1 TITLE PAGE

CLINICAL STUDY REPORT

Sponsor Name	Merck Sharp & Dohme LLC, Rahway, NJ, USA
Compound Name	pembrolizumab (MK-3475)
Protocol Title	Adjuvant Therapy with Pembrolizumab versus Placebo in Resected High-risk Stage II Melanoma: A Randomized, Double-blind Phase 3 Study (KEYNOTE 716)
CSR Identification	P716V04MK3475
Indication	Melanoma
Study Design	Multicenter/Single-center, efficacy, safety, parallel assignment, double-blind, placebo-controlled intervention
Phase	Phase 3
Study Initiation Date	12-SEP-2018 first participant first visit
Study Completion Date	ongoing, data cutoff 04-JAN-2023
Report Date	16-MAY-2023
Revised Report Date	31-MAY-2023
Previous CSR Identification	P716V03MK3475
GCP Compliance	This study was conducted in accordance with local and/or national regulations (including all applicable data protection laws and regulations), ICH GCP, and the ethical principles that have their origin in the Declaration of Helsinki regarding IEC review, informed consent, and the protection of human participants in biomedical research.
Questions about the clinical study report should be directed to the study research staff by using the toll-free number: [redacted]	

2 SYNOPSIS

SPONSOR: Merck Sharp & Dohme LLC, Rahway, NJ, USA (hereafter called the Sponsor or MSD)

COMPOUND NAME: pembrolizumab (MK-3475)

PROTOCOL TITLE: Adjuvant Therapy with Pembrolizumab versus Placebo in Resected High-risk Stage II Melanoma: A Randomized, Double-blind Phase 3 Study (KEYNOTE 716)

STUDY IDENTIFIERS:

IND: 110,080	EudraCT: 2018-000669-35	WHO: Not applicable	NCT: NCT03553836
JAPIC-CTI: Not applicable	UTN: Not applicable	EU CT: Not applicable	

STUDY PHASE: Phase 3

INDICATION: Melanoma

STUDY CENTERS: This study was conducted at 160 centers in 16 countries.

STUDY STATUS:

This study is ongoing; this report is based on the fourth interim analysis of the study.

First Patient, First Visit	Data Cut-off	Database Lock Date
12-SEP-2018	ongoing, data cutoff 04-JAN-2023	09-FEB-2023

NOTE: Patient = Participant

METHODOLOGY:

Part of this study was conducted during the coronavirus disease 2019 (COVID-19) pandemic. The Sponsor continued to follow its standard operating procedures for study conduct, monitoring, and oversight during the pandemic and used a risk-based approach to assess and mitigate impact on study conduct.

KEYNOTE-716 is a randomized, placebo-controlled, parallel-group, crossover/rechallenge, multicenter study of adjuvant pembrolizumab in participants 12 years of age and older with resected high-risk Stage II cutaneous melanoma. Participants must have had newly diagnosed, pathologically confirmed, and completely resected melanoma with negative margins, and could not have received prior systemic therapy for Stage II melanoma.

The treatment phase of the study consists of 2 parts:

- Part 1 (Adjuvant Treatment): Pembrolizumab or placebo administered every 3 weeks (Q3W) for 17 cycles.
- Part 2 (Crossover/Rechallenge after First Recurrence): Pembrolizumab administered Q3W for 17 cycles after resection of recurrent disease if feasible (local recurrence, including local metastatic lymph nodes, or distant metastasis) or up to 35 cycles of pembrolizumab Q3W for unresectable disease recurrence (unresectable local [regional metastatic lymph nodes, in-transit, satellite, and/or microsatellite metastases] or unresectable distant recurrence).

The study treatments are shown below. Participants under 18 years of age who were randomized to receive pembrolizumab at the beginning of Part 1 remained on the pediatric dose of pembrolizumab throughout Part 1.

Study Treatments

Study Treatment Name	Dose Formulation	Unit Dose Strength(s)	Dosage Level(s)	Route of Administration	Regimen/ Treatment Period	Use
Pembrolizumab	Solution for infusion	25 mg/mL vial	2 mg/kg (maximum 200 mg) Q3W for pediatric participants (≥12 and <18 years old); 200 mg Q3W for adults (≥18 years of age)	IV infusion via infusion pump	Part 1: 17 cycles Part 2: 17 or 35 cycles	Experimental
Saline placebo	Solution for infusion	None	None	IV infusion via infusion pump	Part 1: 17 cycles	Placebo

IV=intravenous; Q3W=every 3 weeks

ELIGIBILITY CRITERIA:

Male and female participants ≥12 years of age with surgically resected Stage IIB or IIC cutaneous melanoma who met the following key criteria were eligible for enrollment in the study:

- Histologically/pathologically confirmed, newly diagnosed Stage IIB or IIC cutaneous melanoma (tumor stage of T3b, T4a, or T4b) with pathologically confirmed negative sentinel lymph node (SLN) biopsy, and no evidence of regional [N0] or distant metastatic [M0] disease per American Joint Committee on Cancer (AJCC) eighth edition guidelines.
- Not previously treated for melanoma beyond complete surgical resection.
- No more than 12 weeks between final surgical resection and randomization, with complete surgical wound healing.
- No evidence of metastatic disease on imaging as determined by investigator assessment; suspicious lesions amenable to biopsy confirmed negative for malignancy.

- Performance status of 0 or 1 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale at the time of enrollment, Lansky Performance Status (LPS) score ≥50 (for participants ≤16 years old), or a Karnofsky Performance Status (KPS) score ≥50 (for participants >16 and <18 years old).

OBJECTIVES AND ENDPOINTS:

Male/female participants with Stage IIB or IIC cutaneous melanoma of at least 12 years of age were enrolled in this study.

Objectives	Endpoints
Primary	
Objective: To compare Recurrence-free Survival (RFS) between treatment arms. Hypothesis (H1): Pembrolizumab is superior to placebo with respect to RFS as assessed by the site investigator.	RFS: time from randomization to (1) any recurrence (local or regional [including invasive ipsilateral tumor and invasive loco-regional tumor], or distant) as assessed by the investigator, or (2) death due to any cause (both cancer and noncancer causes of death)
Secondary	
Objective: To compare distant metastasis-free survival (DMFS) between treatment arms. Hypothesis (H2): Pembrolizumab is superior to placebo with respect to DMFS as assessed by the site investigator.	DMFS: The time from randomization to appearance of a distant metastasis as assessed by the investigator. A distant metastasis refers to cancer that has spread from the original (primary) tumor to distant organs or distant lymph nodes.
Objective: To compare overall survival (OS) between treatment arms. Hypothesis (H3): Pembrolizumab is superior to placebo with respect to OS.	OS: The time from randomization to death due to any cause.
Objective: To assess the safety and tolerability of pembrolizumab compared to placebo in the proportion of adverse events (AEs).	• AEs. • Discontinuation of study treatment due to AEs.

NUMBER OF PARTICIPANTS (planned and analyzed): The planned enrollment total was approximately 954 participants. As of the data cutoff date (DCO) date for this report, 976 participants were randomized (487 in the pembrolizumab group and 489 in the placebo group).

STATISTICAL AND ANALYSIS METHODS:

The nonparametric Kaplan-Meier (KM) method was used to estimate the RFS curve in each treatment group. Treatment comparisons for RFS were evaluated using a stratified log-rank test with Efron's tie handling method, and the hazard ratio was estimated using a stratified Cox model. RFS analysis was performed on the intent-to-treat (ITT) population.

Five efficacy interim analyses and a final analysis were planned for this study. The first interim analysis (IA1) was planned after enrollment was completed and approximately 128 RFS events were observed to test the superiority of pembrolizumab over placebo with respect to RFS as assessed by the investigator (primary hypothesis). The second interim analysis (IA2) was planned after approximately 179 RFS events were observed, but the actual number at the final RFS analysis was 187. For the secondary endpoint, DMFS, the third interim analysis (IA3) was planned after approximately 146 DMFS events, but the actual number was 158 DMFS. The fourth interim analysis (IA4) was planned after approximately 195 DMFS events, but the actual number was 193 DMFS; and final analysis of DMFS events are included in this report. The fifth interim analysis (IA5) is planned after approximately 154 OS events. The final analysis is planned after approximately 204 OS events; and will include final analysis of OS.

The multiplicity strategy in this study followed step-down approach from the primary (RFS) hypothesis to the 2 secondary (DMFS and OS) hypotheses. The overall Type I error was strongly controlled at 2.5% (one-sided), with 2.5% initially allocated to the RFS hypothesis. The graphical method of Maurer and Bretz was used to control multiplicity for multiple hypotheses as well as interim analyses. According to this multiplicity strategy and given the RFS comparison was statistically significant at IA1 (DCO 04-DEC-2020) and DMFS comparison was statistically significant at IA3 (DCO 04-JAN-2022) the 2.5% alpha was reallocated to the OS comparison.

Safety analysis followed a tiered approach. There were no Tier 1 events for this study. Point estimates and 95% confidence intervals (CIs) for between treatment comparisons via the Miettinen and Nurminen method were provided for Tier 2 safety endpoints, and only point estimates by treatment group were provided for Tier 3 safety endpoints.

There were no changes in the planned analyses due to the COVID-19 pandemic.

RESULTS:

Participant Disposition:

- Pembrolizumab group: 487 participants were randomized, 483 were treated, 320 (66.3%) completed Part 1 study treatment, 163 (33.7%) had treatment discontinued, and 59 (12.1%) participants were discontinued from the study. Eight participants entered Part 2 of the study and were rechallenged with pembrolizumab after first recurrence. One (12.5%) participant completed Part 2 treatment, 2 (25%) discontinued study treatment due to progressive disease, and 5 (62.5%) participants are ongoing.

- Placebo group: 489 participants were randomized, 486 were treated, 367 (75.5%) completed Part 1 study treatment, 119 (24.5%) had treatment discontinued, and 62 (12.7%) participants were discontinued from the study. Sixty-three participants entered Part 2 of the study and crossed over to the pembrolizumab group after first recurrence. Twenty (31.7%) completed Part 2 treatment, 30 (47.6%) discontinued study treatment, and 13 (20.6%) are ongoing.

Demographics and Baseline Characteristics:

- **Overall Median Age (range):** 61.0 years (16 to 87 years)
- **Sex:** 589 (60.3%) male, 387 (39.7%) female
- **Ethnicity:** 810 (83.0%) not Hispanic or Latino, 68 (7.0%) Hispanic or Latino, 87 (8.9%) not reported, 11 (1.1%) unknown
- **Race:** 1 (0.1%) American Indian or Alaska Native, 5 (0.5%) Asian, 8 (0.8%) black or African American, 1 (0.1%) multiple, 874 (89.5%) white, 87 (8.9%) missing

Efficacy:

- Final DMFS results at IA4, continued to show that with 38.5 months of follow-up, pembrolizumab treatment resulted in a clinically meaningful improvement in DMFS, demonstrating a decreased risk of distant metastasis (HR=0.59; [95% CI: 0.44, 0.79]) compared to placebo. The KM curves for DMFS separated at Month 3 and remained separated through the period assessed.
- Of the 193 participants with a DMFS event, 53 (27.5%) participants underwent subsequent surgery, 37 (19.2%) participants received subsequent radiation, and 135 (69.9%) participants received (non-Part 2) subsequent systemic therapy.
- DMFS subgroup analyses were generally consistent regardless of tumor stage, age, gender, race, ECOG performance status, and region.
- Pembrolizumab provided sustained RFS benefit with additional follow-up when compared with placebo. The HR was 0.62 [95% CI: 0.49, 0.79] in favor of pembrolizumab.
- Of the 291 participants with a RFS event, 152 (52.2%) participants underwent subsequent surgery, 41 (14.1%) participants received subsequent radiation, and 160 (55.0%) participants received (non-Part 2) subsequent systemic therapy.
- Adjuvant pembrolizumab treatment resulted in no clinically meaningful difference in LS mean changes (-2.07 [95% CI: -4.40, 0.26]) in EORTC QLQ-C30 global health status/QoL at Week 72 compared with placebo. The change from baseline to Week 72 in physical functioning and the EQ-5D-5L visual analog scale (VAS) score at Week 72 were similar in the treatment groups.

Safety:

- The overall frequency and type of adverse events (AEs) reported in KEYNOTE-716 at IA4 were generally consistent with prior interim analyses and the established safety profile of pembrolizumab monotherapy.
- As expected for a comparison of active treatment versus placebo, higher incidences of AEs in the following AE categories were reported in the pembrolizumab group: drug-related AEs, Grade 3 to 5 AEs, drug-related Grade 3 to 5 AEs, drug-related serious adverse events (SAEs), and AEs and drug-related AEs leading to discontinuation of study intervention.
- The most frequently reported AEs in the pembrolizumab group (incidence ≥15%) were fatigue, diarrhea, pruritus, arthralgia, rash, headache, and hypothyroidism.
- The overall nature and severity of the adverse events of special interest (AEOSI) were generally similar to the established pembrolizumab monotherapy safety profile. Most AEOSI were Grade 1 or 2 in severity and were generally manageable with treatment interruption, treatment discontinuation, and/or concomitant treatment with corticosteroids and hormone replacement therapy.
- No deaths due to a drug-related AE were reported in either treatment group. One participant in the pembrolizumab group and 5 participants in the placebo group died due to nondrug-related AEs.
- Overall, the most frequent AEs in Part 2 of the study were consistent with the AEs reported in the pembrolizumab group in Part 1.

Adverse Event Summary
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse event	22	(4.6)	40	(8.2)
with drug-related[a] adverse events	399	(82.6)	309	(63.6)
with toxicity grade 3-5 adverse events	137	(28.4)	98	(20.2)
with toxicity grade 3-5 drug-related adverse events	83	(17.2)	25	(5.1)
with serious adverse events	103	(21.3)	96	(19.8)
with serious drug-related adverse events	49	(10.1)	11	(2.3)
who died	1	(0.2)	5	(1.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	83	(17.2)	23	(4.7)
discontinued drug due to a drug-related adverse event	77	(15.9)	12	(2.5)
discontinued drug due to a serious adverse event	38	(7.9)	13	(2.7)
discontinued drug due to a serious drug-related adverse event	33	(6.8)	4	(0.8)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

CONCLUSIONS:

Efficacy

- KEYNOTE-716 results confirm pembrolizumab is an effective adjuvant treatment that prolongs DMFS and RFS for the adjuvant treatment of adult and pediatric (12 years and older) patients with high-risk Stage II melanoma.
- The final DMFS results at IA4 demonstrates that pembrolizumab continues to provide clinically meaningful improvement compared with placebo with longer follow-up.
- DMFS results by subgroup are generally consistent with the overall population.
- Data from subsequent RFS analyses (at IA4) are supportive and demonstrate that pembrolizumab continues to provide a clinically meaningful improvement compared with placebo with longer follow-up.

Safety

- The KEYNOTE-716 safety analyses are consistent with the established safety profile of pembrolizumab and the safety profile observed in the previous IA analyses. The results further confirm that pembrolizumab has a tolerable and manageable safety profile in patients with high-risk Stage II melanoma following complete resection in the adjuvant setting. The incidence of deaths and treatment discontinuations in the study due to AEs is low and similar between the 2 groups.
- The types and severity of AEOSI are consistent with the established pembrolizumab monotherapy safety profile. AEOSI were generally manageable with standard medical care, drug discontinuation/interruption, or corticosteroid use as appropriate.
- No new safety concerns were identified for pembrolizumab based on the IA4 safety data in the KEYNOTE-716 study.

PUBLICATIONS:

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REPORT DATE: 16-MAY-2023

REVISED REPORT DATE: 31-MAY-2023

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4 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

This list serves as the first appearance in text.

The following terms may be used interchangeably in this report:

- Participant and subject
- Intervention and treatment
- Study and trial

Abbreviation/Term	Definition
ADR	adverse drug reaction
AE	adverse event
AEOSI	adverse event(s) of special interest
AJCC	American Joint Committee on Cancer
ALP	alkaline phosphatase
ALT	alanine aminotransferase
APaT	all participants as treated
AST	aspartate aminotransferase
CD	cluster of differentiation
CFR	Code of Federal Regulations
CI	confidence interval
COVID-19	coronavirus disease 2019, caused by severe acute respiratory syndrome coronavirus 2
CRF	case report form
CSR	clinical study report
CTLA-4	cytotoxic T lymphocyte-associated antigen-4
DBL	data base lock
DCO	data cutoff
DILI	drug-induced liver injury
DMFS	distant metastasis-free survival
DNA	deoxyribonucleic acid
EC	Ethics Committee
ECOG	Eastern Cooperative Oncology Group

Abbreviation/Term	Definition
EMA	European Medicines Agency
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EQ-5D-5L	EuroQol 5 Dimension 5 Level Questionnaire
ERC	Ethics Review Committee
FAS	full analysis set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GPvP	Good Pharmacovigilance Practice
HR	hazard ratio
IA1	first interim analysis
IA2	second interim analysis
IA3	third interim analysis
IA4	fourth interim analysis
ICH	International Council for Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IEC	Independent Ethics Committee
IFN-α	interferon-alpha
IHC	Immunohistochemistry
IRB	Institutional Review Board
ITT	intent-to-treat
IV	Intravenous
KM	Kaplan-Meier
KPS	Karnofsky performance status
LPS	Lansky performance status
LS	least squares
MedDRA	Medical Dictionary for Regulatory Activities
MSD	Merck Sharp & Dohme LLC, Rahway, NJ, USA
MSS	melanoma-specific survival
NR	not reached
OS	overall survival

Abbreviation/Term	Definition
PD-1	programmed cell death 1
PD-L1	programmed cell death ligand 1
PD-L2	programmed cell death ligand 2
PRFS2	progression/recurrence-free survival 2
PRO	patient-reported outcome
PT	preferred term
Q3W	every 3 weeks
QA	quality assurance
QoL	quality of life
RECIST 1.1	Response Evaluation Criteria in Solid Tumors Version 1.1
RFS	recurrence-free survival
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SDR	source document review
SDV	source document verification
SLN	sentinel lymph node
SOP	standard operating procedure
TTST	time to subsequent therapy
VAS	visual analog scale
UK	United Kingdom
ULN	upper limit of normal
US	United States

5 ETHICS

5.1 Independent Ethics Committee

The protocol, protocol amendments, informed consent form, investigator's brochure, and other relevant study documents were reviewed and approved by the IEC(s) (also referred to as an IRB, ERC, or any other ethics committee) listed in [16.1.3] before being implemented at each site, in compliance with local and/or national regulations (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]). The IEC(s) consulted for this study met the definition of an "IEC" as outlined in US CFR Title 21, Part 56 or equivalent country specific regulations.

5.2 Ethical Conduct of the Study

This study was conducted in accordance with local and/or national regulations (including all applicable data protection laws and regulations), ICH-GCP and with the ethical principles that have their origin in the Declaration of Helsinki regarding IEC review, informed consent and the protection of human participants in biomedical research (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]).

5.3 Participant Information and Consent

Informed consent was obtained and documented in accordance with the principles and provisions in Section 4.8 of the ICH E6 Guideline for Good Clinical Practice, US CFR Title 21 Part 50, Protection of Human Subjects, and/or local country/cultural consent practices and/or requirements where applicable. Representative written information for the participant and sample informed consent form(s) or applicable assent (if the participant was under the age of consent) are available upon request. A description of any incentives used in the study is available upon request or included, if required [16.1.3.3].

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

A list of investigator(s), including study center information, is provided in [16.1.3]. Information for the administrative structure of the study (eg, monitoring, laboratory facilities and clinical supply) is provided in [16.1.4]. Study governance information is available in the study protocol [16.1.1].

7 INTRODUCTION

KEYNOTE-716 is an ongoing Phase 3, randomized, placebo-controlled, parallel-group, crossover/rechallenge study of adjuvant pembrolizumab in participants 12 years of age and older with resected high-risk Stage II cutaneous melanoma. Recent results from EORTC1325/KEYNOTE-054 showed that adult patients with Stage III melanoma who received approximately 1 year (18 doses) of adjuvant pembrolizumab therapy had a significantly longer RFS compared with placebo (HR=0.57; 98.4% CI: 0.43-0.74; p<0.001) [16.1.12.1]. Further, the 5-year analysis based on extended follow-up from this study confirmed the long-term benefit of adjuvant pembrolizumab [16.1.12.2]. KEYNOTE-716

was initiated to investigate whether pembrolizumab improved RFS relative to placebo in participants with resected Stage II melanoma who were at high-risk for disease recurrence.

Patients with Stage II melanoma are at risk for disease recurrence after complete surgical resection due to vertical growth of the primary melanoma and subsequent lymphogenic or hematogenic spread. Although surgery with curative intent is standard of care in early-stage melanoma that can be completely resected, many patients experience disease recurrence due to micrometastatic disease at diagnosis. Adjuvant immunotherapy after complete resection has shown decreased recurrence and distant metastases in patients with lymphogenic spread to regional lymph nodes. Further, some patients with Stage II melanoma have MSS outcomes similar to patients with Stage III melanoma [16.1.12.3].

Despite clear advances in the treatment of early and advanced melanoma in recent years, adjuvant therapy in the high-risk Stage II melanoma setting has shown modest results with earlier immune therapies such as IFN-α. Therefore, there remains a high unmet medical need and thus, opportunities to improve the outcomes for patients with early-stage melanoma. Anti PD-1 immunotherapies could provide significant benefit over surgery and observation alone. Thus, a study of pembrolizumab in the adjuvant setting for patients with high-risk Stage II melanoma was warranted to determine whether the benefits achieved with pembrolizumab adjuvant therapy in Stage III melanoma translated to high-risk Stage II melanoma populations. The efficacy and tolerable safety profile, in an otherwise untreated population, observed at IA1 supported marketing applications for the adjuvant treatment of high-risk Stage II melanoma in both pediatric and adult participants.

Statistical significance for RFS was reached at KEYNOTE-716 IA1 as of the DCO on 04-DEC-2020. Treatment with adjuvant pembrolizumab, when administered to participants after complete resection of Stage IIB or IIC melanoma, resulted in a 35% decreased risk of disease recurrence or death (HR=0.65 [95% CI: 0.46, 0.92]; p=0.00658), with a median duration of follow-up of 14.3 months. After an additional 6 months of follow-up, the IA2 (DCO 21-JUN-2021) results continued to show a clinically meaningful improvement in RFS compared with placebo. The IA2 analysis was the prespecified final RFS analysis (full information); therefore, no formal hypothesis testing for RFS was conducted. IA3 RFS results demonstrated a continued benefit with longer follow-up (median follow-up of 26.9 months). The HR was 0.64 (95% CI: 0.50, 0.84), and the RFS rate at 18 months was 86.1% (95% CI: 82.6, 88.9) in the pembrolizumab arm and 77.8% (95% CI: 73.7, 81.2) in the placebo arm. IA4 RFS (DCO 04-JAN-2023) results also demonstrated a continued benefit with longer follow-up (291 RFS events; 38.5 months median follow-up duration). The HR was 0.62 (95% CI: 0.49, 0.79). The RFS rate at 36 months was 76.2% (95% CI: 71.9, 79.9) in the pembrolizumab arm and 63.4% (95% CI: 58.7, 67.7) in the placebo arm.

Statistical significance for DMFS was reached at KEYNOTE-716 IA3 as of the DCO on 04-JAN-2022. The IA3 analysis was the first DMFS analysis of pembrolizumab compared to placebo and was triggered by 158 DMFS events. Treatment with pembrolizumab resulted in a statistically significant and clinically meaningful improvement in DMFS compared with placebo, demonstrating a 36% decreased risk of distant metastasis (HR=0.64 [95% CI:0.47, 0.88]; p=0.00292).

This report summarizes the final DMFS analysis and the extended RFS analysis of pembrolizumab compared to placebo at IA4 triggered by 193 events and 291 events, respectively. As of the DCO date of 04-JAN-2023, treatment with pembrolizumab resulted in a clinically meaningful improvement in DMFS (HR=0.59 [95% CI:0.44, 0.79]) and RFS compared with placebo, demonstrating that pembrolizumab continues to provide a clinically meaningful improvement compared with placebo at longer follow-up.

No new safety concerns were identified at IA4, and the overall nature and severity of AEs observed during the study were consistent with the established safety profile for pembrolizumab monotherapy.

The results for global health status/QoL and physical functioning endpoints at Week 72 were similar between groups and were consistent with IA3.

This report also provides data from Part 2 (crossover/rechallenge phase) of the study. KEYNOTE-716 is ongoing and will continue to the next endpoint, OS.

Additional details are available in the study protocol [16.1.1]. A sample CRF is provided in [16.1.2].

Part of this study was conducted during the COVID-19 pandemic. Protocol amendments and other contingency measures implemented to manage study conduct as a result of the pandemic and the impact of these measures on study conduct, data integrity, and analyses are described in [Sec. 9.8]. Effects of the COVID-19 pandemic on participant status, efficacy, and safety results, if any, are described in [Sec. 10, 11, and 12], respectively.

8 STUDY OBJECTIVES AND ENDPOINTS

Male/female participants with Stage IIB or IIC cutaneous melanoma of at least 12 years of age were enrolled in this study.

Objectives	Endpoints
Primary	
Objective: To compare Recurrence-free Survival (RFS) between treatment arms. Hypothesis (H1): Pembrolizumab is superior to placebo with respect to RFS as assessed by the site investigator.	RFS: time from randomization to (1) any recurrence (local or regional [including invasive ipsilateral tumor and invasive loco-regional tumor], or distant) as assessed by the investigator, or (2) death due to any cause (both cancer and noncancer causes of death)
Secondary	
Objective: To compare distant metastasis-free survival (DMFS) between treatment arms. Hypothesis (H2): Pembrolizumab is superior to placebo with respect to DMFS as assessed by the site investigator.	DMFS: The time from randomization to appearance of a distant metastasis as assessed by the investigator. A distant metastasis refers to cancer that has spread from the original (primary) tumor to distant organs or distant lymph nodes.
Objective: To compare overall survival (OS) between treatment arms. Hypothesis (H3): Pembrolizumab is superior to placebo with respect to OS.	OS: The time from randomization to death due to any cause.
Objective: To assess the safety and tolerability of pembrolizumab compared to placebo in the proportion of adverse events (AEs).	• AEs. • Discontinuation of study treatment due to AEs.
Tertiary/Exploratory	
Objective: To compare mean change from baseline during the adjuvant treatment period (up to 21 days after last administration) in global quality of life between the 2 treatment arms using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) global health status/QoL scale	EORTC QLQ-C30 global health status/QoL scale.

Objectives	Endpoints
Objective: To characterize health utilities using the EuroQoL-5 Dimension Questionnaire (EQ-5D-5L) healthy utility scores.	EQ-5D-5L health utility score.
Objective: To compare the time to subsequent therapy (TTST) between treatment arms	TTST: The time from randomization to the date of first subsequent therapy (eg, surgery, radiation therapy, antineoplastic therapy) or death (whatever the cause), whichever occurs first.
Objective: To compare Progression/recurrence-free Survival 2 (PRFS2) between treatment arms	PRFS2: Time from randomization to the earliest of the following: (1) date of 1st disease progression per RECIST 1.1 beyond the initial unresectable disease recurrence; (2) date of 2nd recurrence in patients without evidence of disease after surgery of a resectable 1st recurrence; (3) death.
Objective: To identify molecular (genomic, metabolic, and/or proteomic) biomarkers that may be indicative of clinical response/resistance, safety, pharmacodynamic activity, and/or the mechanism of action of pembrolizumab.	Germline genetic variation, genetic deoxyribonucleic acid (DNA) mutations from tumor, tumor and blood RNA variation, proteomics and immunohistochemistry (IHC), and other biomarkers.

9 INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan

KEYNOTE-716 is a randomized, placebo-controlled, parallel-group, crossover/rechallenge, multicenter study of adjuvant pembrolizumab in participants 12 years of age and older with resected Stage IIB or IIC cutaneous melanoma. Stage IIB and IIC cutaneous melanoma are defined as T category T3b, T4a, or T4b, with no regional nodal metastases (N0) confirmed by a negative SLN biopsy and no evidence of distant metastasis (M0) per AJCC eighth edition guidelines. Participants must have had newly diagnosed, pathologically confirmed, and completely resected melanoma with negative margins, and could not have received prior systemic therapy for Stage II melanoma.

The study enrolled 976 participants that were randomized to receive pembrolizumab or saline placebo.

The treatment phase of the study consists of 2 parts:

- Part 1 (Adjuvant Treatment): Pembrolizumab adult dose of 200 mg IV (≥18 years of age) or pediatric dose of 2 mg/kg IV (≥12 years and <18 years of age) up to a maximum of 200 mg Q3W, or saline placebo IV Q3W for 17 cycles.
- Part 2 (Crossover/Rechallenge after First Recurrence): Pembrolizumab administered Q3W for 17 cycles after resection of recurrent disease if feasible (local recurrence, including local metastatic lymph nodes, or distant metastasis) or up to 35 cycles of pembrolizumab Q3W for unresectable disease recurrence (unresectable local [regional metastatic lymph nodes, in-transit, satellite, and/or microsatellite metastases] or unresectable distant recurrence).

Participants in Part 1 were stratified into 3 strata based on T-stage tumor thickness and ulceration [Table 9-1]. Additional details are provided in the supplemental SAP [16.1.9.1].

Participants under 18 years of age who were randomized to receive pembrolizumab at the beginning of Part 1 remained on the pediatric dose of pembrolizumab throughout Part 1.

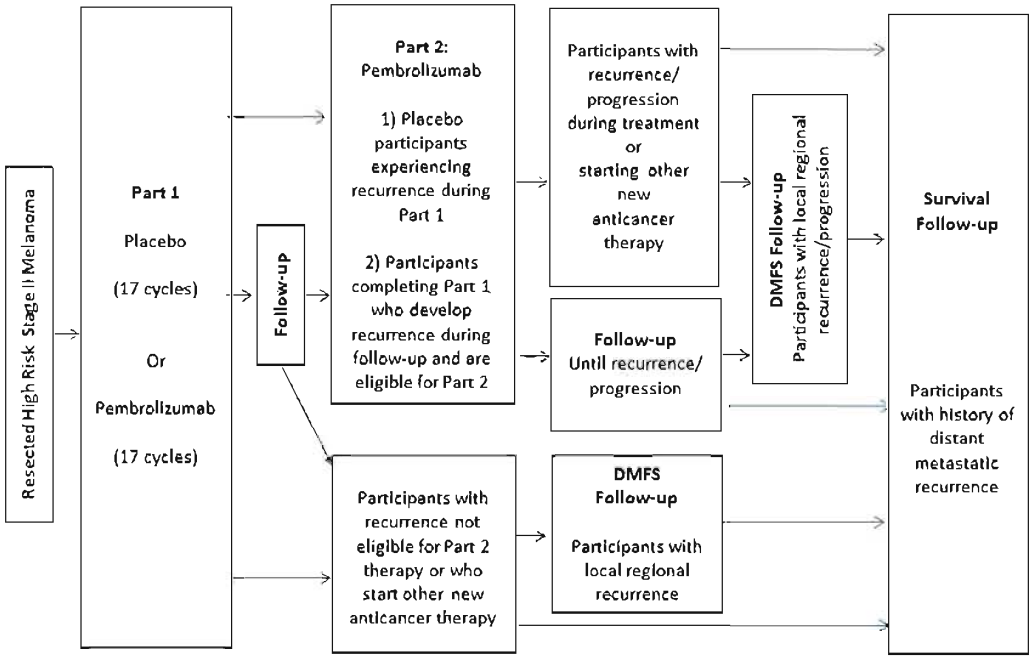
Adult participants who crossed over in Part 2 received the fixed adult dose of pembrolizumab (200 mg Q3W) regardless of their Part 1 dosing regimen.

Table 9-1
Melanoma Stage Stratification

Melanoma Stage	T-Stage	T-Stage Definition (Thickness and Ulceration Status)
IIB	T3b	>2.0-4.0 mm with ulceration
IIB	T4a	>4.0 mm without ulceration
IIC	T4b	>4.0 mm with ulceration
T-stage of disease as defined by thickness and ulceration status per American Joint Committee on Cancer guidelines eighth edition.		

The study design is depicted in [Figure 9-1]. Additional details are available in the study protocol [16.1.1].

Figure 9-1
Study Design



All participants complete the Safety Follow-up visit prior to entering long-term follow up.
See protocol Section 4.1 for details.

9.2 Discussion of Study Design

The scientific rationale for features of the study design, including chosen control group(s), dose(s), and endpoint(s), as applicable, are discussed in the study protocol [16.1.1].

9.3 Selection of Study Population

9.3.1 Inclusion Criteria

Key inclusion criteria included the following:

- Male or female participants who were ≥12 years of age with surgically resected and histologically/pathologically confirmed new diagnosis of Stage IIB or IIC cutaneous melanoma (T-stage of T3b, T4a, or T4b [Figure 9-1] with pathologically confirmed negative SLN biopsy, and no evidence of regional [N0] or distant metastatic [M0] disease) per AJCC eighth edition guidelines.
- Not previously treated for melanoma beyond complete surgical resection.
- No more than 12 weeks had elapsed between final surgical resection and randomization, with complete surgical wound healing.

- Had no evidence of metastatic disease on imaging as determined by investigator assessment. All suspicious lesions amenable to biopsy were confirmed negative for malignancy.
- Performance status of 0 or 1 on the ECOG Performance Scale at the time of enrollment, LPS score ≥50 (for participants ≤16 years old), or a KPS score ≥50 (for participants >16 and <18 years old).

Additional details are available in the study protocol [16.1.1].

9.3.2 Exclusion Criteria

Participants were excluded from the study if any of the following criteria apply:

- Had a known additional malignancy that is progressing or has required active antineoplastic therapy (including hormonal) within the past 5 years.
- Had a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study intervention.

  If participant received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment.
- Had received prior therapy with an anti PD-1, anti PD-L1, or anti PD-L2 agent or with an agent directed to another stimulatory or coinhibitory T-cell receptor (eg, CTLA-4, CD137).
- Had received prior systemic anticancer therapy for melanoma including investigational agents.

Additional details are available in the study protocol [16.1.1].

9.3.3 Participant Withdrawal/Discontinuation Criteria

The specific criteria and procedures for early discontinuation from study intervention or withdrawal from the study are described in the study protocol [16.1.1].

9.4 Study Interventions

9.4.1 Interventions Administered

The study interventions are presented in [Table 9-2].

Table 9-2
Study Interventions

Arm Name	Arm Type	Intervention Name	Intervention Type	Dose Formulation	Unit Dose Strength	Dosage Level(s)	Route of Administration	Regimen/ Treatment Period	Use	IMP/ NIMP	Sourcing
Pembrolizumab	Experimental	Pembrolizumab	Drug	Solution for infusion	25 mg/mL vial	2 mg/kg (max. 200 mg) Q3W for pediatric participants (≥12 and <18 years old); 200 mg Q3W for adults (≥18 years of age)	IV infusion	Part 1: 17 cycles Part 2: 17 or 35 cycles	Experimental	IMP	Provided centrally by Sponsor
Saline Placebo	Placebo Comparator	Placebo	Drug	Solution for infusion	None	None	IV infusion	Part 1: 17 cycles	Placebo	IMP	Provided locally by the study site, subsidiary, or designee

EEA=European Economic Area; IMP=investigational medicinal product; IMP=investigational medicinal product; IV=intravenous; NIMP=noninvestigational medicinal product; Q3W=every 3 weeks

The classification of IMP and NIMP in this table is based on guidance issued by the European Commission and applies to countries in the EEA. Country differences with respect to the definition/classification of IMP/NIMP may exist. In these circumstances, local legislation is followed.

Placebo for pembrolizumab was diluent alone (normal saline); diluent was used for blinding purposes and does not contain active ingredients.

9.4.2 Identity of Investigational Products

The manufacturing lot numbers for the investigational products dispensed in this study are provided in [16.1.6].

9.4.3 Avoidance of Bias in the Study

9.4.3.1 Methods of Assigning Participants to Intervention Groups

The method used to randomize participants to intervention groups, including stratification factors, is described in the study protocol [16.1.1].

9.4.3.2 Blinding

The method used for blinding is described in the study protocol [16.1.1].

9.4.4 Selection and Timing of Doses for Each Participant

The planned dose of pembrolizumab for this study was 200 mg IV Q3W for adults (≥18 years of age) and 2 mg/kg IV Q3W up to a maximum of 200 mg IV Q3W for pediatric participants (≥12 years and <18 years of age). The procedures for selecting each participant's dose of study intervention, timing of dosing, dose modification guidelines, prespecified allowances for dose interruptions or unblinding, and specific instructions to participants about when or how to take the assigned study intervention are described in the study protocol [16.1.1]. A listing of allocation/assignment to study intervention by participant is provided in [16.1.7].

9.4.5 Intervention Compliance

The measures taken to ensure and to document compliance with the randomized study intervention regimen are described in the study protocol [16.1.1].

9.4.6 Prior and Concomitant Therapy

The medication(s)/treatment(s)/vaccination(s) allowed or disallowed before and during the study, including any exceptions to these requirements, are described in the study protocol [16.1.1].

9.5 Study Assessments and Procedures

9.5.1 Planned Measurements and Timing of Assessments

The specific efficacy, safety, and other variables to be assessed, their schedule, and measurement/collection methods are displayed in the Schedule of Activities and described in the Procedures sections of the study protocol [16.1.1]. The collection and assessment of safety information during the study (evaluation, definitions, recording, and reporting of AEs, SAEs and other reportable safety events) are detailed in the AE reporting section of the study protocol [16.1.1].

9.5.2 Appropriateness of Measurements

The endpoints used in this study (eg, efficacy, safety, and other endpoints) were standard, generally reliable, and relevant to the objectives set forth in the protocol [16.1.1].

9.5.3 Protocol Deviations

Protocol deviations were classified as per the ICH E3 classification of protocol deviations as important (those that may significantly impact the quality or integrity of key study data or that may significantly affect a participant's rights, safety, or well-being) or not important. Important protocol deviations were further classified as either clinically important (deviations that may compromise critical data analyses pertaining to primary efficacy and/or safety endpoints or the participant's safety) or not clinically important.

9.5.4 Efficacy Assessments

Efficacy assessments are described in the study protocol [16.1.1]

9.5.5 Safety Assessments

Safety assessments are described in the study protocol [16.1.1]. MedDRA version 25.1 was used at the time of table generation. The following MedDRA PTs were excluded from the statistical safety tables if the AEs were reported as not related to study intervention: neoplasm progression, malignant neoplasm progression, and disease progression.

9.5.5.1 Adverse Events of Special Interest

AEOSI are immune-mediated events and infusion-related reactions associated with pembrolizumab. A predefined list of PTs was developed by the Sponsor to consistently characterize the nature and frequency of each AEOSI regardless of causality as reported by investigators. These PTs are considered to be medically equivalent to the immune-mediated events and infusion-related reactions. The list of PTs is continually updated based on emerging pembrolizumab safety data. A list of AEOSI (Version 23.1) is presented in [16.2.7.2].

9.6 Data Quality Assurance

Quality oversight activities implemented at the study investigative site(s) or centrally by the Sponsor are intrinsic to all clinical study-related activities, in accordance with ICH GCP 5.1. For this study, such activities may have included remote and/or onsite monitoring inclusive of SDV, SDR, centralized in-house medical monitoring of clinical study data (including monitoring protocol deviations), and relevant reviews of regulatory submission documents.

Investigative study sites were monitored to assess compliance with the study protocol and with GCP. Study data were reviewed for accuracy, completeness, and consistency and verified versus source documentation according to standard operating procedures (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]).

The Sponsor held investigator meeting(s) before study initiation to review all protocol procedures and investigator responsibilities under GCP. At the meeting(s), the conduct of the study was explained and instructions were provided to ensure accuracy and consistency in data collection and performance.

Quality was also evaluated by independent GCP QA activities, which may have included QA audits of study investigative sites and third-party suppliers. The conduct of QA audits was based on a risk-based approach to assess adherence with the protocol, applicable GCP/GPvP regulations and guidance as well as applicable company policies and procedures. Audit information is provided in [16.1.8].

No GCP compliance issues occurred that were assessed as having had a significant impact on the rights, safety or mental integrity of the study participants and/or the scientific integrity or validity of the study results.

The CSR authors reviewed this document for accuracy of scientific content; their signatures are included in [16.1.5.2]. The coordinating investigator's signature is included in [16.1.5.1].

9.7 Statistical Analysis Plan

The planned analyses, comparisons, statistical tests, and determination of sample size are described in the protocol [16.1.1].

9.8 Changes in the Conduct of the Study or Planned Analyses

Part of this study was conducted during the COVID-19 pandemic. Clinical investigator study sites were in the following 16 countries: Australia, Belgium, Brazil, Canada, Chile, France, Germany, Israel, Italy, Japan, Poland, South Africa, Spain, Switzerland, United Kingdom, and US.

9.8.1 Changes in the Conduct of the Study

Changes in the conduct of the study implemented by protocol amendment are summarized in [Table 9-3]. There were no changes in the planned conduct of the study implemented by protocol amendment due to the COVID-19 pandemic.

Table 9-3
Protocol Amendments for MK-3475-716

Document	Date of Issue	Overall Rationale
Amendment 5	13-OCT-2022	Remove PRO objective related to comparison of average change from baseline after the adjuvant period as measured using EORTC QLQ-C30
Amendment 4	11-MAY-2021	Alignment with the USPI requirement for Pembrolizumab Dose Modifications
Amendment 3	28-SEP-2020	Clarify imaging schedule
Amendment 2 Country Specific	05-AUG-2019	Alignment with UK-specific Requirements
Amendment 1	18-MAR-2019	Conformation with FDA and other country-specific requirements
Original Protocol	17-MAY-2018	N/A

EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; FDA=Food and Drug Administration; N/A=not applicable; PRO=patient-reported outcome; UK=United Kingdom; USPI=US Package Insert

Source: [16.1.1]

A risk-based approach, consistent with Health Authority (FDA, EMA) guidance on conducting clinical studies during the COVID-19 pandemic, was used to assess and mitigate the impact of the pandemic on study conduct in order to 1) ensure the safety of study participants, study staff, and health care providers, 2) maintain compliance with GCP principles, and 3) minimize risks to study data integrity. The Sponsor continued to follow its SOPs for study conduct, monitoring, and oversight during the COVID-19 pandemic. Any contingency measures used to manage study conduct during the pandemic were implemented as per the Sponsor's SOP for exception and deviation management and as appropriate for the country, region, and individual study site. Exceptions and deviations from SOPs were documented.

Study sites were advised to follow local and national guidance regarding the pandemic and to share any mitigation plans for study participant management with the IRB/EC and the Sponsor. Study sites were also advised to remain in contact with study participants to monitor for safety concerns, help ensure participants adhered to their study treatment schedule, and to keep participants informed of changes to the study and other study activities.

Measures implemented by the Sponsor to manage key aspects of study conduct during the COVID-19 pandemic are summarized in [Table 9-4] (implementation date shown in parentheses). Not all measures were implemented at all study sites due to differences in local conditions and impact of the pandemic.

Table 9-4
Measures Implemented by the Sponsor to Manage Study Conduct During the COVID-19 Pandemic for MK-3475-716

Process	**Measure (Date Implemented)**
Study site monitoring	Modifications to the frequency of on-site and remote monitoring were allowed due to national and local travel restrictions and/or study site restrictions to on-site monitoring (21-MAR-2020). Alternate methods for source data review and verification for critical data points in absence of remote access to electronic medical records were allowed under documented circumstances (06-MAR-2020). Source data review and/or verification before database lock was/were waived for this study where remote access to the site electronic medical records was not available and per risk assessment (13-MAR-2020). Critical data points for source document verification were reassessed and the study management plan updated without the usual approval workflow for resumption of on-site monitoring (01-MAY-2020).
Protocol deviations	Study sites were queried as to the relationship of reported deviations to the COVID-19 pandemic. The responses were documented (20-MAR-2020).
AE reporting	COVID-19 infection was to be reported following the protocol's AE and SAE reporting instructions, as well as the standard COVID-19 Data Entry Guidelines.
Clinical supplies (including study treatment)	Clinical supply shipments were carefully monitored to ensure timely delivery (15-MAR-2020). An alternate location (eg, primary care center, pharmacy) for infusion administration of study treatment/other clinical supplies was allowed when participant travel was impacted, and administration could not be postponed (21-APR-2020).
Data management	Alternative procedures were allowed for study sites using shared electronic devices to complete clinical outcome assessments (08-APR-2020). Study sites were queried, and responses documented about the relationship of the following to the COVID-19 pandemic (08-APR-2020): • Missing participant study visits and data • Participants who discontinued study treatment and/or the study
Clinical laboratory and other facilities	Alternate clinical laboratory facilities were allowed for collection of samples for study participants unable to visit the study site, where supported by the clinical site processes, HA and/or IRB/IEC guidance (16-APR-2020). Alternate imaging facilities and delayed schedules for study site and alternate facility imaging were allowed for protocol-required imaging (each to be reported as a protocol deviation) (24-MAR-2020).
Informed consent	Oral confirmation of participant consent (eg, via telephone) was allowed when in-person discussion and signature was not possible (30-MAR-2020).

Process	Measure (Date Implemented)
Home health care services	Home health services could be used to perform protocol-specified activities (eg, physical examination, completion of participant questionnaires, sample collection) for study participants unable to visit the study site (31-MAR-2020). For participants who only completed telemedicine visits, a complete physical examination was required to ensure AE and disease recurrence evaluations were completed (06-NOV-2020).
EQ-5D-5L and EORTC QLQ-C30	Participants were permitted to complete paper QoL questionnaires with IRB/IEC approval if they did not want to use the shared electronic device on site (15-APR-2020).

AE=adverse event; COVID-19=coronavirus disease 2019; EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EQ-5D-5L=EuroQol 5 Dimension 5 Level Questionnaire; HA=health authority; IEC=Independent Ethics Committee; IRB=Institutional Review Board; QoL=quality of life; SAE=serious adverse event.

Missing participant study visits and/or data were queried as per the Sponsor's standard processes, and were to be reported as protocol deviations for that participant. Procedures and study visits conducted outside protocol-defined windows were also to be reported as protocol deviations. Participants with protocol deviations due to the pandemic are described in [Sec. 10.2].

9.8.2 Changes in the Planned Analyses

The following change in the planned analyses occurred after the final version of the SAP, before complete unblinding of the study: Descriptive analyses by cancer stage (IIB and IIC) were performed that were not predefined analyses. The study was not powered to show efficacy in either of these subgroups. A characterization of EQ-5D-5L utility values was added for this CSR to address the tertiary exploratory objective for completeness.

All other changes to the planned analyses are included in a protocol amendment [16.1.1].

There were no changes in the planned analyses of the study due to the COVID-19 pandemic.

9.8.3 Changes Following Study Unblinding and Post-hoc Analyses

There were no changes following study unblinding between IA3 and IA4.

10 STUDY PARTICIPANTS

Participant data listings are available upon request or, if required, provided in [16.2.1, 16.2.4, 16.2.5, 16.2.6, 16.2.7, 16.2.8] with electronic data sets provided in [16.4]. Participant CRFs are available upon request or linked, as applicable [16.3].

Tables for the 2 pediatric participants are provided in [Table 14.1-1] through [Table 14.1-4].

10.1 Disposition of Participants

Participants were randomized across 160 centers in 16 countries [Table 14.1-9] [Sec.9.8]; 19 study sites did not randomize study participants [16.1.3.1].

As of the DCO date, 976 participants were randomized to receive pembrolizumab 200 mg (for participants ≥18 years of age) or 2 mg/kg up to a maximum of 200 mg (for participants ≥12 years and <18 years of age) or placebo (normal saline solution) IV Q3W [Table 14.1-9]. Of the randomized participants, 7 participants did not receive study treatment [Table 14.1-13]. The remaining 969 participants received at least 1 dose of study treatment in Part 1 [Figure 10-1] [Table 14.1-13].

As of the DCO date, the majority of participants remained in the study ([87.9%] and [87.3%] in the pembrolizumab and placebo groups, respectively) [Table 10-1] [Figure 10-1].

Overall, 33.7% participants in the pembrolizumab group discontinued study intervention and 24.5% discontinued study intervention in the placebo group. AEs, relapse/recurrence, and withdrawal by participant were the most common reasons for discontinuing study intervention in both groups. More participants in the pembrolizumab group discontinued study intervention due to AEs compared with the placebo group (17.6% vs 4.9%). Fewer participants in the pembrolizumab group discontinued study intervention due to relapse/recurrence compared with the placebo group (5.0% vs 12.6%) [16.2.1] [16.4]. Note: For 1 participant in the placebo group, relapse/recurrence was inadvertently reported in the eCRF as associated with COVID-19. After DBL, this was changed to not associated with COVID-19.

Overall, 71 participants entered Part 2 of the study [Figure 10-1] [Table 14.1-8] [Table 14.1-13]. Participants that discontinued study intervention (45.1%) in Part 2 were primarily due to AEs, progressive disease, or relapse/recurrence. As of the DCO date 18 participants were still receiving study intervention [Table 10-1].

All nonrandomized participants were screen failures [Figure 10-1], [Table 14.1-6], [Table 14.1-7] [16.4].

Figure 10-1
Disposition of Participants
(ITT Population)

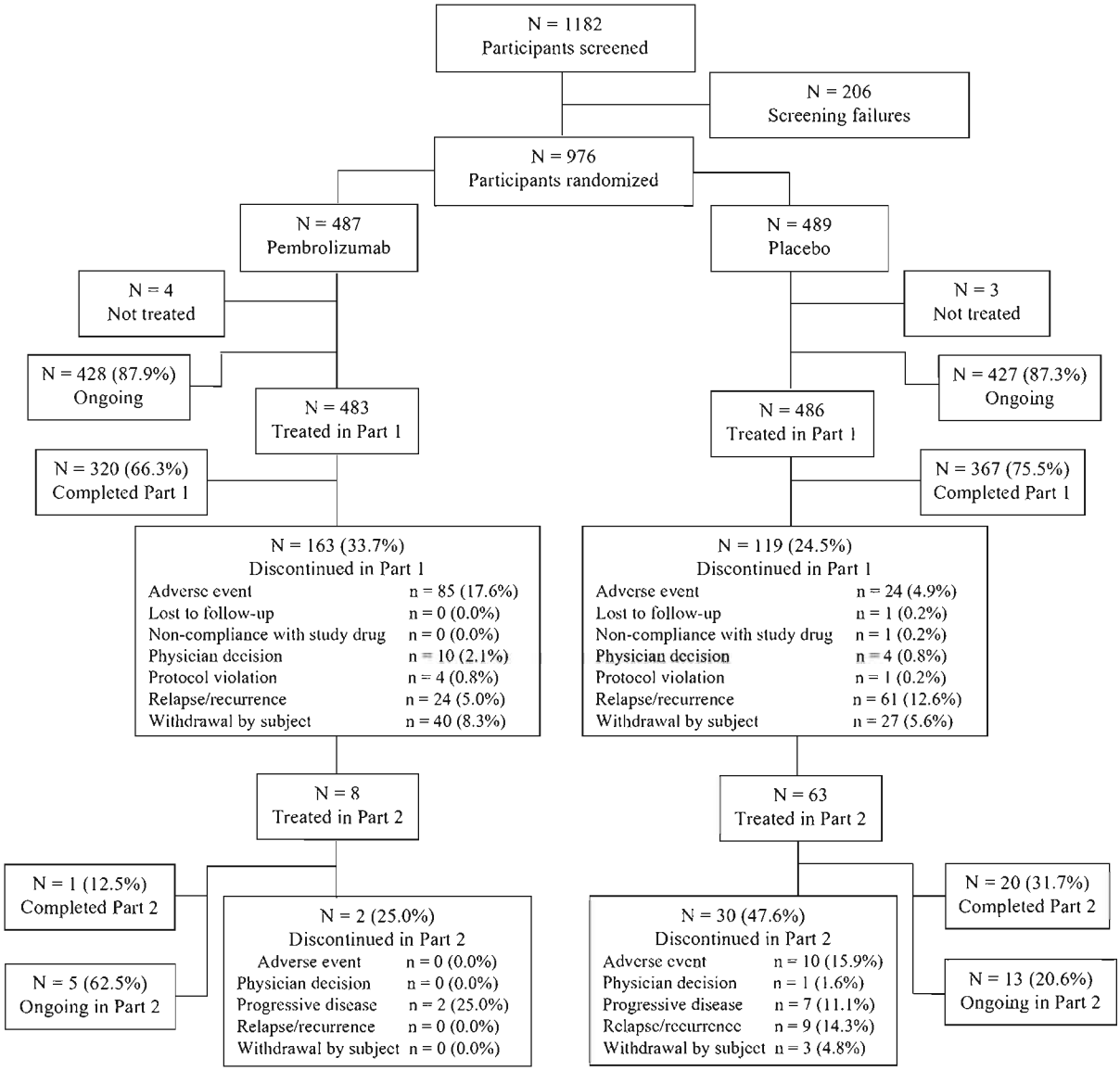


Table 10-1
Disposition of Participant
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participant in population	487		489		976	
Trial Disposition						
Discontinued	59	(12.1)	62	(12.7)	121	(12.4)
Death	38	(7.8)	39	(8.0)	77	(7.9)
Associated with COVID-19	3	(0.6)	1	(0.2)	4	(0.4)
Lost To Follow-Up	2	(0.4)	3	(0.6)	5	(0.5)
Not Associated with COVID-19, No Further Information	2	(0.4)	3	(0.6)	5	(0.5)
Physician Decision	1	(0.2)	3	(0.6)	4	(0.4)
Not Associated with COVID-19, No Further Information	1	(0.2)	3	(0.6)	4	(0.4)
Withdrawal By Subject	18	(3.7)	17	(3.5)	35	(3.6)
Associated with COVID-19, No Further Information	1	(0.2)	0	(0.0)	1	(0.1)
Not Associated with COVID-19, No Further Information	15	(3.1)	14	(2.9)	29	(3.0)
Not Associated with COVID-19, Subsequently Died	2	(0.4)	3	(0.6)	5	(0.5)
Participants Ongoing	428	(87.9)	427	(87.3)	855	(87.6)
Participant Study Medication Disposition in Part 1						
Started	483		486		969	
Completed	320	(66.3)	367	(75.5)	687	(70.9)
Discontinued	163	(33.7)	119	(24.5)	282	(29.1)
Adverse Event	85	(17.6)	24	(4.9)	109	(11.2)
Associated with COVID-19	1	(0.2)	1	(0.2)	2	(0.2)
Lost To Follow-Up	0	(0.0)	1	(0.2)	1	(0.1)
Non-Compliance With Study Drug	0	(0.0)	1	(0.2)	1	(0.1)
Physician Decision	10	(2.1)	4	(0.8)	14	(1.4)
Associated with COVID-19	0	(0.0)	2	(0.4)	2	(0.2)
Protocol Violation	4	(0.8)	1	(0.2)	5	(0.5)
Relapse/Recurrence	24	(5.0)	61	(12.6)	85	(8.8)
Associated with COVID-19	0	(0.0)	1	(0.2)	1	(0.1)
Withdrawal By Subject	40	(8.3)	27	(5.6)	67	(6.9)
Associated with COVID-19	6	(1.2)	7	(1.4)	13	(1.3)
Participant Study Medication Disposition in Part 2						
Started	8		63		71	

Disposition of Participant
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participant Study Medication Disposition in Part 2						
Completed	1	(12.5)	20	(31.7)	21	(29.6)
Discontinued	2	(25.0)	30	(47.6)	32	(45.1)
Adverse Event	0	(0.0)	10	(15.9)	10	(14.1)
Physician Decision	0	(0.0)	1	(1.6)	1	(1.4)
Progressive Disease	2	(25.0)	7	(11.1)	9	(12.7)
Relapse/Recurrence	0	(0.0)	9	(14.3)	9	(12.7)
Withdrawal By Subject	0	(0.0)	3	(4.8)	3	(4.2)
Participants Ongoing	5	(62.5)	13	(20.6)	18	(25.4)

If the overall count of participant is calculated and displayed within a section in the first row, then it is used as the denominator for the percentage calculation. Otherwise, participant in population is used as the denominator for the percentage calculation.
Trial Disposition includes information from Part 1 and Part 2, where each participant is counted once for trial disposition.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

10.1.1 Confirmed Premature Unblinding Events

As of the DCO, 29 participants were prematurely unblinded. Of these, 25 were unblinded by the site due to safety reasons (as allowed by the procedures for emergency unblinding in Section 8.1.11 of the study protocol [16.1.1]) and 4 were inadvertently unblinded by the site. None of these premature unblinding events led to exclusion from the analysis.

10.2 Protocol Deviations

Important protocol deviations were reported for 57 (5.8%) participants [Table 14.1-10]. The important protocol deviations are not expected to impact the overall safety or integrity of the study.

No participant's data were excluded from analysis due to an important protocol deviation [Sec. 10.3].

No protocol deviations were classified as a serious GCP compliance issue.

Most participants had no clinically important protocol deviations. Thirty-three (3.4%) participants had clinically important protocol deviations during the study; of these, 2 were reported since IA3. The types of clinically important protocol deviations were similar across the treatment groups [Table 10-2].

As described in [Sec. 9.8], part of this study was conducted during the COVID-19 pandemic. The percentages and types of protocol deviations in Part 1 that were associated with the pandemic were similar across treatment groups; most were visit deviations (eg, missed, delayed, or early) or dose deviations (eg, missed or delayed) [Table 14.1-12]. No

participant's data were excluded from analyses due to a protocol deviation associated with the pandemic [Sec. 10.3]. No protocol deviations that occurred due to the COVID-19 pandemic were considered important protocol deviations. A listing of important protocol deviations is presented by participant, study site, and clinical importance in [16.2.2].

Table 10-2
Summary of Important Protocol Deviations Considered to be Clinically Important
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
with one or more clinically important protocol deviations	14	(2.9)	19	(3.9)	33	(3.4)
with no clinically important protocol deviations	473	(97.1)	470	(96.1)	943	(96.6)
Discontinuation Criteria	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Participant developed trial specific discontinuation criteria but was not discontinued from the trial.	1	(0.2)	0	(0.0)	1	(0.1)
Inclusion/ Exclusion Criteria	**7**	**(1.4)**	**7**	**(1.4)**	**14**	**(1.4)**
Participant did not meet inclusion criteria 01. (Male/female participants who are ≥ 12 years of age on the day of signing informed consent/assent [unless local regulations and/or institutional policies do not allow for participants < 18 years of age to participate; for those sites, the eligible population is ≥ 18 years of age] with surgically resected and histologically/pathologically confirmed new diagnosis of Stage IIB or IIC cutaneous melanoma per AJCC 8th edition guidelines.)	4	(0.8)	3	(0.6)	7	(0.7)
Participants entered into the trial, i.e. progressed beyond screening, who did not meet key inclusion/exclusion criteria.	3	(0.6)	4	(0.8)	7	(0.7)
Safety Reporting	**4**	**(0.8)**	**12**	**(2.5)**	**16**	**(1.6)**
Participant had a reportable Safety Event and/or follow up Safety Event information that was not reported per the timelines outlined in the protocol.	4	(0.8)	12	(2.5)	16	(1.6)
Study Intervention	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Participant was dispensed study intervention other than what was assigned in the allocation schedule, i.e. incorrect medication or potential cross-treatment.	2	(0.4)	0	(0.0)	2	(0.2)
Every participant is counted a single time for each applicable row and column. Database Cutoff Date: 04JAN2023						

Source: [P716V04MK3475: adam-adsl] [P716V04MK3475: sdtm-dv; suppdv]

10.3 Data Sets Analyzed

10.3.1 Efficacy Analysis Population(s)

Efficacy analyses were based on the ITT population, which consisted of all 976 randomized participants [Table 10-3]. Participants were analyzed according to the treatment group assigned at randomization.

No participants were excluded from the efficacy analysis population [16.2.3].

10.3.2 Safety Analysis Population

Safety analyses were based on the APaT population, which included all 969 randomized participants who received at least 1 dose of study intervention [Table 10-3].

Table 10-3
Study Population

	Pembrolizumab	Placebo	Total
Number of Participants Screened			1182
Number of Participants Randomized (Planned Treatment) (ITT)	487	489	976
Number of Participants Received Treatment in Part 1(Actual Treatment) (APaT)	483	486	969
Number of Participants Randomized and Did not Receive Treatment	4	3	7
Number of Participants Received Treatment in Part 2(Actual Part 1 Treatment) (APaT)	8	63	71
Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl]

10.3.3 Patient-reported Outcome Analysis Population

PRO analyses for the EORTC QLQ-C30 and EQ-5D-5L questionnaires [Sec. 11.1.3] were based on the PRO FAS population, which included all participants who had at least 1 PRO assessment and received at least 1 dose of study treatment.

10.4 Demographics and Other Baseline Characteristics

10.4.1 Demographics and Baseline Disease Characteristics

The demographic and baseline characteristics for Parts 1 and 2 of the study were balanced across the treatment groups and were generally unchanged from IA3 [Ref. 5.3.5.1: P716V03MK3475: Table 10-4] [Table 10-4] [Table 14.1-15]. Almost all participants had Stage IIB or IIC melanoma without nodal involvement or evidence of distant metastasis. Overall, 625 (64.0%) participants had Stage IIB melanoma, and 340 (34.8%) participants had Stage IIC melanoma [Table 14.1-14].

Participants' medical history conditions are presented in [Table 14.1-16].

Table 10-4
Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
Sex						
Male	300	(61.6)	289	(59.1)	589	(60.3)
Female	187	(38.4)	200	(40.9)	387	(39.7)
Age (Years)						
12 - 17	1	(0.2)	1	(0.2)	2	(0.2)
18 - 64	302	(62.0)	294	(60.1)	596	(61.1)
≥ 65	184	(37.8)	194	(39.7)	378	(38.7)
Mean	59.0		59.6		59.3	
SD	12.6		13.3		12.9	
Median	60.0		61.0		61.0	
Range	[redacted] to 84		[redacted] to 87		16 to 87	
Race						
American Indian Or Alaska Native	1	(0.2)	0	(0.0)	1	(0.1)
Asian	4	(0.8)	1	(0.2)	5	(0.5)
Black Or African American	4	(0.8)	4	(0.8)	8	(0.8)
Multiple	1	(0.2)	0	(0.0)	1	(0.1)
Black Or African American White	1	(0.2)	0	(0.0)	1	(0.1)
White	435	(89.3)	439	(89.8)	874	(89.5)
Missing	42	(8.6)	45	(9.2)	87	(8.9)
Ethnicity						
Hispanic Or Latino	44	(9.0)	24	(4.9)	68	(7.0)
Not Hispanic Or Latino	395	(81.1)	415	(84.9)	810	(83.0)
Not Reported	42	(8.6)	45	(9.2)	87	(8.9)
Unknown	6	(1.2)	5	(1.0)	11	(1.1)
Geographic Region						
US	95	(19.5)	80	(16.4)	175	(17.9)
Non-US	392	(80.5)	409	(83.6)	801	(82.1)
ECOG						
0	454	(93.2)	452	(92.4)	906	(92.8)
1	32	(6.6)	35	(7.2)	67	(6.9)
2	0	(0.0)	1	(0.2)	1	(0.1)

Redacted under section 40 of the FOI Act

Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Not Applicable	1	(0.2)	1	(0.2)	2	(0.2)
KPS Status						
100 - Normal. No complaints. No evidence of disease.	1	(0.2)	1	(0.2)	2	(0.2)
Not Applicable	486	(99.8)	488	(99.8)	974	(99.8)
T-Stage						
T3a	2	(0.4)	0	(0.0)	2	(0.2)
T3b	200	(41.1)	201	(41.1)	401	(41.1)
T4a	113	(23.2)	116	(23.7)	229	(23.5)
T4b	172	(35.3)	172	(35.2)	344	(35.2)
Nodal Involvement						
NX	2	(0.4)	1	(0.2)	3	(0.3)
N0	481	(98.8)	487	(99.6)	968	(99.2)
N1C	4	(0.8)	1	(0.2)	5	(0.5)
Metastatic Staging						
M0	487	(100.0)	487	(99.6)	974	(99.8)
M1C	0	(0.0)	1	(0.2)	1	(0.1)
M1D	0	(0.0)	1	(0.2)	1	(0.1)
Overall Cancer Stage						
IIA	1	(0.2)	0	(0.0)	1	(0.1)
IIB	309	(63.4)	316	(64.6)	625	(64.0)
IIC	171	(35.1)	169	(34.6)	340	(34.8)
IIIC	4	(0.8)	1	(0.2)	5	(0.5)
IV	0	(0.0)	2	(0.4)	2	(0.2)
Missing	2	(0.4)	1	(0.2)	3	(0.3)
Stratification						
Pediatric Age 12 to 17	1	(0.2)	1	(0.2)	2	(0.2)
IIB T3b >2.0-4.0 mm with ulceration	199	(40.9)	198	(40.5)	397	(40.7)
IIB T4a >4.0 mm without ulceration	112	(23.0)	114	(23.3)	226	(23.2)

Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
IIC T4b >4.0 mm with ulceration	175	(35.9)	176	(36.0)	351	(36.0)
ECOG is not applicable for pediatric participants. KPS is not applicable for adult participants. Database Cutoff Date: 04JAN2023.						

Source: [P716V04MK3475: adam-adsl]

10.4.2 Concomitant Treatments

Consistent with IA3, similar proportions of participants received concomitant medications in both treatment groups (95.2% vs 91.6% in the pembrolizumab and placebo groups, respectively) [Table 14.1-17] [Ref. 5.3.5.1: P716V03MK3475: 10.4.2].

The most frequently reported categories of concomitant medications (in >40% of participants in either treatment group) were ophthalmologicals, analgesics, stomatological preparations, corticosteroids for systemic use, antidiarrheals/intestinal anti-inflammatory/anti-infective agents, and corticosteroids for dermatological preparations [Table 14.1-17]:

Use of systemic corticosteroids for management of AEOSI is described in [Sec. 12.2.3.1].

10.5 Measurements of Study Intervention Compliance

Study treatment was administered in the clinic by qualified personnel as described in the protocol [16.1.1]. Important protocol deviations associated with administration of study intervention were reported for 13 participants (7 in the pembrolizumab group and 6 in the placebo group) [Table 14.1-10]. No AEs associated with an overdose of study intervention were reported [Sec. 12.1.3.1].

10.6 Extent of Exposure

As of the DCO, the median duration of exposure to study intervention was unchanged from IA3, and was the same in both treatment groups (337.0 days) [Table 10-5].

In the pembrolizumab and placebo groups, 68.9% and 79.2% of participants had at least 10 months of exposure, respectively [Table 10-6].

Table 10-5
Summary of Drug Exposure
(APaT Population)

	Pembrolizumab (N=483)	Placebo (N=486)	Total (N=969)
Number of Days on Therapy			
Mean	281.6	309.5	295.6
Median	337.0	337.0	337.0
SD	114.86	88.43	103.35
Range	1.0 to 498.0	1.0 to 475.0	1.0 to 498.0
Number of Administrations			
Mean	13.8	15.1	14.4
Median	17.0	17.0	17.0
SD	5.20	3.97	4.68
Range	1.0 to 17.0	1.0 to 17.0	1.0 to 17.0
Number of Days on Therapy is calculated as last dose date - first dose date +1. Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl; adexsum]

Table 10-6
Exposure by Duration
(APaT Population)

	Pembrolizumab (N=483)		Placebo (N=486)		Total (N=969)	
	n	(%)	n	(%)	n	(%)
Duration of Exposure						
> 0 m	483	(100.0)	486	(100.0)	969	(100.0)
≥ 1 m	455	(94.2)	472	(97.1)	927	(95.7)
≥ 3 m	430	(89.0)	461	(94.9)	891	(92.0)
≥ 6 m	376	(77.8)	428	(88.1)	804	(83.0)
≥ 9 m	341	(70.6)	400	(82.3)	741	(76.5)
≥ 10 m	333	(68.9)	385	(79.2)	718	(74.1)
≥ 12 m	52	(10.8)	51	(10.5)	103	(10.6)

Each participant is counted once on each applicable duration category row.
Duration of exposure is the time from the first dose date to the last dose date.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adexsum]

11 EFFICACY AND OTHER EVALUATIONS

11.1 Efficacy Results

The results presented in this CSR are based on IA4, with 193 DMFS and 291 RFS events as of the DCO [Table 14.2-2]. The median duration of follow-up for all participants (ITT population) was 38.5 months (range: 4.6 to 51.2 months) with a similar median duration of follow-up in both treatment groups [Table 11-1].

Table 11-1
Summary of Follow-up Duration
(ITT Population)

	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
Follow-up duration (months)[a]			
Median (Range)	38.6 (10.3 - 51.1)	38.5 (4.6 - 51.2)	38.5 (4.6 - 51.2)
Mean (SD)	38.2 (6.7)	37.8 (7.7)	38.0 (7.2)

[a]Follow-up duration is defined as the time from randomization date to the date of death or the database cutoff date if the patient was still alive.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adintdt]

11.1.1 Distant Metastasis-free Survival

11.1.1.1 Distant Metastasis-free Survival in All Participants

According to the multiplicity strategy for this study, after a statistically significant RFS comparison at IA1, and statistically significant DMFS comparison at IA3 the 2.5% alpha was reallocated to the OS comparison. KEYNOTE-716 achieved the success criterion for the secondary DMFS endpoint and hypothesis based on IA3 results. In IA4 pembrolizumab treatment resulted in a clinically meaningful improvement in DMFS compared with placebo, demonstrating a continued decreased risk of distant metastasis (HR=0.59; [95% CI: 0.44, 0.79]) [Table 11-2].

The KM curves for DMFS separated at approximately 3 months and remained separated through the assessment period [Figure 11-1].

As of the DCO, the median DMFS was not yet reached in either group [Table 11-2]. The DMFS rates by KM estimation at each analyzed timepoint were higher in the pembrolizumab group compared with the placebo group and remained higher through 48 months [Table 11-3].

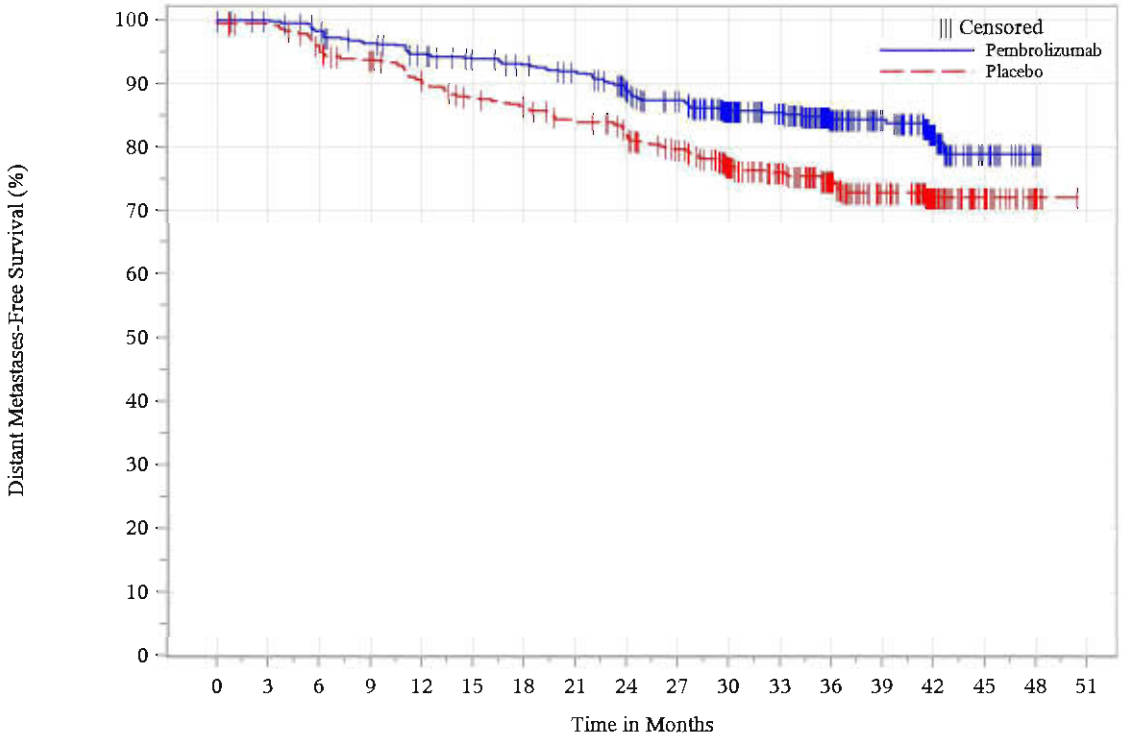
Table 11-2
Analysis of Distant Metastases-Free Survival
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	487	74 (15.2)	15505.8	0.5	NR (NR, NR)	84.4 (80.6, 87.5)
Placebo	489	119 (24.3)	14891.4	0.8	NR (NR, NR)	74.7 (70.4, 78.5)
Pairwise Comparisons					Hazard Ratiob (95% CI)[b]	
Pembrolizumab vs. Placebo					0.59 (0.44, 0.79)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T Stage (T3b vs. T4a vs. T4b).
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Figure 11-1
Kaplan-Meier Estimates of Distant Metastases-Free Survival
(ITT Population)



At Risk

Pembrolizumab	487	480	469	456	444	434	427	417	396	376	322	276	185	130	71	22	5	0
Placebo	489	482	463	449	427	412	402	389	372	350	287	243	176	131	62	32	7	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 11-3
Distant Metastases-Free Survival Rate Over Time
(ITT Population)

	Pembrolizumab (N=487) % (95% CI)[a]	Placebo (N=489) % (95% CI)[a]
Distant Metastases-Free Survival rate at time point		
6 months	98.3 (96.7, 99.2)	95.9 (93.7, 97.3)
12 months	94.7 (92.3, 96.4)	90.4 (87.4, 92.7)
18 months	93.0 (90.3, 95.0)	86.4 (83.0, 89.2)
24 months	89.3 (86.1, 91.7)	82.0 (78.3, 85.2)
30 months	85.8 (82.2, 88.7)	76.9 (72.8, 80.5)
36 months	84.4 (80.6, 87.5)	74.7 (70.4, 78.5)
42 months	82.2 (77.5, 85.9)	72.2 (67.4, 76.5)
48 months	79.0 (72.2, 84.2)	72.2 (67.4, 76.5)

[a] From product-limit (Kaplan-Meier) method for censored data.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

11.1.1.1.1 Subsequent Therapies After First Distant Metastasis

Subsequent therapies received among the participants after first distant metastasis included surgical resection, radiation therapy, and systemic therapy.

Among the 193 participants with a DMFS event, 53 (27.5%) participants underwent surgical procedures (21 [28.4%] in the pembrolizumab group and 32 [26.9%] in the placebo group). Fewer participants underwent lung metastasis resection in the pembrolizumab group (10 [13.5%] participants) compared to the placebo group (22 [18.5%] participants) [Table 11-4].

A total of 37 (19.2%) of participants received subsequent radiation for palliation or control of metastatic disease post first distant metastasis (21 [28.4%] and 16 [13.4%] participants in the pembrolizumab and placebo groups, respectively) [Table 11-5].

A total of 135 (69.9%) of participants received subsequent therapy (excluding treatment with pembrolizumab in Part 2 of the study); 56 [75.7%] and 79 [66.4%] participants in the pembrolizumab and placebo groups, respectively) following first distant metastasis [Table 11-6]. Ten (13.5%) in the pembrolizumab group and 23 (19.3%) participants in the placebo group received anti PD-1 monotherapy (excluding treatment with pembrolizumab in Part 2 of the study). Nineteen (25.7%) participants in the pembrolizumab group and 33 (27.7) in the placebo group received anti PD-1/anti-CTLA-4 combination therapy. Sixteen (21.6%) in the pembrolizumab group and 14 (11.8%) in the placebo group received BRAF/MEK targeted therapy. Participants who received multiple therapies following first distant metastasis were included in multiple categories [Table 11-6] [Table 14.2-18].

Table 11-4
Subsequent Surgical Procedure Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Participants with Surgical Procedure Post First Distant Metastasisa	**21 (28.4)**	**32 (26.9)**	**53 (27.5)**
Lung Metastasis Resection	10 (13.5)	22 (18.5)	32 (16.6)
Craniotomy	3 (4.1)	2 (1.7)	5 (2.6)
Skin Metastasis Resection	2 (2.7)	1 (0.8)	3 (1.6)
Skin Excisional Biopsy	1 (1.4)	0 (0.0)	1 (0.5)
Lymphadenectomy	1 (1.4)	2 (1.7)	3 (1.6)
Adrenal Metastasis Resection	1 (1.4)	0 (0.0)	1 (0.5)
Intestinal Metastasis Resection	1 (1.4)	1 (0.8)	2 (1.0)
Pleural Biopsy	1 (1.4)	0 (0.0)	1 (0.5)
Spinal Metastasis Resection	1 (1.4)	0 (0.0)	1 (0.5)
Tonsillectomy	1 (1.4)	0 (0.0)	1 (0.5)
Parotidectomy	0 (0.0)	1 (0.8)	1 (0.5)
Cholecystectomy	0 (0.0)	1 (0.8)	1 (0.5)
Lymph Node Biopsy	0 (0.0)	1 (0.8)	1 (0.5)
Thyroid Gland Biopsy	0 (0.0)	1 (0.8)	1 (0.5)
Retroperitoneal Metastasis Resection	0 (0.0)	1 (0.8)	1 (0.5)

[a] Participants with multiple surgeries are counted in multiple categories.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 11-5
Subsequent Radiation Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Subsequent Radiation Post First Distant Metastasis	**21 (28.4)**	**16 (13.4)**	**37 (19.2)**
Control of Brain Metastases	11 (14.9)	4 (3.4)	15 (7.8)
Control of Recurrent Disease	3 (4.1)	4 (3.4)	7 (3.6)
Palliative Treatment or Symptom Control	1 (1.4)	2 (1.7)	3 (1.6)
Palliative Treatment or Symptom Control of Metastatic Disease	6 (8.1)	6 (5.0)	12 (6.2)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 11-6
Subsequent Therapy Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

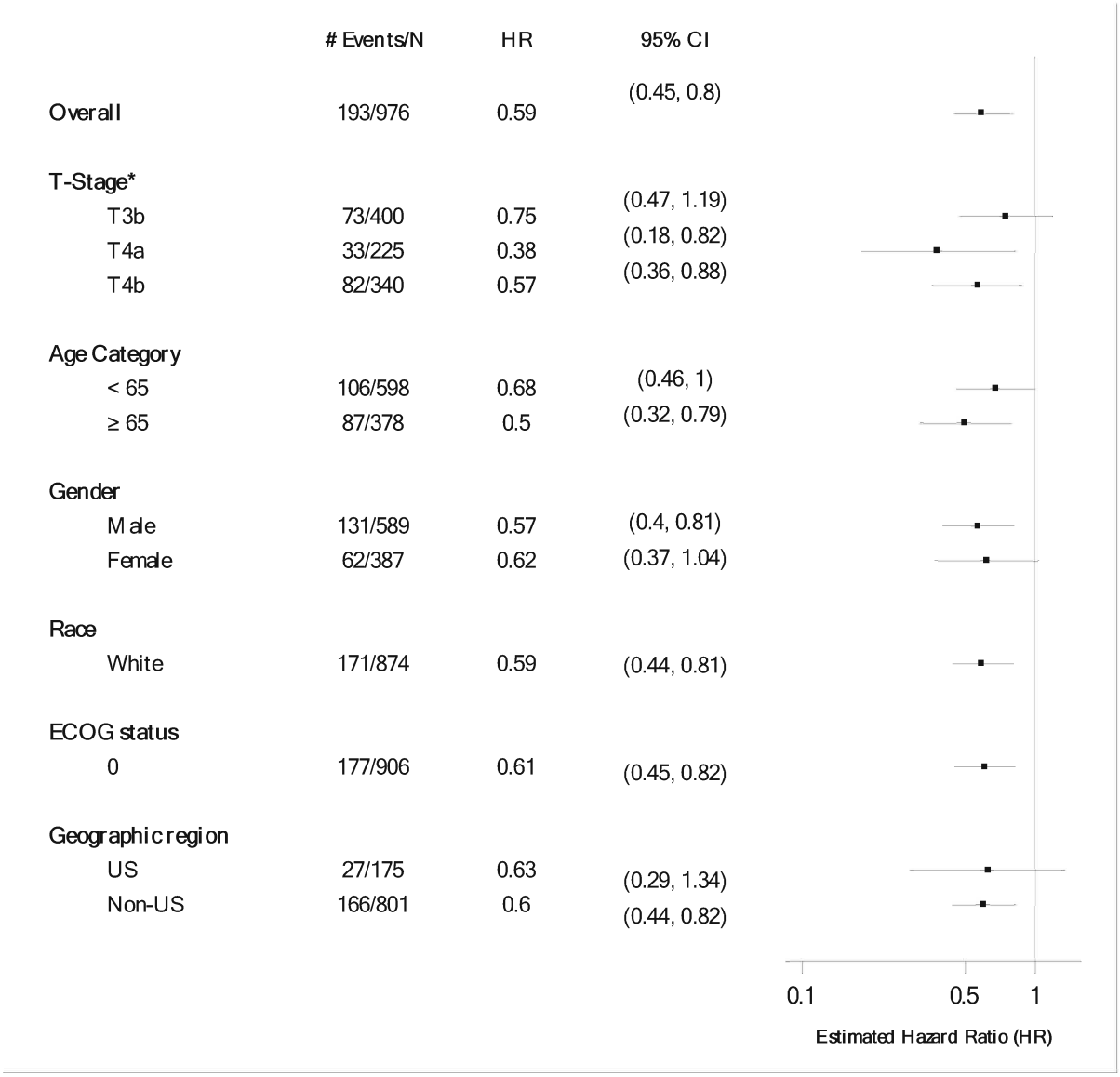
	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Subsequent Therapy Post First Distant Metastasis	**56 (75.7)**	**79 (66.4)**	**135 (69.9)**
Anti PD-1 Therapy	10 (13.5)	23 (19.3)	33 (17.1)
Anti CTLA-4 Therapy	4 (5.4)	4 (3.4)	8 (4.1)
Immunotherapy	2 (2.7)	1 (0.8)	3 (1.6)
Protein Kinase Inhibitor	1 (1.4)	0 (0.0)	1 (0.5)
BRAF/MEK Targeted Therapy	16 (21.6)	14 (11.8)	30 (15.5)
Anti PD-1/Anti CTLA-4 Combination Therapy	19 (25.7)	33 (27.7)	52 (26.9)
Anti PD-1/Immunotherapy Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Anti CTLA-4 /Immunotherapy Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Anti CTLA-4/TKI Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Other Targeted Combination Therapy	1 (1.4)	0 (0.0)	1 (0.5)
Chemotherapy	2 (2.7)	0 (0.0)	2 (1.0)
Anti PD-1/TKI Combination Therapy	0 (0.0)	2 (1.7)	2 (1.0)
Other Targeted Therapy	1 (1.4)	0 (0.0)	1 (0.5)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

11.1.1.2 Distant Metastasis-free Survival by Subgroup

DMFS results in prespecified subgroups were generally consistent with the primary analysis for the ITT population. The subgroup analyses by region and T-stage had small numbers of participants and events in the US compared with non-US regions and T4a compared with T3b and T4b T-stages, respectively [Figure 11-2]. Thus, the resulting HRs had wide 95% CIs [Table 14.2-5] [Table 14.2-6] [Table 14.2-7] [Table 14.2-8] [Table 14.2-9]. The tails of the KM curves by subgroup should be interpreted with caution due to the small number of participants at risk [Figure 14.2-3] [Figure 14.2-4] [Figure 14.2-5] [Figure 14.2-6] [Figure 14.2-7] [Figure 14.2-8] [Figure 14.2-9] [Figure 14.2-10].

Figure 11-2
Forest Plot of Distant Metastases-Free Survival Hazard Ratio by Subgroup Factors
(ITT Population)



A subgroup with number of participants < 10% ITT population is not displayed on the plot.
*Based on actual baseline tumor stage collected on eCRF.
Source: [P716V04MK3475: adam-adsl; adtte]

11.1.1.3 Distant Metastasis-free Survival Sensitivity Analyses

A sensitivity analysis that included deaths as part of the DMFS analysis was performed at IA4 to evaluate the robustness of the DMFS results. The results were consistent with the analysis in the overall population, with an improvement in DMFS in the pembrolizumab group compared with the placebo group (HR=0.61 [95% CI: 0.46, 0.81]) [Table 14.2-25] [Figure 14.2-21].

Consistent with the overall population, the DMFS rates for the sensitivity analysis at 12, 24, 36 and 48 months in the pembrolizumab group were higher than in the placebo group [Table 14.2-26].

Further details about the sensitivity analyses are provided in the protocol [16.1.1].

11.1.2 Recurrence-free Survival

11.1.2.1 Recurrence-free Survival in All Participants

KEYNOTE-716 achieved the success criterion for the primary RFS endpoint and hypothesis based on IA1 results. The descriptive IA2, IA3, and IA4 results for RFS supported the primary analysis at IA1 with additional follow-up.

At IA4, adjuvant pembrolizumab treatment continued to result in a clinically meaningful improvement in RFS compared with placebo, demonstrating a decreased risk of disease recurrence or death (HR=0.62 [95% CI: 0.49, 0.79]) [Table 11-7]. This result is consistent with the IA1 (HR=0.65 [95% CI: 0.46, 0.92]; p=0.00658), IA2 RFS results (HR=0.61; 95% CI: 0.45, 0.82), and IA3 RFS (HR=0.64 [95% CI:0.50, 0.84]) [Ref. 5.3.5.1: P716V01MK3475: Table 11-2] [Ref. 5.3.5.1: P716V02MK3475: Table 11-2] [Ref. 5.3.5.1: P716V03MK3475: Table 11-7].

As of the DCO, the median RFS was not reached in the pembrolizumab group or in the placebo group [Table 11-7].

The median RFS in the pembrolizumab group will be reached when the last participant at risk in the pembrolizumab group experiences an event.

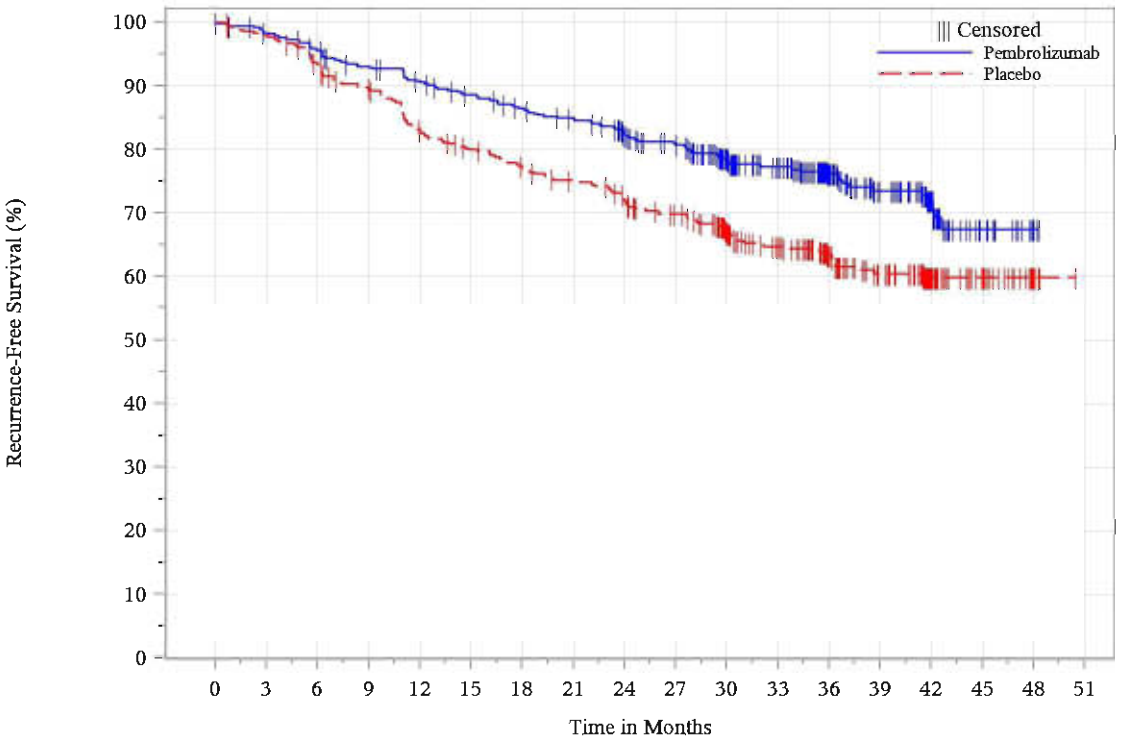
The KM curves for RFS separated at Month 6 and remain separated through the timeframe evaluated. Results beyond 48 months should be interpreted with caution due to the small numbers of participants at risk beyond this timepoint in both treatment groups [Figure 11-3].

The RFS rates by KM estimation from Month 6 through Month 48 were higher in the pembrolizumab group compared with the placebo group [Table 11-8].

Overall, during Part 1 of the study, fewer participants in the pembrolizumab group experienced disease recurrence compared with the placebo group [Table 11-7]. Fewer participants in the pembrolizumab group experienced distant metastases compared with the placebo group (52 [10.68%] vs 97 [19.84%]). Local, regional, and loco-regional recurrence were similar in the pembrolizumab and placebo groups [Table 14.2-2]. Overall, 15 deaths

contributed to the RFS events: 7 deaths in the pembrolizumab group, and 8 deaths in the placebo group [Table 14.2-2] [16.2.7].

Figure 11-3
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule)
(ITT Population)



At Risk

Pembrolizumab	487	472	457	441	426	413	400	390	371	353	300	254	173	117	62	18	4	0
Placebo	489	477	452	430	395	378	363	350	331	311	252	210	149	113	51	30	7	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 11-7
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	487	117 (24.0)	14728.3	0.8	NR (NR, NR)	76.2 (71.9, 79.9)
Placebo	489	174 (35.6)	13729.1	1.3	NR (NR, NR)	63.4 (58.7, 67.7)
Pairwise Comparisons					Hazard Ratiob (95% CI)[b]	
Pembrolizumab vs. Placebo					0.62 (0.49, 0.79)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T Stage (T3b vs. T4a vs. T4b).
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 11-8
Recurrence-Free Survival Rate Over Time
(ITT Population)

	Pembrolizumab (N=487) % (95% CI)[a]	Placebo (N=489) % (95% CI)[a]
Recurrence-Free Survival rate at time point		
6 months	95.6 (93.4, 97.1)	93.4 (90.8, 95.3)
12 months	90.6 (87.6, 92.9)	83.0 (79.3, 86.1)
18 months	86.5 (83.1, 89.3)	77.3 (73.2, 80.8)
24 months	82.6 (78.8, 85.7)	72.1 (67.8, 75.9)
30 months	78.6 (74.6, 82.1)	66.8 (62.4, 70.9)
36 months	76.2 (71.9, 79.9)	63.4 (58.7, 67.7)
42 months	72.0 (66.8, 76.5)	59.9 (54.8, 64.7)
48 months	67.4 (60.0, 73.7)	59.9 (54.8, 64.7)

[a] From product-limit (Kaplan-Meier) method for censored data.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

11.1.2.1.1 Subsequent Therapies After First Recurrence

Subsequent therapies received among participants who experienced disease recurrence included surgical resection, radiation therapy, and systemic therapy.

Among the 291 participants with an RFS event, approximately half (152 [52.2%] participants) underwent surgical resection due to disease recurrence (65 [55.6%] and 87 [50.0%] in the pembrolizumab and placebo groups, respectively). More participants in the placebo group underwent lung metastasis resection compared with the pembrolizumab group. The proportions of participants that underwent other surgical procedures (eg, skin metastasis resection and lymphadenectomy) were generally similar in both treatment groups [Table 11-9].

A total of 41 (14.1%) participants with a recurrence event received subsequent radiation therapy for palliation or control of recurrent/metastatic disease (24 [20.5%] and 17 [9.8%] participants in the pembrolizumab and placebo groups, respectively) [Table 11-10].

Overall, 73 (62.4%) participants in the pembrolizumab group and 87 (50.0%) in the placebo group received subsequent therapy (excluding treatment with pembrolizumab in Part 2 of the study) following first recurrence. The use of subsequent anti PD-1 monotherapy was numerically higher in the placebo group (34 [19.5%] participants) compared with the pembrolizumab group (15 [12.8%] participants). The use of BRAF/MEK targeted therapy was numerically higher in the pembrolizumab group (23 [19.7%] participants) compared

with the placebo group (14 [8.0%] participants). Similar proportions of participants in the pembrolizumab and placebo groups received other types of subsequent systemic therapy. Participants who received multiple therapies following first recurrence were included in multiple categories [Table 11-11] [Table 14.2-18]. An additional 8 participants in the pembrolizumab arm were rechallenged with pembrolizumab and 63 participants in the placebo group crossed over to receive pembrolizumab during Part 2 of the study after first recurrence [Table 14.2-12].

Table 11-9
Subsequent Surgical Procedure in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Participants with Surgical Procedure in Part 1 Post First Recurrencea	**65 (55.6)**	**87 (50.0)**	**152 (52.2)**
Lymphadenectomy	21 (17.9)	33 (19.0)	54 (18.6)
Skin Excisional Biopsy	13 (11.1)	15 (8.6)	28 (9.6)
Skin Metastasis Resection	12 (10.3)	15 (8.6)	27 (9.3)
Lung Metastasis Resection	10 (8.5)	21 (12.1)	31 (10.7)
Amputation	3 (2.6)	0 (0.0)	3 (1.0)
Craniotomy	2 (1.7)	1 (0.6)	3 (1.0)
Parotidectomy	1 (0.9)	1 (0.6)	2 (0.7)
Adrenal Metastasis Resection	1 (0.9)	0 (0.0)	1 (0.3)
Intestinal Metastasis Resection	1 (0.9)	1 (0.6)	2 (0.7)
Lymph Node Biopsy	1 (0.9)	3 (1.7)	4 (1.4)
Pleural Biopsy	1 (0.9)	0 (0.0)	1 (0.3)
Spinal Metastasis Resection	1 (0.9)	0 (0.0)	1 (0.3)
Tonsillectomy	1 (0.9)	0 (0.0)	1 (0.3)
Thyroid Gland Biopsy	0 (0.0)	1 (0.6)	1 (0.3)
Retroperitoneal Metastasis Resection	0 (0.0)	1 (0.6)	1 (0.3)

[a] Participants with multiple surgeries are counted in multiple categories.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 11-10
Subsequent Radiation in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Subsequent Radiation in Part 1 Post First Recurrence	**24 (20.5)**	**17 (9.8)**	**41 (14.1)**
Control of Brain Metastases	9 (7.7)	3 (1.7)	12 (4.1)
Control of Recurrent Disease	8 (6.8)	9 (5.2)	17 (5.8)
Palliative Treatment or Symptom Control	1 (0.9)	2 (1.1)	3 (1.0)
Palliative Treatment or Symptom Control of Metastatic Disease	6 (5.1)	3 (1.7)	9 (3.1)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 11-11
Subsequent Therapy in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Subsequent Therapy in Part 1 Post First Recurrence	**73 (62.4)**	**87 (50.0)**	**160 (55.0)**
Anti PD-1 Therapy	15 (12.8)	34 (19.5)	49 (16.8)
Anti CTLA-4 Therapy	4 (3.4)	1 (0.6)	5 (1.7)
Immunotherapy	3 (2.6)	0 (0.0)	3 (1.0)
Protein Kinase Inhibitor	2 (1.7)	0 (0.0)	2 (0.7)
BRAF/MEK Targeted Therapy	23 (19.7)	14 (8.0)	37 (12.7)
Anti PD-1/Anti CTLA-4 Combination Therapy	21 (17.9)	28 (16.1)	49 (16.8)
Anti PD-1/Immunotherapy Combination Therapy	2 (1.7)	4 (2.3)	6 (2.1)
Anti PD-1/Anti CTLA-4 /Immunotherapy Combination Therapy	0 (0.0)	1 (0.6)	1 (0.3)
Anti PD-1/Anti CTLA-4/TKI Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Anti PD-1/Anti Lag-3 Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Chemotherapy	2 (1.7)	0 (0.0)	2 (0.7)
Anti PD-1/TKI Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Other Targeted Therapy	1 (0.9)	0 (0.0)	1 (0.3)
Database Cutoff Date: 04JAN2023			

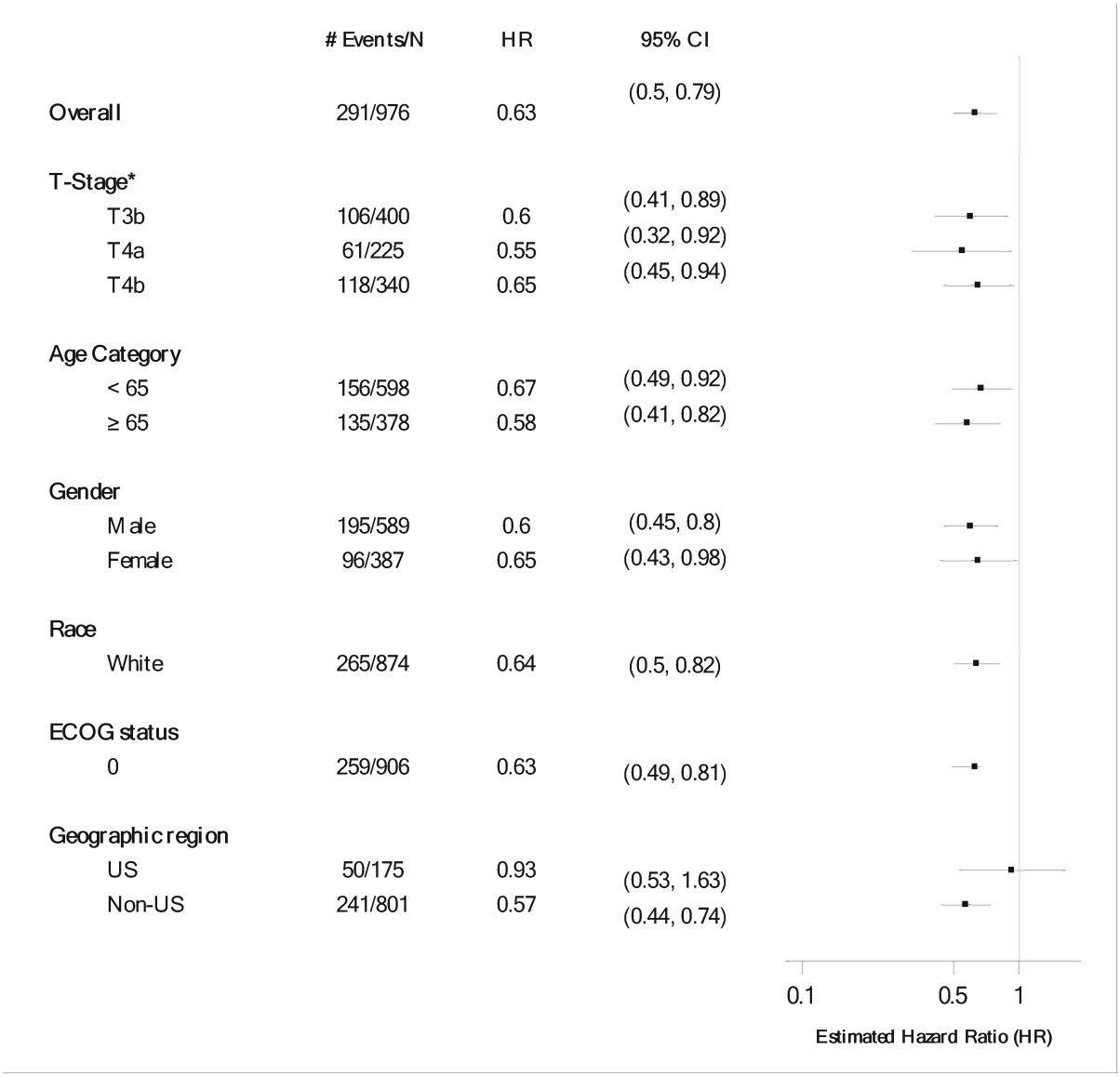
Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

11.1.2.2 Recurrence-free Survival by Subgroup

RFS results in prespecified subgroups at IA4 were generally consistent with the primary analysis at IA1 and with the supportive analyses at IA2 and IA3.The subgroup analysis by region had small numbers of participants and events in the US compared with ex-US regions, resulting in a wide 95% CI for the HR [Figure 11-4].

With additional follow-up since IA3, the RFS benefit remained favorable for pembrolizumab across subgroups, which supports the robustness of the RFS benefit [Table 14.2-13] through [Table 14.2-17]. However, the tails of the KM curves by subgroup should be interpreted with caution due to the small number of participants at risk [Figure 14.2-13] through [Figure 14.2-20].

Figure 11-4
Forest Plot of Recurrence-Free Survival Hazard Ratio by Subgroup Factors
(ITT Population)



A subgroup with number of participants < 10% ITT population is not displayed on the plot.
*Based on actual baseline tumor stage collected on eCRF.
Source: [P716V04MK3475: adam-adsl; adtte]

11.1.2.3 Recurrence-free Survival Sensitivity Analyses

No sensitivity analyses were conducted at IA4 or IA3. At IA2, two sensitivity analyses were performed to evaluate the robustness of the RFS endpoint, and the results were consistent with the primary analysis at IA1 [Ref. 5.3.5.1: P716V02MK3475: 11.1.1.3].

Further details about the sensitivity analyses are provided in the protocol [16.1.1]

11.1.3 Patient-reported Outcomes

A description of the PRO analyses conducted during this study is provided in the protocol [16.1.1]. Note: Physical functioning and EQ-5D-5L VAS scores are endpoints included in the sSAP [16.1.9.1] and analyzed for previous IAs.

EORTC QLQ-C30

To maintain consistency with IA3, updated Week 48 and Week 72 were selected as the timepoints for analyzing change from baseline for the EORTC QLQ-C30 in IA4 [Table 14.2-28]. At Week 48 the completion rates were 73.3% and 78.2%, in the pembrolizumab and placebo groups respectively, and the compliance rates were 85.5% and 91.1%, in the pembrolizumab and placebo groups, respectively. At Week 72 the completion rates were 61.1% and 60.3% in the pembrolizumab and placebo groups respectively, and the compliance rates were 85.0% and 86.4%, in the pembrolizumab and placebo groups, respectively [Table 14.2-27].

Adjuvant pembrolizumab treatment at Weeks 48 and 72 did not result in a clinically meaningful difference of global health status/QoL, respectively, [-3.68 (95% CI: -5.88, -1.47)] and [-2.07 (95% CI: -4.40, 0.26)] compared with placebo [Table 14.2-29]. The mean change in physical functioning from baseline to Weeks 48 and 72 was similar in the treatment groups [Table 14.2-30] [Table 14.2-31].

The mean changes from baseline in global health status/QoL, functional scales, and symptom scales between treatment groups at Weeks 48 [Figure 14.2-22] [Figure 14.2-23] and 72 [Figure 14.2-24] [Figure 14.2-25] were similar.

The mean changes from baseline in the global health status/QoL and physical functioning scores over time were stable within each treatment group and similar across treatment groups [Figure 11-5] [Figure 14.2-27]. The proportions of participants for whom the change from baseline in the global health status/QoL score and physical functioning score had improved or remained stable were similar across treatment groups [Table 14.2-32] [Table 14.2-33].

EQ-5D-5L

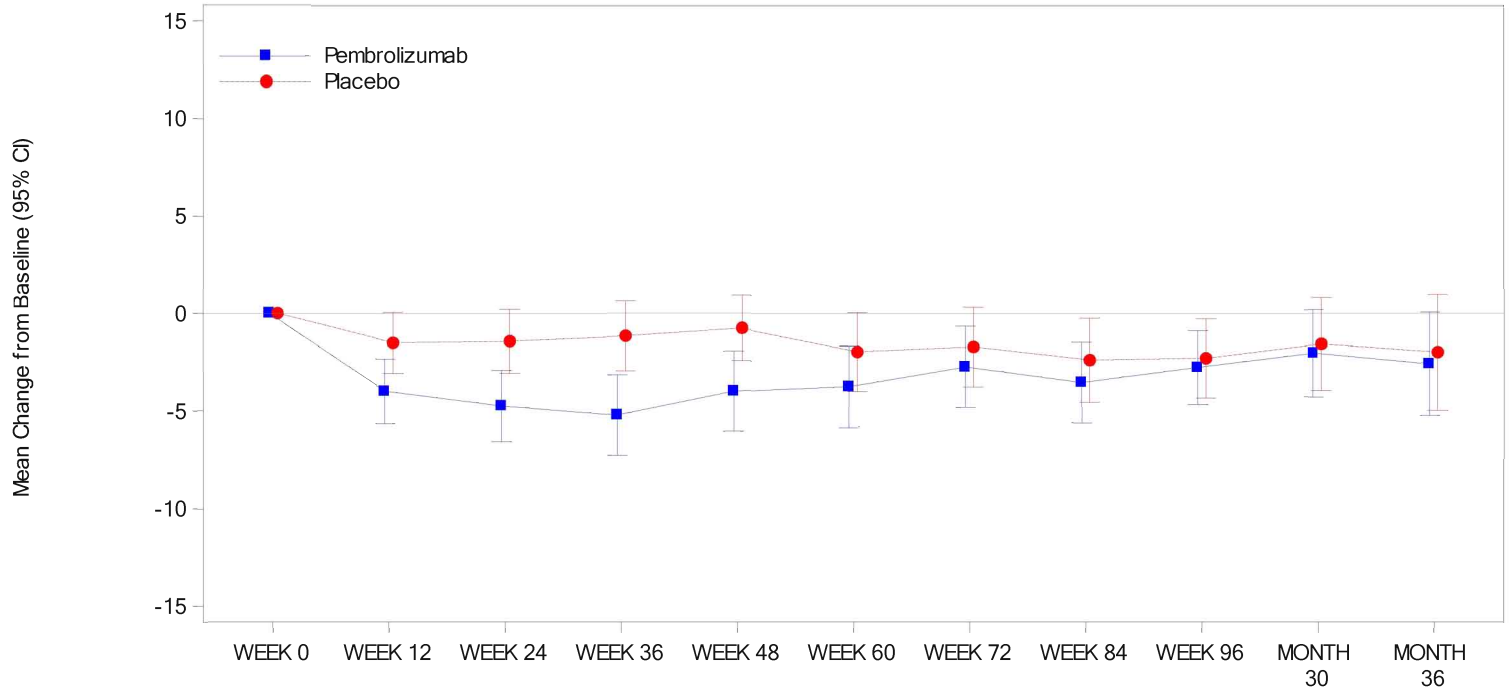
To maintain consistency with IA3, updated Week 48 and Week 72 were selected as the timepoints for analyzing change from baseline for the EQ-5D-5L in IA4. At Week 48 the completion rates were 73.9% and 80.7%, in the pembrolizumab and placebo groups, respectively, and the compliance rates were 86.2% and 91.6%, in the pembrolizumab and placebo groups, respectively [Table 14.2-34]. At Week 72 the completion rates were 61.9%

and 63.6%, in the pembrolizumab and placebo groups, respectively, and the compliance rates were 86.2% and 86.3%, in the pembrolizumab and placebo groups, respectively [Table 14.2-34].

The mean change from baseline analysis of the EQ-5D-5L VAS score at Weeks 48 and 72 was not meaningfully different in the pembrolizumab and placebo groups [Table 14.2-35] [Table 14.2-36]. Over time, the mean change from baseline analysis of the EQ-5D-5L index score using the UK crosswalk value set was not meaningfully different in either group [Figure 14.2-28].

Figure 11-5
Empirical Mean Change from Baseline and 95% CI for the EORTC QLQ-C30 Global Health Status/QoL Over Time by Treatment Group

(PRO FAS Population)



Number of Participants

Pembrolizumab	449	387	359	329	329	295	278	268	291	243	142
Placebo	459	418	372	351	360	289	274	260	285	241	138

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

11.2 Efficacy Results Summary

- Final DFMS results at IA4, continued to show that with 38.5 months of follow-up, pembrolizumab treatment resulted in a clinically meaningful improvement in DMFS, demonstrating a decreased risk of distant metastasis (HR=0.59; [95% CI: 0.44, 0.79]) compared to placebo. The KM curves for DMFS separated at Month 3 and remained separated through the period assessed.
- Of the 193 participants with a DMFS event, 53 (27.5%) participants underwent subsequent surgery, 37 (19.2%) participants received subsequent radiation, and 135 (69.9%) participants received (non-Part 2) subsequent systemic therapy.
- DMFS subgroup analyses were generally consistent regardless of tumor stage, age, gender, race, ECOG performance status, and region.
- Pembrolizumab provided sustained RFS benefit with additional follow-up when compared with placebo. The HR was 0.62 [95% CI: 0.49, 0.79] in favor of pembrolizumab.
- Of the 291 participants with a RFS event, 152 (52.2%) participants underwent subsequent surgery, 41 (14.1%) participants received subsequent radiation, and 160 (55.0%) participants received (non-Part 2) subsequent systemic therapy.
- Adjuvant pembrolizumab treatment resulted in no clinically meaningful difference in LS mean changes (-2.07 [95% CI: -4.40, 0.26]) in EORTC QLQ-C30 global health status/QoL at Week 72 compared with placebo. The change from baseline to Week 72 in physical functioning and the EQ-5D-5L VAS score at Week 72 were similar in the treatment groups.

12 SAFETY EVALUATION

12.1 Adverse Events

Listings of AEs by participant are provided in [16.2.7] [16.4]. MedDRA version 25.1 was used for IA4 table generation.

Separate safety tables for the 2 pediatric participants are provided in [Table 14.3-1] through Table 14.3-4]. A listing of AEs for the pediatric participants are provided in [16.2.7]. Safety summaries for the pediatric participants are provided in [16.2.7.1.5].

Data for Part 1 of the study are the primary focus of the safety analyses in this report. Therefore, analyses presented are for Part 1 unless otherwise indicated. A subset of safety tables for Part 2 of the study are provided in the corresponding section.

Exposure-adjusted safety data are provided in [Table 14.3-7], [Table 14.3-20], [Table 14.3-21], [Table14.3-32], [Table 14.3-33], [Table 14.3-40], [Table 14.3-41],[Table 14.3-53], [Table 14.3-54], [Table 14.3-89], and [Table 14.3-90].

12.1.1 Brief Summary of Adverse Events

Of the 969 participants in the APaT population, the majority had at least 1 AE (461 [95.4%] in the pembrolizumab group and 446 [91.8%] in the placebo group). Consistent with IA1, IA2, and IA3, and as expected for a comparison of active treatment vs placebo, higher incidences of AEs were reported in the pembrolizumab group compared with the placebo group in the following categories: drug-related AEs, Grade 3 to 5 AEs, Grade 3 to 5 drug-related AEs, drug-related SAEs, and AEs and drug-related AEs leading to discontinuation of study intervention [Table 12-1].

No deaths due to a drug-related AE were reported [Table 12-1]. Deaths considered unrelated to study intervention or drug by the investigator were reported in 1 participant in the pembrolizumab group (COVID-19 pneumonia) and 5 participants in the placebo group (COVID-19 pneumonia, pneumonia, completed suicide, malignant lung neoplasm, and recurrent cancer) [Table 12-1] [Table 14.3-19] [Table 14.3-22].

Subgroup analyses by age, sex, race, ECOG performance status, and region showed that the incidences and types of AEs were generally similar to those in the overall population [Table 14.3-8] through [Table 14.3-14].

Of the 71 participants enrolled in Part 2 of the study, the majority of participants (75% in the pembrolizumab rechallenge group and 85.7% in the crossover to pembrolizumab group) experienced 1 or more AEs. Most of the participants in each group experienced a drug-related AE. Grade 3 to 5 drug-related AEs were only reported in the crossover to pembrolizumab group (9.5%). No deaths were reported due to a drug-related AE in either group. Only participants in the crossover to pembrolizumab group discontinued pembrolizumab due to an AE (15.9%) [Table 12-2].

Table 12-1
Adverse Event Summary
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse event	22	(4.6)	40	(8.2)
with drug-relateda adverse events	399	(82.6)	309	(63.6)
with toxicity grade 3-5 adverse events	137	(28.4)	98	(20.2)
with toxicity grade 3-5 drug-related adverse events	83	(17.2)	25	(5.1)
with serious adverse events	103	(21.3)	96	(19.8)
with serious drug-related adverse events	49	(10.1)	11	(2.3)
who died	1	(0.2)	5	(1.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	83	(17.2)	23	(4.7)
discontinued drug due to a drug-related adverse event	77	(15.9)	12	(2.5)
discontinued drug due to a serious adverse event	38	(7.9)	13	(2.7)
discontinued drug due to a serious drug-related adverse event	33	(6.8)	4	(0.8)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 12-2
Adverse Event Summary
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	6	(75.0)	54	(85.7)
with no adverse event	2	(25.0)	9	(14.3)
with drug-relateda adverse events	4	(50.0)	36	(57.1)
with toxicity grade 3-5 adverse events	1	(12.5)	15	(23.8)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	6	(9.5)
with serious adverse events	1	(12.5)	10	(15.9)
with serious drug-related adverse events	0	(0.0)	3	(4.8)
who died	0	(0.0)	1	(1.6)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	10	(15.9)
discontinued drug due to a drug-related adverse event	0	(0.0)	8	(12.7)
discontinued drug due to a serious adverse event	0	(0.0)	5	(7.9)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	3	(4.8)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.1.2 Most Frequently Reported Adverse Events

The most frequently reported AEs in the pembrolizumab group (in ≥10% of participants) were fatigue, diarrhea, pruritus, arthralgia, rash, headache, hypothyroidism, nausea, cough, increased ALT, asthenia, hyperthyroidism, and myalgia [Table 12-3] [Table 14.3-15] through [Table 14.3-20].

AEs that occurred at a higher percentage in the pembrolizumab group than in the placebo group, and with the greatest difference in incidence between the treatment groups (≥8%), were pruritus, rash, hypothyroidism, and hyperthyroidism; these AEs are known ADRs (or clinical manifestations of ADRs) for pembrolizumab [Table 12-1] [Table 12-3].

Most AEs were Grades 1 and 2 in severity in both the pembrolizumab group (20.1% and 47.0%, respectively) and placebo group (31.7% and 39.9%, respectively) [Table 14.3-19] [Table 14.3-22].

The AEs reported in Part 2 of the study were consistent with the pembrolizumab group in Part 1.The most frequently reported AEs in the pembrolizumab rechallenge group (in ≥15% of participants) were arthralgia, asthenia, and fatigue. The most frequently reported AEs in the crossover to pembrolizumab group (in ≥5% of participants) were pruritis, hyperthyroidism, headache, asthenia, rash, arthralgia, diarrhea, increased ALT, hypothyroidism , insomnia, abdominal pain, increased AST, dizziness, nausea, dry mouth, hypophosphatemia, pyrexia, and urinary tract infection [Table 14.3-16].

Table 12-3
Participants With Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse events	22	(4.6)	40	(8.2)
Fatigue	143	(29.6)	127	(26.1)
Diarrhoea	136	(28.2)	100	(20.6)
Pruritus	134	(27.7)	66	(13.6)
Arthralgia	114	(23.6)	85	(17.5)
Rash	91	(18.8)	42	(8.6)
Headache	83	(17.2)	55	(11.3)
Hypothyroidism	82	(17.0)	17	(3.5)
Nausea	67	(13.9)	56	(11.5)
Cough	61	(12.6)	58	(11.9)
Alanine aminotransferase increased	57	(11.8)	29	(6.0)
Asthenia	56	(11.6)	52	(10.7)
Hyperthyroidism	51	(10.6)	3	(0.6)
Myalgia	51	(10.6)	28	(5.8)
Hypertension	43	(8.9)	43	(8.8)
Rash maculo-papular	42	(8.7)	11	(2.3)
Back pain	41	(8.5)	39	(8.0)
Constipation	40	(8.3)	41	(8.4)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Dizziness	33	(6.8)	27	(5.6)
Pyrexia	33	(6.8)	26	(5.3)
Dry mouth	32	(6.6)	9	(1.9)
Vomiting	32	(6.6)	16	(3.3)
Abdominal pain	31	(6.4)	24	(4.9)
Decreased appetite	28	(5.8)	13	(2.7)
Oedema peripheral	28	(5.8)	24	(4.9)
Pain in extremity	28	(5.8)	28	(5.8)
Dyspnoea	22	(4.6)	27	(5.6)
Nasopharyngitis	21	(4.3)	30	(6.2)
Basal cell carcinoma	17	(3.5)	27	(5.6)

Participants With Adverse Events by Decreasing Incidence (Incidence ≥ 5% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hyperglycaemia	15	(3.1)	28	(5.8)

Every participant is counted a single time for each applicable row and column.

A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

NCI CTCAE version 4.03.

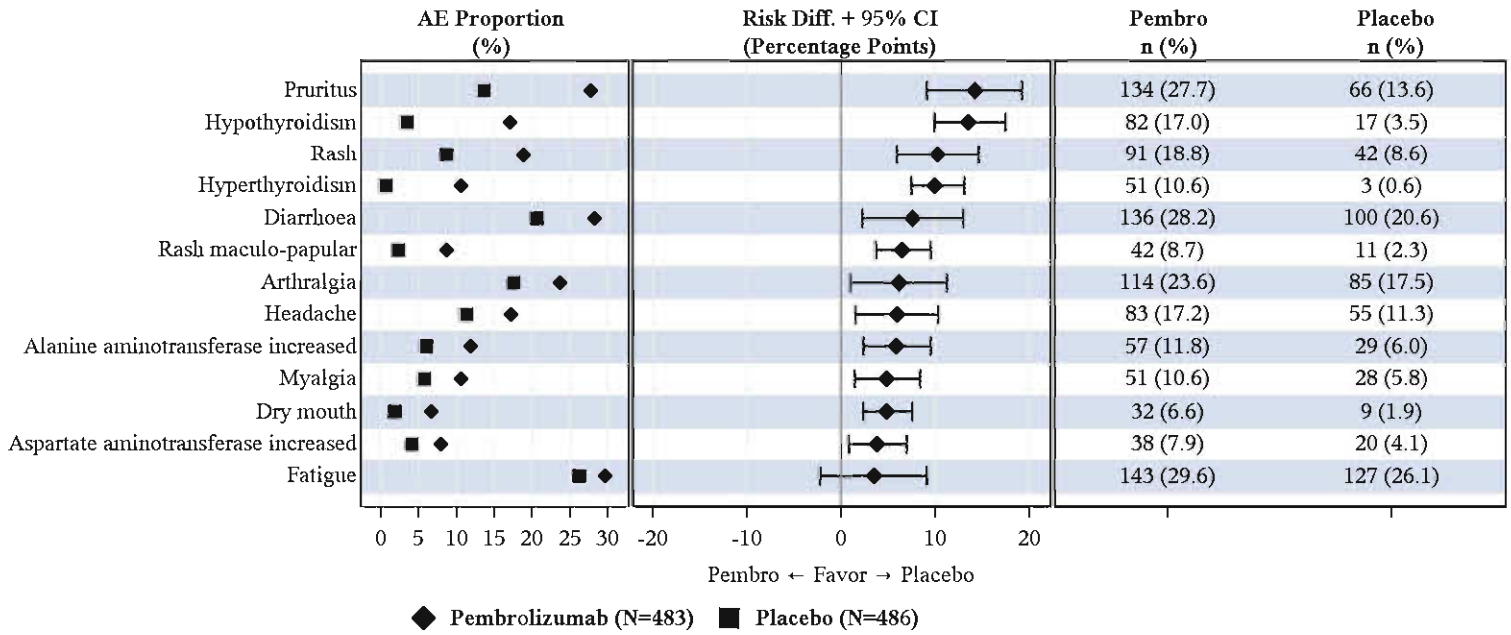
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

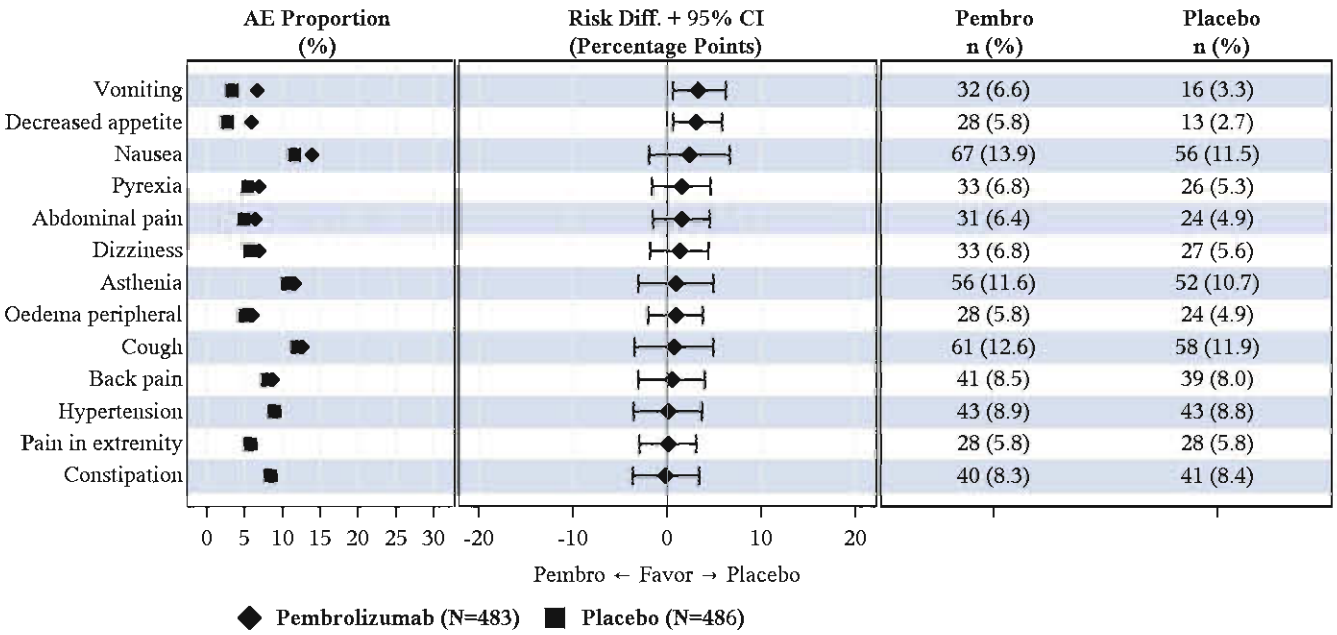
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

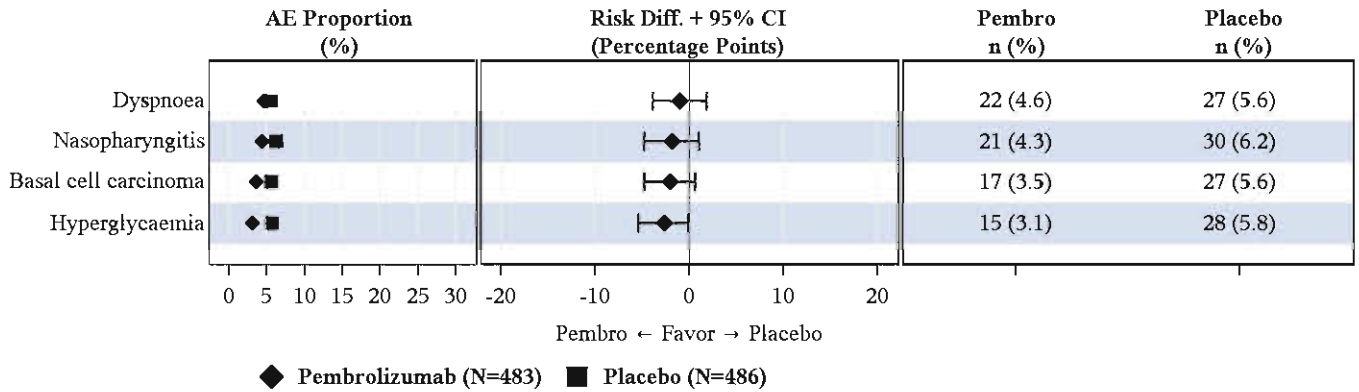
Figure 12-1
Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)



Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population) (Continued)



Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population) (Continued)



Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adae]

12.1.3 Classification of Adverse Events

12.1.3.1 Related to Study Intervention

The overall incidence of drug-related AEs was higher in the pembrolizumab group (82.6%) compared with the placebo group (63.6%) [Table 12-4] [Table 14.3-26].

The most frequently reported drug-related AEs (in ≥10% of participants in either treatment group) were pruritus, fatigue, diarrhea, arthralgia, rash, hypothyroidism, and hyperthyroidism [Table 12-4] [Table 14.3-26].

The drug-related AEs of pruritus, arthralgia, rash, hypothyroidism, and hyperthyroidism were reported at higher incidences (≥8.0% difference between groups) in the pembrolizumab group than in the placebo group [Table 12-4] [Table 14.3-26]. These AEs are known ADRs (or clinical manifestations of ADRs) for pembrolizumab.

Most drug-related AEs were Grade 1 or Grade 2 in severity in both the pembrolizumab group (28.0% and 37.5%, respectively) and placebo group (42.4% and 16.0%, respectively) [Table 14.3-25] [Table 14.3-27].

The drug-related AEs reported in Part 2 of the study were consistent with the pembrolizumab group in Part 1.The most frequently reported drug-related AEs in the pembrolizumab rechallenge group (in ≥ 10% of participants) were arthralgia, asthenia, arthritis, back pain, constipation, diarrhea, fatigue, insomnia, myalgia, paresthesia, and pruritis; and the most frequently reported AEs in the crossover to pembrolizumab (in ≥ 5% of participants) were rash, hyperthyroidism, diarrhea, asthenia, pruritis, and hypothyroidism [Table 14.3-24].

Table 12-4
Participants With Drug-Related Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	399	(82.6)	309	(63.6)
with no adverse events	84	(17.4)	177	(36.4)
Pruritus	119	(24.6)	52	(10.7)
Fatigue	104	(21.5)	93	(19.1)
Diarrhoea	90	(18.6)	56	(11.5)
Arthralgia	79	(16.4)	39	(8.0)
Rash	78	(16.1)	34	(7.0)
Hypothyroidism	77	(15.9)	13	(2.7)
Hyperthyroidism	49	(10.1)	3	(0.6)
Asthenia	47	(9.7)	40	(8.2)
Alanine aminotransferase increased	39	(8.1)	22	(4.5)
Nausea	37	(7.7)	33	(6.8)
Rash maculo-papular	36	(7.5)	9	(1.9)
Myalgia	32	(6.6)	16	(3.3)
Aspartate aminotransferase increased	31	(6.4)	11	(2.3)

Every participant is counted a single time for each applicable row and column.
A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.1.3.2 Grade 3 to 5 Adverse Events

The overall incidence of Grade 3 to 5 AEs was higher in the pembrolizumab group compared with the placebo group (28.4% vs 20.2%) [Table 14.3-28] [Table 14.3-29].

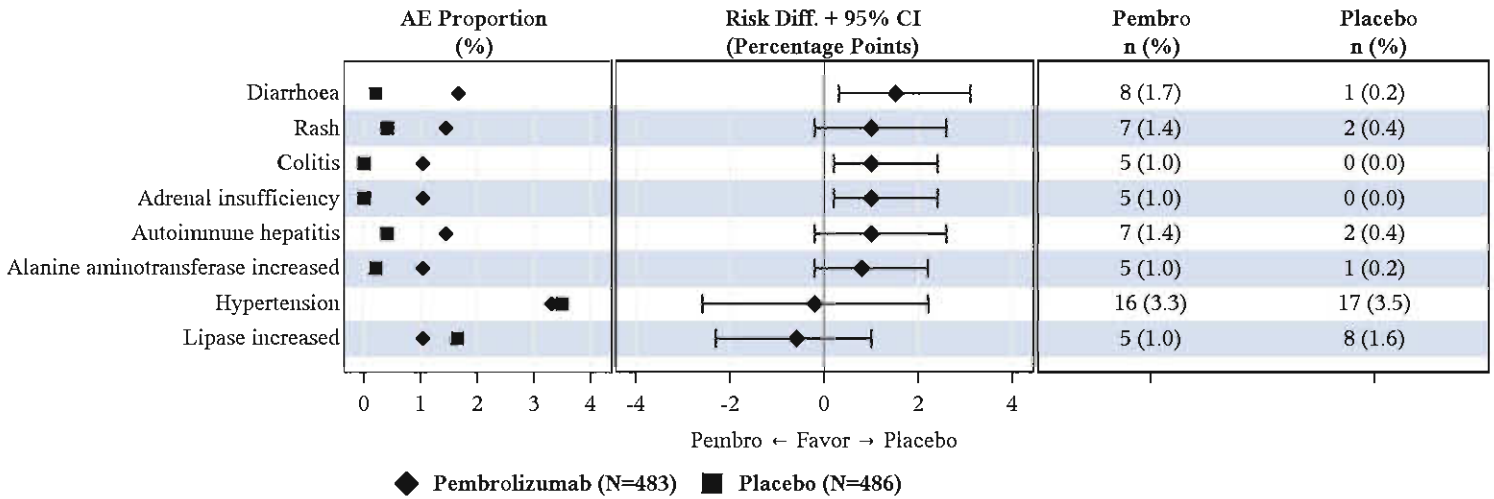
The most frequently reported Grade 3 to 5 AEs (in ≥1.0% of participants in either treatment group) were hypertension, diarrhea, autoimmune hepatitis, rash, increased lipase, adrenal insufficiency, increased ALT, and colitis [Table 14.3-28] [Table 14.3-29] [Figure 12-2].

Most Grade 3 to 5 AEs were Grade 3 in severity in both the pembrolizumab group (24.8%) and placebo group (17.1%). One participant in the pembrolizumab group and 5 participants in the placebo group had Grade 5 AEs[Sec. 12.2.1.1] [Table 14.3-19] [Table 14.3-22].

The median time to onset of participants' first Grade 3 to 5 AE was shorter in the pembrolizumab group (125.0 days) than in the placebo group (168.5 days) [Table 14.3-31].

In Part 2 of the study, most participants in the pembrolizumab rechallenge group (87.5%) and crossover to pembrolizumab group (76.2%) had no Grade 3 to 5 AEs. The most frequently reported Grade 3 to 5 AE in the pembrolizumab rechallenge group (in ≥0% of participants) were dysphagia and seizure. The most frequently reported Grade 3 to 5 AE was increased AST (in ≥3% of participants) in the crossover to pembrolizumab group [Table 14.3-30].

Figure 12-2
Rainfall Plot for Grade 3-5 Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 1% in One or More Treatment Groups)
(APaT Population)



Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adae]

12.1.3.3 Grade 3 to 5 Adverse Events Related to Study Intervention

The overall incidence of drug-related Grade 3 to 5 AEs was higher in the pembrolizumab group compared with the placebo group (17.2% vs 5.1%) [Table 12-5].

The most frequently reported drug-related Grade 3 to 5 AEs in the pembrolizumab group (in ≥1.0% of participants) were autoimmune hepatitis, rash, increased lipase, adrenal insufficiency, colitis, and diarrhea [Table 12-5]. These are known ADRs (or clinical manifestations of ADRs) for pembrolizumab.

Most drug-related Grade 3 to 5 AEs were Grade 3 in severity in both the pembrolizumab group (14.7%) and placebo group (4.7%), and none were Grade 5 [Table 14.3-27].

Table 12-5
Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	83	(17.2)	25	(5.1)
with no adverse events	400	(82.8)	461	(94.9)
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Rash	7	(1.4)	1	(0.2)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Diarrhoea	5	(1.0)	1	(0.2)
Lipase increased	5	(1.0)	8	(1.6)
Alanine aminotransferase increased	4	(0.8)	1	(0.2)
Amylase increased	3	(0.6)	2	(0.4)
Blood creatine phosphokinase increased	3	(0.6)	2	(0.4)
Pruritus	3	(0.6)	0	(0.0)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Rash maculo-papular	2	(0.4)	0	(0.0)
Rash pruritic	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Arthralgia	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Asthenia	1	(0.2)	0	(0.0)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood sodium decreased	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Decreased appetite	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Fatigue	1	(0.2)	1	(0.2)

Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)
Hypertension	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophosphataemia	1	(0.2)	2	(0.4)
Hypophysitis	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lip dry	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Polyarthritis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Transaminases increased	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)

Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.2 Serious Adverse Events and Other Clinically Meaningful Adverse Events

SAEs, interruptions/discontinuations due to AEs, and other clinically meaningful AE listings by participant are available in [16.2.7.1] [16.4].

12.2.1 Serious Adverse Events

12.2.1.1 Deaths Due to Adverse Events

No deaths due to a drug-related AE were reported in either treatment group. Six participants had AEs that resulted in death and considered unrelated to drug by the investigator: 1 participant (COVID-19 pneumonia) in the pembrolizumab group and 5 participants (COVID-19 pneumonia, pneumonia, lung neoplasm malignant, recurrent cancer, and completed suicide) in the placebo group. No new deaths due to AEs were reported in the pembrolizumab group since IA2 or IA3 [Table 12-6] [16.2.7.1.3].

Table 12-6
Participants With Adverse Events Resulting in Death
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	1	(0.2)	5	(1.0)
with no adverse events	482	(99.8)	481	(99.0)
Infections and infestations	**1**	**(0.2)**	**2**	**(0.4)**
COVID-19 pneumonia	1	(0.2)	1	(0.2)
Pneumonia	0	(0.0)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**2**	**(0.4)**
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Recurrent cancer	0	(0.0)	1	(0.2)
Psychiatric disorders	**0**	**(0.0)**	**1**	**(0.2)**
Completed suicide	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Recurrent Cancer: recurrence of disease under the study
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.2.1.2 Other Serious Adverse Events

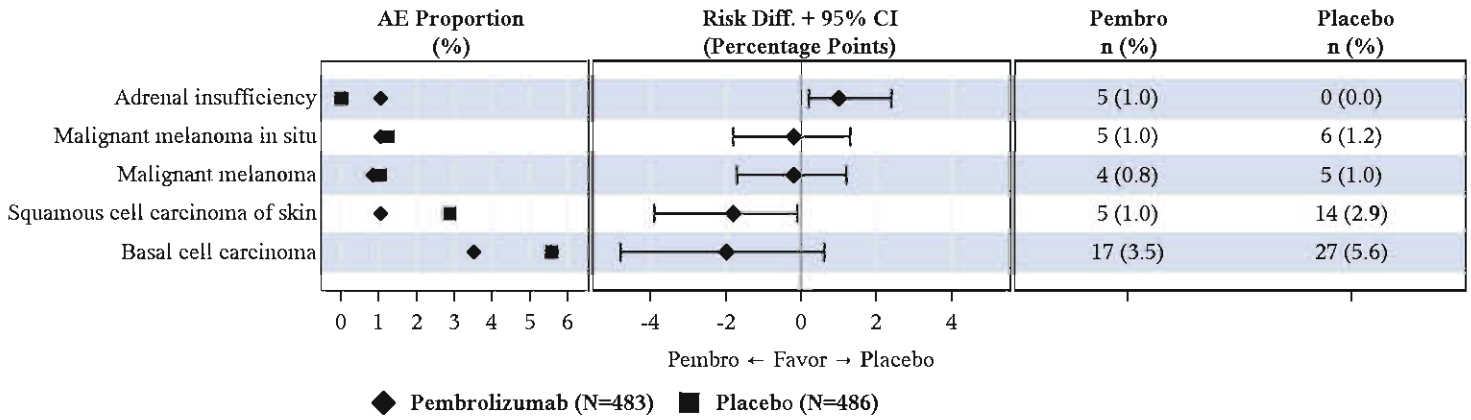
The overall incidence of SAEs was similar in the pembrolizumab group (21.3%) and placebo group (19.8%) [Table 14.3-37] through [Table 14.3-42].

The most frequently reported SAEs (in ≥1.0% of participants in either treatment group) were basal cell carcinoma, squamous cell carcinoma, adrenal insufficiency, malignant melanoma, and malignant melanoma in situ [Table 14.3-38] [Figure 12-3]. Secondary skin cancers are not unexpected in an adjuvant melanoma population where patients are at higher risk and are often under close surveillance for possible recurrence.

Serious drug-related AEs occurred in 10.1% of the pembrolizumab group and 2.3% of the placebo group [Table 14.3-43]

The SAEs reported in Part 2 of the study were consistent with the pembrolizumab group in Part 1.The overall incidence of SAEs was similar in the pembrolizumab rechallenge group (12.5%) and the crossover to pembrolizumab group (15.9%) [Table 14.3-39].

Figure 12-3
Rainfall Plot for Serious Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 1% in One or More Treatment Groups)
(APaT Population)



Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adae]

12.2.1.2.1 Intervention-related Serious Adverse Events

The overall incidence of drug-related SAEs was higher in the pembrolizumab group (10.1%) compared with the placebo group (2.3%) [Table 12-7].

The most frequently reported drug-related SAEs in the pembrolizumab group were adrenal insufficiency and colitis (reported in 5 and 4 participants, respectively). Both are known ADRs for pembrolizumab [Table 12-7].

A listing of participants with drug-related SAEs is provided in [16.2.7.1.1].

Table 12-7
Participants With Serious Drug-Related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	49	(10.1)	11	(2.3)
with no adverse events	434	(89.9)	475	(97.7)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Colitis	4	(0.8)	0	(0.0)
Autoimmune hepatitis	3	(0.6)	1	(0.2)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Diarrhoea	2	(0.4)	1	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Abscess soft tissue	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Cough	1	(0.2)	0	(0.0)
Decreased appetite	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Muscular weakness	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pneumonia	1	(0.2)	0	(0.0)

Participants With Serious Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pneumonitis	1	(0.2)	0	(0.0)
Sarcoidosis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Facial paralysis	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	1	(0.2)
Infusion site urticaria	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.2.2 Discontinuations and Interruptions of Study Intervention Due to Adverse Events

12.2.2.1 Adverse Events Leading to Study Intervention Discontinuation

The overall incidence of AEs that led to discontinuation of study intervention was higher in the pembrolizumab group (17.2%) compared with the placebo group (4.7%) [Table 14.3-45].

The overall incidence of drug-related AEs that led to discontinuation of study intervention was higher in the pembrolizumab group (15.9%) compared with the placebo group (2.5%) [Table 14.3-46] [Table 14.3-47].

Each PT for an AE that led to discontinuation of study intervention was reported for ≤1.2% of participants in each treatment group. The most frequently reported of these AEs were autoimmune hepatitis and colitis in the pembrolizumab group, and diarrhea and autoimmune hepatitis in the placebo group [Table 14.3-45]; these same AEs were reported as drug-related [Table 14.3-46]. Colitis and autoimmune hepatitis are known ADRs for pembrolizumab.

In Part 2 of the study, no participants in the pembrolizumab rechallenge group discontinued due to an AE; in contrast, 15.9% of participants in the crossover to pembrolizumab group discontinued treatment due to an AE [Table 14.3-6].

Guidance for treatment discontinuation in response to high toxicity grade events and recurrent events were provided in the study protocol [16.1.1].

A listing of participants with drug-related AEs that led to discontinuation of study intervention is provided in [16.2.7.1.2].

12.2.2.2 Adverse Events Leading to Study Intervention Interruption

The overall incidence of AEs that led to interruption of study intervention was similar in the pembrolizumab group (21.9%) and placebo group (16.7%) [Table 14.3-48].

The most frequently reported AEs resulting in study treatment interruption (in >1.0% of participants in either treatment group) were diarrhea, arthralgia, pyrexia, hyperthyroidism, and cough in the pembrolizumab group and pyrexia and diarrhea in the placebo group [Table 14.3-48].

The overall incidence of drug-related AEs that led to interruption of study treatment was higher in the pembrolizumab group (15.1%) compared with the placebo group (6.6%). The most frequently reported drug-related AEs resulting in treatment interruption (in ≥1.0% of participants in either treatment group) were arthralgia, diarrhea, and hyperthyroidism in the pembrolizumab group and diarrhea in the placebo group [Table 14.3-49].

12.2.3 Adverse Events of Special Interest

12.2.3.1 Overall Adverse Events of Special Interest

The overall nature and severity of AEOSI observed in the pembrolizumab group during the study were similar to the established safety profile for pembrolizumab monotherapy. No new indication-specific, immune-mediated AEOSI were associated with pembrolizumab. The AEOSI were manageable with standard medical care, including drug interruption and corticosteroids.

The overall incidence of AEOSI was higher in the pembrolizumab group compared with the placebo group (37.9% vs 9.5%) [Table 12-8] [Table 14.3-81]. Fewer than 10% of participants in the pembrolizumab group discontinued study intervention due to an AEOSI. In both treatment groups, no participant died due to an AEOSI [Table 12-8] [Table 14.3-55] through [Table 14.3-78]. Most AEOSI were Grade 1 or 2 in severity in both the pembrolizumab group (7.9% and 19.0%, respectively) and placebo group (4.5% and 3.7%, respectively) [Table 14.3-79] [Table 14.3-87] [Table 14.3-88].

The most frequently reported AEOSI (>10%) in the pembrolizumab group were hypothyroidism and hyperthyroidism [Table 12-9] [Table 12-8] [Table 14.3-81]. A listing of all participants with AEOSI is provided in [16.2.7.1.4].

In the pembrolizumab group, the median time to onset of participants' first AEOSI episode was 67.0 days. The median duration of AEOSI episodes in the pembrolizumab group was 109.0 days, with an average of 1.5 AEOSI episodes per participant [Table 14.3-82].

In the pembrolizumab group, use of systemic corticosteroids was reported for management of some or all episodes of AEOSI [Table 14.3-83] [Table 14.3-84] [Table 14.3-85], with the following exceptions: hyperthyroidism, infusion reactions, myocarditis, type 1 diabetes mellitus, and uveitis.

Narratives for participants in the pembrolizumab group who experienced AEOSI are presented in [16.2.7.2].

Among participants in the pembrolizumab group who had 1 or more AEOSI, most AEOSI were resolved (60.7%) or resolving (12.0%) at the time of the DCO. Unresolved AEOSI included myelitis, arthritis, pancreatitis, pneumonitis, hepatitis, and myasthenic syndrome; other unresolved AEOSI were endocrinopathies (eg, hypothyroidism, adrenal insufficiency, hypophysitis, thyroiditis and hyperthyroidism) that may require long-term hormone replacement therapy [Table 14.3-86].

In Part 2 of the study, no participants in the pembrolizumab rechallenge group had an AEOSI and 30.2% of participants in the crossover to pembrolizumab group had one or more AEOSI. Most AEOSI were Grade 1 or 2 in the crossover to pembrolizumab group [Table 14.3-80]; 4.8% discontinued study drug due to a drug-related AEOSI and 3.2% discontinued due to a serious drug-related AEOSI. There were no deaths due to an AEOSI [Table 14.3-51].

Table 12-8
Adverse Event Summary
AEOSI Overall
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
with no adverse event	300	(62.1)	440	(90.5)
with drug-relateda adverse events	176	(36.4)	33	(6.8)
with toxicity grade 3-5 adverse events	53	(11.0)	6	(1.2)
with toxicity grade 3-5 drug-related adverse events	52	(10.8)	4	(0.8)
with serious adverse events	38	(7.9)	4	(0.8)
with serious drug-related adverse events	36	(7.5)	3	(0.6)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	47	(9.7)	4	(0.8)
discontinued drug due to a drug-related adverse event	47	(9.7)	4	(0.8)
discontinued drug due to a serious adverse event	27	(5.6)	2	(0.4)
discontinued drug due to a serious drug-related adverse event	27	(5.6)	2	(0.4)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 12-9
Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
with no adverse events	300	(62.1)	440	(90.5)
Adrenal Insufficiency	**13**	**(2.7)**	**0**	**(0.0)**
Adrenal insufficiency	13	(2.7)	0	(0.0)
Arthritis	**2**	**(0.4)**	**2**	**(0.4)**
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Colitis	**20**	**(4.1)**	**5**	**(1.0)**
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	16	(3.3)	5	(1.0)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Hepatitis	**11**	**(2.3)**	**3**	**(0.6)**
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Hepatitis	3	(0.6)	1	(0.2)
Hyperthyroidism	**51**	**(10.6)**	**3**	**(0.6)**
Hyperthyroidism	51	(10.6)	3	(0.6)
Hypophysitis	**12**	**(2.5)**	**0**	**(0.0)**
Hypophysitis	7	(1.4)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Hypothyroidism	**83**	**(17.2)**	**18**	**(3.7)**
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Hypothyroidism	82	(17.0)	17	(3.5)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)
Infusion Reactions	**3**	**(0.6)**	**7**	**(1.4)**
Drug hypersensitivity	1	(0.2)	2	(0.4)
Hypersensitivity	0	(0.0)	1	(0.2)
Infusion related reaction	2	(0.4)	4	(0.8)

Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Myasthenic Syndrome	**2**	**(0.4)**	**0**	**(0.0)**
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis	**1**	**(0.2)**	**0**	**(0.0)**
Myelitis transverse	1	(0.2)	0	(0.0)
Myocarditis	**1**	**(0.2)**	**1**	**(0.2)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Myositis	**6**	**(1.2)**	**1**	**(0.2)**
Myopathy	2	(0.4)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Nephritis	**7**	**(1.4)**	**0**	**(0.0)**
Autoimmune nephritis	2	(0.4)	0	(0.0)
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Nephritis	3	(0.6)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Pancreatitis	**2**	**(0.4)**	**0**	**(0.0)**
Pancreatitis	2	(0.4)	0	(0.0)
Pneumonitis	**13**	**(2.7)**	**4**	**(0.8)**
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Sarcoidosis	**5**	**(1.0)**	**0**	**(0.0)**
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Sarcoidosis	3	(0.6)	0	(0.0)
Severe Skin Reactions	**15**	**(3.1)**	**3**	**(0.6)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Erythema multiforme	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Severe Skin Reactions	**15**	**(3.1)**	**3**	**(0.6)**
Pruritus	3	(0.6)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Thyroiditis	**8**	**(1.7)**	**2**	**(0.4)**
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Thyroiditis	2	(0.4)	1	(0.2)
Type 1 Diabetes Mellitus	**2**	**(0.4)**	**0**	**(0.0)**
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Uveitis	**1**	**(0.2)**	**0**	**(0.0)**
Iridocyclitis	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

12.2.4 Participant Narratives

A list of participants for whom narratives were written (including events qualifying the participants for a narrative), conventions for preparing narratives and individual participant narratives (with links to corresponding CRFs, if applicable) are presented in [16.2.7.2] [16.3].

Participant narratives used data from the datasets in [16.4].

12.3 Clinical Laboratory Evaluation

12.3.1 Individual Laboratory Measurements by Participant

Listings of laboratory measurements by participant are included in [16.2.8] [16.4].

12.3.2 Evaluation of Laboratory Values

12.3.2.1 Laboratory Values Over Time

Changes over time from baseline laboratory measurements were generally representative of the preexisting, underlying disease state of participants and/or were consistent with the previously established safety profile of pembrolizumab.

Most changes in toxicity grade from baseline to the worst postbaseline value were changes to toxicity Grades ≤2 [Table 14.4-1] [Table 14.4-2]. Shifts to a highest postbaseline value of Grades 3 and 4 were reported for the following laboratory test results in >1% of participants in the pembrolizumab group: increased triacylglycerol lipase (5.0%), decreased phosphate (4.5%), decreased glucose (3.3%), increased glucose (3.3%), decreased lymphocytes (3.1%), increased GGT (3.2%), increased ALT (2.9%), decreased potassium (2.3%), increased potassium (2.3%), increased AST (1.7%), decreased sodium (1.7%), and increased sodium (1.7%) [Table 14.4-2].

12.3.2.2 Specific Clinically Meaningful Laboratory Abnormalities

No participant met the predetermined criteria for potential DILI (ALT or AST ≥3 × ULN, bilirubin ≥2 × ULN, and ALP <2 × ULN) [Table 14.4-3].

The percentages of participants who had at least 1 postbaseline abnormality in ALT or AST (eg, toxicity Grade 1, 2, 3, or 4) were 28.7% and 25.2%, in the pembrolizumab group, respectively, compared with 15.2% and 13.8% in the placebo group, respectively [Table 14.4-2].

Listings of participants with liver function laboratory findings that met predetermined criteria and participant liver function laboratory values are provided in [16.2.8.1] and [16.2.8.2], respectively.

12.4 Vital Signs, Physical Examinations and Other Observations Related to Safety

There were no clinically meaningful differences over time in vital signs between the 2 treatment groups [Table 14.5-1].

Listing(s) of observations by participant are provided in [16.2.8] [16.4].

12.5 Safety Results Summary

- The overall frequency and type of adverse events (AEs) reported in KEYNOTE-716 at IA4 were generally consistent with prior interim analyses and the established safety profile of pembrolizumab monotherapy.
- As expected for a comparison of active treatment versus placebo, higher incidences of AEs in the following AE categories were reported in the pembrolizumab group: drug-related AEs, Grade 3 to 5 AEs, drug-related Grade 3 to 5 AEs, drug-related SAEs, and AEs and drug-related AEs leading to discontinuation of study intervention.

- The most frequently reported AEs in the pembrolizumab group (incidence ≥15%) were fatigue, diarrhea, pruritus, arthralgia, rash, headache, and hypothyroidism.
- The overall nature and severity of the adverse events of special interest (AEOSI) were generally similar to the established pembrolizumab monotherapy safety profile. Most AEOSI were Grade 1 or 2 in severity and were generally manageable with treatment interruption, treatment discontinuation, and/or concomitant treatment with corticosteroids and hormone replacement therapy.
- No deaths due to a drug-related AE were reported in either treatment group. One participant in the pembrolizumab group and 5 participants in the placebo group died due to nondrug-related AEs.
- Overall, the most frequent AEs in Part 2 of the study were consistent with the AEs reported in the pembrolizumab group in Part 1.

13 CONCLUSIONS

Efficacy

- KEYNOTE-716 results confirm pembrolizumab is an effective adjuvant treatment that prolongs DMFS and RFS for the adjuvant treatment of adult and pediatric (12 years and older) patients with high-risk Stage II melanoma.
- The final DMFS results at IA4 demonstrates that pembrolizumab continues to provide clinically meaningful improvement compared with placebo with longer follow-up.
- DMFS results by subgroup are generally consistent with the overall population.
- Data from subsequent RFS analyses (at IA4) are supportive and demonstrate that pembrolizumab continues to provide a clinically meaningful improvement compared with placebo with longer follow-up.

Safety

- The KEYNOTE-716 safety analyses are consistent with the established safety profile of pembrolizumab and the safety profile observed in the previous IA analyses. The results further confirm that pembrolizumab has a tolerable and manageable safety profile in patients with high-risk Stage II melanoma following complete resection in the adjuvant setting. The incidence of deaths and treatment discontinuations in the study due to AEs is low and similar between the 2 groups.
- The types and severity of AEOSI are consistent with the established pembrolizumab monotherapy safety profile. AEOSI were generally manageable with standard medical care, drug discontinuation/interruption, or corticosteroid use as appropriate.
- No new safety concerns were identified for pembrolizumab based on the IA4 safety data in the KEYNOTE-716 study.

14 SUPPLEMENTAL TABLES AND/OR FIGURES

14.1 Participant Disposition, Protocol Deviations, Baseline Characteristics, Medical History, and Drug Exposure

14.1.1 Pediatric Participant Disposition, Baseline Characteristics, and Drug Exposure

Table 14.1-1
Disposition of Participant
(ITT Population - Pediatric Patients)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participant in population	1		1		2	
Trial Disposition						
Started	1		1		2	
Participants Ongoing	1	(100.0)	1	(100.0)	2	(100.0)
Participant Study Medication Disposition						
Completed	1	(100.0)	1	(100.0)	2	(100.0)

If the overall count of participant is calculated and displayed within a section in the first row, then it is used as the denominator for the percentage calculation. Otherwise, participant in population is used as the denominator for the percentage calculation.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

Table 14.1-2
Study Population - Pediatric Patients

	Pembrolizumab	Placebo	Total
Number of Participants Screened			2
Number of Participants Randomized (Planned Treatment) (ITT)	1	1	2
Number of Participants Received Treatment in Part 1(Actual Treatment) (APaT)	1	1	2
Number of Participants Randomized and Did not Receive Treatment	0	0	0
Number of Participants Received Treatment in Part 2(Actual Part 1 Treatment) (APaT)	0	0	0
Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl]

Table 14.1-3
Participant Characteristics
(ITT Population - Pediatric Patients)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	1		1		2	
Sex						
[redacted]	1	(100.0)	1	(100.0)	2	(100.0)
Age (Years)						
12 - 17	1	(100.0)	1	(100.0)	2	(100.0)
18 - 64	0	(0.0)	0	(0.0)	0	(0.0)
≥ 65	0	(0.0)	0	(0.0)	0	(0.0)
Mean	[redacted]					
SD						
Median						
Range						
Race						
White	1	(100.0)	1	(100.0)	2	(100.0)
Ethnicity						
Not Hispanic Or Latino	1	(100.0)	1	(100.0)	2	(100.0)
Geographic Region						
Non-US	1	(100.0)	1	(100.0)	2	(100.0)
ECOG						
Not Applicable	1	(100.0)	1	(100.0)	2	(100.0)
KPS Status						
100 - Normal. No complaints. No evidence of disease.	1	(100.0)	1	(100.0)	2	(100.0)
T-Stage						
T3b	0	(0.0)	1	(100.0)	1	(50.0)
T4a	1	(100.0)	0	(0.0)	1	(50.0)
Nodal Involvement						
N0	1	(100.0)	1	(100.0)	2	(100.0)
Metastatic Staging						

Redacted under section 40 of the FOI Act

Redacted under section 40 of the FOI Act

Participant Characteristics
(ITT Population - Pediatric Patients)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
M0	1	(100.0)	1	(100.0)	2	(100.0)
Overall Cancer Stage						
IIB	1	(100.0)	1	(100.0)	2	(100.0)
Stratification						
Pediatric Age 12 to 17	1	(100.0)	1	(100.0)	2	(100.0)
ECOG is not applicable for pediatric participants. KPS is not applicable for adult participants. Database Cutoff Date: 04JAN2023.						

Source: [P716V04MK3475: adam-adsl]

Table 14.1-4
Summary of Drug Exposure
(APaT Population - Pediatric Patients)

	Pembrolizumab (N=1)	Placebo (N=1)	Total (N=2)
Number of Days on Therapy			
Mean	356.0	356.0	356.0
Median	356.0	356.0	356.0
SD	NA	NA	0.00
Range	356.0 to 356.0	356.0 to 356.0	356.0 to 356.0
Number of Administrations			
Mean	17.0	17.0	17.0
Median	17.0	17.0	17.0
SD	NA	NA	0.00
Range	17.0 to 17.0	17.0 to 17.0	17.0 to 17.0
Number of Days on Therapy is calculated as last dose date - first dose date +1. Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl; adexsum]

14.1.2 Participant Disposition

Table 14.1-5
Disposition of Participant
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participant in population	487		489		976	
Trial Disposition						
Discontinued	59	(12.1)	62	(12.7)	121	(12.4)
Death	38	(7.8)	39	(8.0)	77	(7.9)
Associated with COVID-19	3	(0.6)	1	(0.2)	4	(0.4)
Lost To Follow-Up	2	(0.4)	3	(0.6)	5	(0.5)
Not Associated with COVID-19, No Further Information	2	(0.4)	3	(0.6)	5	(0.5)
Physician Decision	1	(0.2)	3	(0.6)	4	(0.4)
Not Associated with COVID-19, No Further Information	1	(0.2)	3	(0.6)	4	(0.4)
Withdrawal By Subject	18	(3.7)	17	(3.5)	35	(3.6)
Associated with COVID-19, No Further Information	1	(0.2)	0	(0.0)	1	(0.1)
Not Associated with COVID-19, No Further Information	15	(3.1)	14	(2.9)	29	(3.0)
Not Associated with COVID-19, Subsequently Died	2	(0.4)	3	(0.6)	5	(0.5)
Participants Ongoing	428	(87.9)	427	(87.3)	855	(87.6)
Participant Study Medication Disposition in Part 1						
Started	483		486		969	
Completed	320	(66.3)	367	(75.5)	687	(70.9)
Discontinued	163	(33.7)	119	(24.5)	282	(29.1)
Adverse Event	85	(17.6)	24	(4.9)	109	(11.2)
Associated with COVID-19	1	(0.2)	1	(0.2)	2	(0.2)
Lost To Follow-Up	0	(0.0)	1	(0.2)	1	(0.1)
Non-Compliance With Study Drug	0	(0.0)	1	(0.2)	1	(0.1)
Physician Decision	10	(2.1)	4	(0.8)	14	(1.4)
Associated with COVID-19	0	(0.0)	2	(0.4)	2	(0.2)
Protocol Violation	4	(0.8)	1	(0.2)	5	(0.5)
Relapse/Recurrence	24	(5.0)	61	(12.6)	85	(8.8)
Associated with COVID-19	0	(0.0)	1	(0.2)	1	(0.1)
Withdrawal By Subject	40	(8.3)	27	(5.6)	67	(6.9)
Associated with COVID-19	6	(1.2)	7	(1.4)	13	(1.3)
Participant Study Medication Disposition in Part 2						
Started	8		63		71	

Disposition of Participant
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participant Study Medication Disposition in Part 2						
Completed	1	(12.5)	20	(31.7)	21	(29.6)
Discontinued	2	(25.0)	30	(47.6)	32	(45.1)
Adverse Event	0	(0.0)	10	(15.9)	10	(14.1)
Physician Decision	0	(0.0)	1	(1.6)	1	(1.4)
Progressive Disease	2	(25.0)	7	(11.1)	9	(12.7)
Relapse/Recurrence	0	(0.0)	9	(14.3)	9	(12.7)
Withdrawal By Subject	0	(0.0)	3	(4.8)	3	(4.2)
Participants Ongoing	5	(62.5)	13	(20.6)	18	(25.4)

If the overall count of participant is calculated and displayed within a section in the first row, then it is used as the denominator for the percentage calculation. Otherwise, participant in population is used as the denominator for the percentage calculation.

Trial Disposition includes information from Part 1 and Part 2, where each participant is counted once for trial disposition.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

Table 14.1-6
Disposition of Participants Not Randomized

	n (%)
Not Randomized	206
Screen Failure	206 (100.0)
Database Cutoff Date: 04JAN2023.	

Source: [P716V04MK3475: adam-adsl]

Table 14.1-7
Summary of Non-Randomized Participants Who Did Not Meet Inclusion Criteria or Did Meet Exclusion Criteria

		n	(%)
	Non-randomized participants	206	
	Non-randomized participants who did not meet inclusion criteria or did meet exclusion criteria	206	
Code	**Inclusion Criteria**		
IN09_01	The participant (or legally acceptable representative if applicable) provides written informed consent/assent for the study and agrees to DMFS and OS data collection until these study endpoints are reached.	46	(22.3)
IN01_01	Male/female participants who are ≥12 years of age on the day of signing informed consent/assent (unlesslocal regulations and/or institutional policies do not allow for participants <18 years of age to participate; for those sites, the eligible population is ≥18 years of age) withsurgically resected and histologically/pathologicallyconfirmed new diagnosis of Stage IIB or IICcutaneous melanoma per AJCC 8th edition guidelines. Note: Participants must have T stage of T3b, T4a, or T4b (Table 3) with pathologically confirmed negative SLNbiopsy, and no evidence of regional (N0) or distant metastatic disease (M0)per AJCC 8th edition guidelines (Appendix 11). Surgical considerations can be found in Appendix10.	31	(15.0)
IN04_01	Have no evidence of metastatic disease on imaging as determined by investigator assessment. All suspicious lesions amenable to biopsy should be confirmed negative for malignancy.	30	(14.6)
IN09_00	The participant (or legally acceptable representative if applicable) provides written informed consent/assent for the study and agrees to DMFS and OS data collection until these study endpoints are reached.	21	(10.2)
IN04_00	Have no evidence of metastatic disease on imaging as determined by investigator assessment. All suspicious lesions amenable to biopsy should be confirmed negative for malignancy.	15	(7.3)
IN01_00	Male/female participants who are at least 12 years of age on the day of signing informed consent/assent with surgically resected and histologically/pathologically confirmed new diagnosis of Stage IIB or IIC cutaneous melanoma per AJCC 8th edition guidelines.Note: Participants must have T stage of T3b, T4a, or T4b (Table 3) with pathologically confirmed negative sentinel lymph node biopsy, and no evidence of regional (N0) or distant metastatic disease (M0) per AJCC 8th edition guidelines (Appendix 11). Surgical considerations can be found in Appendix 10.	12	(5.8)

Summary of Non-Randomized Participants Who Did Not Meet Inclusion Criteria or Did Meet Exclusion Criteria

		n	(%)
IN03_01	No more than 12weeks may elapse between finalsurgical resection and randomization. Treatment should startonly after complete wound healingfromthe surgery. If there is a delay of 1to 7 days exceeding 12weeks due to unforeseen circumstances, the eligibility should be discussed with the Sponsorand the decision documented. A delay of 1to 7 days for screening imaging requirementswill be allowed if sponsor has allowed 1week extension between surgical resection and randomization. Note: Final surgical resection is defined in this protocol as complete resection of melanoma and a SLN biopsy. If the wide excision is followed by the SLN biopsy (ie, they are not performed at the same time), no more than 12 weeks may elapse between the 2 surgical procedures. If a second wide excision needs to be completed after SLN biopsy, this date will be used to calculate final surgical resection date.	10	(4.9)
IN03_00	No more than 12 weeks may elapse between full surgical resection and first study treatment. Treatment should start only after complete wound healing from the surgery. If there is a delay of 1-7 days exceeding 12 weeks due to extreme unforeseen circumstances, the eligibility should be discussed with the Sponsor and the decision documented.	5	(2.4)
IN10_00	The participant provides consent/assent for future biomedical research. However, the participant may take part in the main study without participating in future biomedical research.	4	(1.9)
IN11_00	Have adequate organ function as defined in Table 1. Specimens must be collected within 10 days prior to the start of study treatment.	4	(1.9)
IN11_01	Have adequate organ function as defined in Table 1. Specimens must be collected within 10 days prior to the start of study treatment.	4	(1.9)
IN10_01	The participant provides consent/assent for future biomedical research. However, the participant may take part in the main study without participating in future biomedical research.	1	(0.5)
Code	**Exclusion Criteria**		
EX16_01	Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the participants participation for the full duration of the study, or is not in the best interest of the participant to participate, in the opinion of the treating investigator.	12	(5.8)

Summary of Non-Randomized Participants Who Did Not Meet Inclusion Criteria or Did Meet Exclusion Criteria

		n	(%)
EX01_00	Has a known additional malignancy that is progressing or has required active antineoplastic therapy (including hormonal) or surgery treatment within the past 5 years. Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, non-ulcerated primary melanoma <1 mm in depth with no nodal involvement, or carcinoma in situ (eg, breast carcinoma, cervical cancer in situ) that have undergone potentially curative therapy are not excluded.	5	(2.4)
EX01_01	Has a known additional malignancy that is progressing or has required active antineoplastic therapy (including hormonal)within the past 5 years. Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinomain situ (eg, breast carcinoma, cervical cancer in situ) that have undergone potentially curative therapy are not excluded. Note: Participants with a history of non ulcerated cutaneous/acral primary melanoma <1 mm in depth with no nodal involvement are allowed in this trial. Participants with any previous melanoma that was ulcerated, ≥1 mm in depth, with nodal involvement, metastasis, or was treated beyond surgical resection (for example, radiation therapy) are not eligible for this trial. Participants with synchronous melanomas where lesions not under study are not ulcerated and <1 mm in depth are allowed on the study. Participants with a history of mucosal or uveal melanoma are excluded from thistrial even if diagnosis and treatment were completed >5 years ago.	5	(2.4)
EX16_00	Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the participants participation for the full duration of the study, or is not in the best interest of the participant to participate, in the opinion of the treating investigator.	4	(1.9)
EX03_01	If participant received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment.	2	(1.0)
EX14_00	Has a known history of Hepatitis B (defined as Hepatitis B surface antigen reactive) or known active Hepatitis C virus (defined as Hepatitis C virus RNA [qualitative] is detected) infection. No testing for Hepatitis B and Hepatitis C is required unless mandated by local health authority. Note: For Germany, Hepatitis B and C testing is mandatory (Appendix 6).	2	(1.0)
EX15_01	Has a history of active tuberculosis (Bacillus tuberculosis). Note: For Germany and the UK, Tuberculosis testing is mandatory (Appendix 6).	2	(1.0)

Summary of Non-Randomized Participants Who Did Not Meet Inclusion Criteria or Did Meet Exclusion Criteria

		n	(%)
EX10_00	Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.	1	(0.5)
EX10_01	Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.	1	(0.5)
EX11_01	Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis.	1	(0.5)
EX17_01	Has a known psychiatric or substance abuse disorder that would interfere with the participants ability to cooperate with the requirements of the study.	1	(0.5)

Although a participant may appear for two or more trial entry criteria in this report, the participant is counted only once in the overall total.
For the calculation of percentage, the denominator is the number of non-randomized participants who did not meet inclusion criteria or did meet exclusion criteria.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl] [P716V04MK3475: sdtm-ie]

Table 14.1-8
Participants in Crossover/re-treatment with Pembrolizumab in Part 2
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
Participants Crossover/re-treat in Part 2	8	(1.6)	63	(12.9)	71	(7.3)
Database Cutoff Date: 04JAN2023						

Source: [P716V04MK3475: adam-adsl]

Table 14.1-9
Participants Randomized by Investigator and Treatment Group
(ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
AUS		[redacted]	**46**	**35**	**81**
	3475-716-0851		12	10	22
	3475-716-0852		8	8	16
	3475-716-0853		3	7	10
	3475-716-0856		10	3	13
	3475-716-0857		5	2	7
	3475-716-0858		3	1	4
	3475-716-0859		4	1	5
	3475-716-0860		0	1	1
	3475-716-0861		1	2	3
BEL			**17**	**9**	**26**
	3475-716-0251		6	2	8
	3475-716-0252		6	3	9
	3475-716-0256		3	2	5
	3475-716-0259		2	2	4
BRA			**20**	**10**	**30**
	3475-716-0151		4	1	5
	3475-716-0154		4	1	5
	3475-716-0155		0	1	1
	3475-716-0156		1	0	1
	3475-716-0158		2	4	6

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
BRA		[redacted]	**20**	**10**	**30**
	3475-716-0160		1	1	2
	3475-716-0161		1	1	2
	3475-716-0162		3	0	3
	3475-716-0164		4	1	5
CAN			**27**	**26**	**53**
	3475-716-0053		2	2	4
	3475-716-0054		2	2	4
	3475-716-0055		1	1	2
	3475-716-0056		1	2	3
	3475-716-0057		4	2	6
	3475-716-0058		3	2	5
	3475-716-0059		5	4	9
	3475-716-0060		3	5	8
	3475-716-0061		4	5	9
	3475-716-0062		2	1	3
CHE			**23**	**22**	**45**
	3475-716-0551		7	6	13
	3475-716-0552		1	4	5
	3475-716-0553		6	4	10
	3475-716-0554		0	1	1
	3475-716-0555		3	1	4

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
CHE		[redacted]	**23**	**22**	**45**
	3475-716-0556		4	1	5
	3475-716-0557		1	2	3
	3475-716-0558		1	2	3
	3475-716-0559		0	1	1
CHL			**21**	**11**	**32**
	3475-716-0200		3	2	5
	3475-716-0201		0	1	1
	3475-716-0203		6	1	7
	3475-716-0204		5	1	6
	3475-716-0207		7	6	13
DEU			**34**	**48**	**82**
	3475-716-0351		2	4	6
	3475-716-0352		2	6	8
	3475-716-0353		2	2	4
	3475-716-0354		3	3	6
	3475-716-0355		5	3	8
	3475-716-0356		0	2	2
	3475-716-0357		0	4	4
	3475-716-0358		8	6	14
	3475-716-0359		2	4	6
	3475-716-0360		1	5	6

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
DEU		[redacted]	**34**	**48**	**82**
	3475-716-0361		9	9	18
ESP			**29**	**39**	**68**
	3475-716-0451		4	7	11
	3475-716-0452		1	5	6
	3475-716-0454		6	3	9
	3475-716-0455		11	11	22
	3475-716-0456		5	6	11
	3475-716-0457		2	7	9
FRA			**42**	**45**	**87**
	3475-716-0300		4	5	9
	3475-716-0301		4	2	6
	3475-716-0302		5	6	11
	3475-716-0303		4	2	6
	3475-716-0304		0	2	2
	3475-716-0305		3	4	7
	3475-716-0306		2	8	10
	3475-716-0312		2	1	3
	3475-716-0316		6	7	13

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
FRA		[redacted]	**42**	**45**	**87**
	3475-716-0317		4	3	7
	3475-716-0320		3	1	4
	3475-716-0321		4	3	7
	3475-716-0322		1	1	2
GBR			**8**	**10**	**18**
	3475-716-0600		2	2	4
	3475-716-0601		0	4	4
	3475-716-0604		4	2	6
	3475-716-0612		1	1	2
	3475-716-0613		1	1	2
ISR			**22**	**22**	**44**
	3475-716-0651		3	7	10
	3475-716-0652		7	6	13
	3475-716-0653		4	2	6
	3475-716-0654		4	4	8
	3475-716-0655		4	1	5
	3475-716-0656		0	2	2
ITA			**64**	**91**	**155**
	3475-716-0400		9	8	17
	3475-716-0401		4	3	7
	3475-716-0402		10	7	17
	3475-716-0403		2	4	6
	3475-716-0404		9	19	28

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
ITA		[redacted]	**64**	**91**	**155**
	3475-716-0405		7	10	17
	3475-716-0406		4	10	14
	3475-716-0407		9	13	22
	3475-716-0408		10	17	27
JPN			**2**	**1**	**3**
	3475-716-0910		2	1	3
POL			**34**	**39**	**73**
	3475-716-0751		13	17	30
	3475-716-0753		9	14	23
	3475-716-0754		3	2	5
	3475-716-0765		1	3	4
	3475-716-0769		4	1	5
	3475-716-0773		4	2	6
USA			**95**	**80**	**175**
	3475-716-0001		2	1	3
	3475-716-0006		1	0	1
	3475-716-0007		2	1	3
	3475-716-0008		1	3	4
	3475-716-0014		4	6	10

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
USA		[redacted]	**95**	**80**	**175**
	3475-716-0016		1	1	2
	3475-716-0019		2	1	3
	3475-716-0022		4	4	8
	3475-716-0024		0	1	1
	3475-716-0025		3	1	4
	3475-716-0026		1	3	4
	3475-716-0027		4	7	11
	3475-716-0029		5	4	9
	3475-716-0030		1	0	1
	3475-716-0032		1	3	4
	3475-716-0035		0	2	2
	3475-716-0042		0	1	1
	3475-716-0043		6	5	11
	3475-716-0044		3	3	6
	3475-716-0046		3	1	4
	3475-716-0047		4	5	9
	3475-716-0115		5	2	7
	3475-716-0116		1	1	2
	3475-716-0121		5	4	9
	3475-716-0124		6	2	8
	3475-716-0126		2	0	2
	3475-716-0130		2	0	2

Participants Randomized by Investigator and Treatment Group (ITT Population)

Location	Trial-Site	Investigator Name	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
USA		[redacted]	**95**	**80**	**175**
	3475-716-0131		8	3	11
	3475-716-0134		4	6	10
	3475-716-0135		4	4	8
	3475-716-0137		7	2	9
	3475-716-0141		0	1	1
	3475-716-0142		1	0	1
	3475-716-0143		2	2	4
ZAF			**3**	**1**	**4**
	3475-716-0801		0	1	1
	3475-716-0803		2	0	2
	3475-716-0806		1	0	1

N = Number of participants randomized in the treatment group.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

14.1.3 Protocol Deviations

Table 14.1-10
Summary of Important Protocol Deviations
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
with one or more important protocol deviations	28	(5.7)	29	(5.9)	57	(5.8)
with no important protocol deviations	459	(94.3)	460	(94.1)	919	(94.2)
Discontinuation Criteria	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Participant developed trial specific discontinuation criteria but was not discontinued from the trial.	1	(0.2)	1	(0.2)	2	(0.2)
Inclusion/ Exclusion Criteria	**7**	**(1.4)**	**7**	**(1.4)**	**14**	**(1.4)**
Participant did not meet inclusion criteria 01. (Male/female participants who are ≥ 12 years of age on the day of signing informed consent/assent [unless local regulations and/or institutional policies do not allow for participants < 18 years of age to participate; for those sites, the eligible population is ≥ 18 years of age] with surgically resected and histologically/pathologically confirmed new diagnosis of Stage IIB or IIC cutaneous melanoma per AJCC 8th edition guidelines.)	4	(0.8)	3	(0.6)	7	(0.7)
Participants entered into the trial, i.e. progressed beyond screening, who did not meet key inclusion/exclusion criteria.	3	(0.6)	4	(0.8)	7	(0.7)
Informed Consent	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Participant had no documented initial consent to enter the trial.	1	(0.2)	1	(0.2)	2	(0.2)

Summary of Important Protocol Deviations
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Prohibited Medications	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Antineoplastic systemic chemotherapy, biologic therapy, immunotherapy, other investigational agents given while on treatment or before study entry during screening (unless allowed per protocol).	0	(0.0)	1	(0.2)	1	(0.1)
Safety Reporting	**12**	**(2.5)**	**14**	**(2.9)**	**26**	**(2.7)**
Participant had a reportable Safety Event and/or follow up Safety Event information that was not reported per the timelines outlined in the protocol.	12	(2.5)	14	(2.9)	26	(2.7)
Study Intervention	**7**	**(1.4)**	**6**	**(1.2)**	**13**	**(1.3)**
Participant was administered improperly stored study intervention that was deemed unacceptable for use.	5	(1.0)	6	(1.2)	11	(1.1)
Participant was dispensed study intervention other than what was assigned in the allocation schedule, i.e. incorrect medication or potential cross-treatment.	2	(0.4)	0	(0.0)	2	(0.2)

Every participant is counted a single time for each applicable row and column.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl] [P716V04MK3475: sdtm-dv; suppdv]

Table 14.1-11
Summary of Important Protocol Deviations Considered to be Clinically Important (ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
with one or more clinically important protocol deviations	14	(2.9)	19	(3.9)	33	(3.4)
with no clinically important protocol deviations	473	(97.1)	470	(96.1)	943	(96.6)
Discontinuation Criteria	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Participant developed trial specific discontinuation criteria but was not discontinued from the trial.	1	(0.2)	0	(0.0)	1	(0.1)
Inclusion/ Exclusion Criteria	**7**	**(1.4)**	**7**	**(1.4)**	**14**	**(1.4)**
Participant did not meet inclusion criteria 01. (Male/female participants who are ≥ 12 years of age on the day of signing informed consent/assent [unless local regulations and/or institutional policies do not allow for participants < 18 years of age to participate; for those sites, the eligible population is ≥ 18 years of age] with surgically resected and histologically/pathologically confirmed new diagnosis of Stage IIB or IIC cutaneous melanoma per AJCC 8th edition guidelines.)	4	(0.8)	3	(0.6)	7	(0.7)
Participants entered into the trial, i.e. progressed beyond screening, who did not meet key inclusion/exclusion criteria.	3	(0.6)	4	(0.8)	7	(0.7)
Safety Reporting	**4**	**(0.8)**	**12**	**(2.5)**	**16**	**(1.6)**
Participant had a reportable Safety Event and/or follow up Safety Event information that was not reported per the timelines outlined in the protocol.	4	(0.8)	12	(2.5)	16	(1.6)
Study Intervention	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Participant was dispensed study intervention other than what was assigned in the allocation schedule, i.e. incorrect medication or potential cross-treatment.	2	(0.4)	0	(0.0)	2	(0.2)

Every participant is counted a single time for each applicable row and column.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl] [P716V04MK3475: sdtm-dv; suppdv]

Table 14.1-12
Accounting of Selected Protocol Deviations Associated With COVID-19
in Part 1 of Study
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
Subjects with ≥1 Dose deviation	**53**	**(10.9)**	**61**	**(12.5)**	**114**	**(11.7)**
≥1 Dose Missed	7	(1.4)	7	(1.4)	14	(1.4)
≥1 Dose Delayed	48	(9.9)	55	(11.2)	103	(10.6)
≥1 Dose Early	1	(0.2)	0	(0.0)	1	(0.1)
Subjects with ≥1 Imaging Scan deviation	**43**	**(8.8)**	**45**	**(9.2)**	**88**	**(9.0)**
≥1 Imaging Scan Missed	8	(1.6)	16	(3.3)	24	(2.5)
≥1 Imaging Scan Delayed	25	(5.1)	22	(4.5)	47	(4.8)
≥1 Imaging Scan Early	9	(1.8)	8	(1.6)	17	(1.7)
≥1 Imaging Scan Other	1	(0.2)	1	(0.2)	2	(0.2)
Subjects with ≥1 Safety Assessment deviation	**138**	**(28.3)**	**129**	**(26.4)**	**267**	**(27.4)**
≥1 Safety Assessment Missed	82	(16.8)	75	(15.3)	157	(16.1)
≥1 Safety Assessment Delayed	70	(14.4)	62	(12.7)	132	(13.5)
≥1 Safety Assessment Early	3	(0.6)	5	(1.0)	8	(0.8)
≥1 Safety Assessment Other	2	(0.4)	2	(0.4)	4	(0.4)

Database Cutoff Date: 04JAN2023.

This table reflects all protocol deviations reported as associated with COVID-19 that are deemed to have the potential to impact interpretation of study results.

Each block of rows (i.e., within horizontal grid lines) reflects deviations recorded according to the bolded text (e.g., visit, dose). Impacts of COVID-19 counted in the blocks of rows subsequent to visit deviations may or may not also be counted within the block of rows for visit deviations, and vice versa, depending on whether the impacts were reported both as visit deviations and as other deviations.

Source: [P716V04MK3475: adam-adsl; adpdev2]

14.1.4 Data Sets Analyzed

Table 14.1-13
Study Population

	Pembrolizumab	Placebo	Total
Number of Participants Screened			1182
Number of Participants Randomized (Planned Treatment) (ITT)	487	489	976
Number of Participants Received Treatment in Part 1(Actual Treatment) (APaT)	483	486	969
Number of Participants Randomized and Did not Receive Treatment	4	3	7
Number of Participants Received Treatment in Part 2(Actual Part 1 Treatment) (APaT)	8	63	71
Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl]

14.1.5 Demographic and Other Baseline Characteristics

Table 14.1-14
Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
Sex						
Male	300	(61.6)	289	(59.1)	589	(60.3)
Female	187	(38.4)	200	(40.9)	387	(39.7)
Age (Years)						
12 - 17	1	(0.2)	1	(0.2)	2	(0.2)
18 - 64	302	(62.0)	294	(60.1)	596	(61.1)
≥ 65	184	(37.8)	194	(39.7)	378	(38.7)
Mean	59.0		59.6		59.3	
SD	12.6		13.3		12.9	
Median	60.0		61.0		61.0	
Range	[redacted] to 84		[redacted] to 87		16 to 87	
Race						
American Indian Or Alaska Native	1	(0.2)	0	(0.0)	1	(0.1)
Asian	4	(0.8)	1	(0.2)	5	(0.5)
Black Or African American	4	(0.8)	4	(0.8)	8	(0.8)
Multiple	1	(0.2)	0	(0.0)	1	(0.1)
Black Or African American White	1	(0.2)	0	(0.0)	1	(0.1)
White	435	(89.3)	439	(89.8)	874	(89.5)
Missing	42	(8.6)	45	(9.2)	87	(8.9)
Ethnicity						
Hispanic Or Latino	44	(9.0)	24	(4.9)	68	(7.0)
Not Hispanic Or Latino	395	(81.1)	415	(84.9)	810	(83.0)
Not Reported	42	(8.6)	45	(9.2)	87	(8.9)
Unknown	6	(1.2)	5	(1.0)	11	(1.1)
Geographic Region						
US	95	(19.5)	80	(16.4)	175	(17.9)
Non-US	392	(80.5)	409	(83.6)	801	(82.1)
ECOG						
0	454	(93.2)	452	(92.4)	906	(92.8)
1	32	(6.6)	35	(7.2)	67	(6.9)
2	0	(0.0)	1	(0.2)	1	(0.1)

Redacted under section 40 of the FOI Act

Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Not Applicable	1	(0.2)	1	(0.2)	2	(0.2)
KPS Status						
100 - Normal. No complaints. No evidence of disease.	1	(0.2)	1	(0.2)	2	(0.2)
Not Applicable	486	(99.8)	488	(99.8)	974	(99.8)
T-Stage						
T3a	2	(0.4)	0	(0.0)	2	(0.2)
T3b	200	(41.1)	201	(41.1)	401	(41.1)
T4a	113	(23.2)	116	(23.7)	229	(23.5)
T4b	172	(35.3)	172	(35.2)	344	(35.2)
Nodal Involvement						
NX	2	(0.4)	1	(0.2)	3	(0.3)
N0	481	(98.8)	487	(99.6)	968	(99.2)
N1C	4	(0.8)	1	(0.2)	5	(0.5)
Metastatic Staging						
M0	487	(100.0)	487	(99.6)	974	(99.8)
M1C	0	(0.0)	1	(0.2)	1	(0.1)
M1D	0	(0.0)	1	(0.2)	1	(0.1)
Overall Cancer Stage						
IIA	1	(0.2)	0	(0.0)	1	(0.1)
IIB	309	(63.4)	316	(64.6)	625	(64.0)
IIC	171	(35.1)	169	(34.6)	340	(34.8)
IIIC	4	(0.8)	1	(0.2)	5	(0.5)
IV	0	(0.0)	2	(0.4)	2	(0.2)
Missing	2	(0.4)	1	(0.2)	3	(0.3)
Stratification						
Pediatric Age 12 to 17	1	(0.2)	1	(0.2)	2	(0.2)
IIB T3b >2.0-4.0 mm with ulceration	199	(40.9)	198	(40.5)	397	(40.7)
IIB T4a >4.0 mm without ulceration	112	(23.0)	114	(23.3)	226	(23.2)

Participant Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
IIC T4b >4.0 mm with ulceration	175	(35.9)	176	(36.0)	351	(36.0)

ECOG is not applicable for pediatric participants. KPS is not applicable for adult participants.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

Table 14.1-15
Participant Characteristics
(ITT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	8		63		71	
Sex						
Male	5	(62.5)	43	(68.3)	48	(67.6)
Female	3	(37.5)	20	(31.7)	23	(32.4)
Age (Years)						
12 - 17	0	(0.0)	0	(0.0)	0	(0.0)
18 - 64	7	(87.5)	34	(54.0)	41	(57.7)
≥ 65	1	(12.5)	29	(46.0)	30	(42.3)
Mean	51.5		61.4		60.3	
SD	10.9		12.0		12.2	
Median	54.5		63.0		61.0	
Range	33 to 69		20 to 81		20 to 81	
Race						
White	7	(87.5)	57	(90.5)	64	(90.1)
Missing	1	(12.5)	6	(9.5)	7	(9.9)
Ethnicity						
Hispanic Or Latino	3	(37.5)	3	(4.8)	6	(8.5)
Not Hispanic Or Latino	4	(50.0)	54	(85.7)	58	(81.7)
Not Reported	1	(12.5)	6	(9.5)	7	(9.9)
Geographic Region						
US	1	(12.5)	7	(11.1)	8	(11.3)
Non-US	7	(87.5)	56	(88.9)	63	(88.7)
ECOG						
0	6	(75.0)	58	(92.1)	64	(90.1)
1	2	(25.0)	5	(7.9)	7	(9.9)
LDH						
≤ ULN	2	(25.0)	34	(54.0)	36	(50.7)
> ULN but < 2X ULN	1	(12.5)	3	(4.8)	4	(5.6)
Missing	5	(62.5)	26	(41.3)	31	(43.7)

Participant Characteristics
(ITT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
KPS Status						
Not Applicable	8	(100.0)	63	(100.0)	71	(100.0)
T-Stage						
T3b	2	(25.0)	24	(38.1)	26	(36.6)
T4a	4	(50.0)	16	(25.4)	20	(28.2)
T4b	2	(25.0)	23	(36.5)	25	(35.2)
Nodal Involvement						
N0	8	(100.0)	63	(100.0)	71	(100.0)
Metastatic Staging						
M0	8	(100.0)	63	(100.0)	71	(100.0)
Overall Cancer Stage						
IIB	6	(75.0)	40	(63.5)	46	(64.8)
IIC	2	(25.0)	23	(36.5)	25	(35.2)
Stratification						
IIB T3b >2.0-4.0 mm with ulceration	3	(37.5)	23	(36.5)	26	(36.6)
IIB T4a >4.0 mm without ulceration	3	(37.5)	17	(27.0)	20	(28.2)
IIC T4b >4.0 mm with ulceration	2	(25.0)	23	(36.5)	25	(35.2)

ECOG is not applicable for pediatric participants. KPS is not applicable for adult participants.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl]

Table 14.1-16
Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more conditions	448	(92.8)	442	(90.9)
with no conditions	35	(7.2)	44	(9.1)
Blood and lymphatic system disorders	**25**	**(5.2)**	**29**	**(6.0)**
Anaemia	10	(2.1)	14	(2.9)
Anaemia macrocytic	0	(0.0)	1	(0.2)
Eosinophilia	1	(0.2)	0	(0.0)
Hyperleukocytosis	0	(0.0)	1	(0.2)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Iron deficiency anaemia	2	(0.4)	2	(0.4)
Lymphadenopathy	1	(0.2)	3	(0.6)
Lymphopenia	2	(0.4)	3	(0.6)
Neutropenia	1	(0.2)	1	(0.2)
Pernicious anaemia	0	(0.0)	1	(0.2)
Polycythaemia	2	(0.4)	1	(0.2)
Pseudolymphoma	0	(0.0)	1	(0.2)
Splenic cyst	0	(0.0)	1	(0.2)
Splenic infarction	1	(0.2)	0	(0.0)
Splenic lesion	1	(0.2)	0	(0.0)
Splenomegaly	1	(0.2)	0	(0.0)
Thrombocytopenia	3	(0.6)	3	(0.6)
Thrombocytosis	1	(0.2)	0	(0.0)
Cardiac disorders	**85**	**(17.6)**	**72**	**(14.8)**
Acute myocardial infarction	3	(0.6)	8	(1.6)
Angina pectoris	0	(0.0)	4	(0.8)
Aortic valve sclerosis	0	(0.0)	1	(0.2)
Aortic valve stenosis	3	(0.6)	0	(0.0)
Arrhythmia	6	(1.2)	4	(0.8)
Arteriosclerosis coronary artery	1	(0.2)	4	(0.8)
Atrial fibrillation	20	(4.1)	20	(4.1)
Atrial flutter	3	(0.6)	0	(0.0)
Atrioventricular block	2	(0.4)	0	(0.0)
Atrioventricular block complete	1	(0.2)	0	(0.0)
Atrioventricular block first degree	3	(0.6)	3	(0.6)
Bradycardia	6	(1.2)	3	(0.6)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cardiac disorders	**85**	**(17.6)**	**72**	**(14.8)**
Bundle branch block left	1	(0.2)	2	(0.4)
Bundle branch block right	3	(0.6)	2	(0.4)
Cardiac aneurysm	1	(0.2)	0	(0.0)
Cardiac disorder	1	(0.2)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Cardiac failure congestive	1	(0.2)	1	(0.2)
Cardiac valve disease	1	(0.2)	1	(0.2)
Cardiomyopathy	0	(0.0)	1	(0.2)
Chronic left ventricular failure	0	(0.0)	1	(0.2)
Coronary artery disease	10	(2.1)	11	(2.3)
Defect conduction intraventricular	1	(0.2)	0	(0.0)
Diastolic dysfunction	0	(0.0)	1	(0.2)
Extrasystoles	1	(0.2)	2	(0.4)
Hypertensive heart disease	1	(0.2)	0	(0.0)
Left ventricular dysfunction	1	(0.2)	2	(0.4)
Left ventricular failure	1	(0.2)	0	(0.0)
Left ventricular hypertrophy	1	(0.2)	0	(0.0)
Mitral valve incompetence	1	(0.2)	3	(0.6)
Mitral valve prolapse	1	(0.2)	3	(0.6)
Myocardial infarction	8	(1.7)	6	(1.2)
Myocardial ischaemia	12	(2.5)	7	(1.4)
Palpitations	0	(0.0)	1	(0.2)
Sinus bradycardia	5	(1.0)	4	(0.8)
Sinus node dysfunction	1	(0.2)	1	(0.2)
Sinus tachycardia	2	(0.4)	0	(0.0)
Stress cardiomyopathy	0	(0.0)	1	(0.2)
Supraventricular extrasystoles	0	(0.0)	1	(0.2)
Supraventricular tachycardia	0	(0.0)	3	(0.6)
Tachycardia	3	(0.6)	2	(0.4)
Tricuspid valve incompetence	0	(0.0)	1	(0.2)
Ventricular extrasystoles	2	(0.4)	1	(0.2)
Ventricular tachycardia	0	(0.0)	1	(0.2)
Wolff-Parkinson-White syndrome	1	(0.2)	0	(0.0)
Congenital, familial and genetic disorders	**16**	**(3.3)**	**16**	**(3.3)**
Adrenogenital syndrome	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Congenital, familial and genetic disorders	**16**	**(3.3)**	**16**	**(3.3)**
Arteriovenous malformation	0	(0.0)	1	(0.2)
Atrial septal defect	1	(0.2)	0	(0.0)
Benign familial pemphigus	0	(0.0)	1	(0.2)
Congenital cystic kidney disease	1	(0.2)	1	(0.2)
Congenital naevus	0	(0.0)	1	(0.2)
Cryptorchism	0	(0.0)	1	(0.2)
Deaf mutism	0	(0.0)	1	(0.2)
Dysplastic naevus syndrome	1	(0.2)	1	(0.2)
Factor V Leiden mutation	0	(0.0)	1	(0.2)
Factor VII deficiency	0	(0.0)	1	(0.2)
Familial tremor	0	(0.0)	1	(0.2)
Fibrous dysplasia of bone	1	(0.2)	0	(0.0)
Gilbert's syndrome	3	(0.6)	4	(0.8)
Hydrocele	1	(0.2)	1	(0.2)
Myotonia congenita	1	(0.2)	0	(0.0)
Phimosis	1	(0.2)	0	(0.0)
Pyloric stenosis	1	(0.2)	0	(0.0)
Renal aplasia	1	(0.2)	0	(0.0)
Renal fusion anomaly	1	(0.2)	1	(0.2)
Talipes	0	(0.0)	1	(0.2)
Thalassaemia beta	1	(0.2)	0	(0.0)
Venous angioma of brain	1	(0.2)	0	(0.0)
Ear and labyrintb disorders	**27**	**(5.6)**	**26**	**(5.3)**
Deafness	7	(1.4)	8	(1.6)
Deafness bilateral	1	(0.2)	0	(0.0)
Deafness neurosensory	1	(0.2)	0	(0.0)
Deafness unilateral	0	(0.0)	2	(0.4)
Hypoacusis	5	(1.0)	7	(1.4)
Middle ear inflammation	0	(0.0)	1	(0.2)
Motion sickness	1	(0.2)	0	(0.0)
Sudden hearing loss	1	(0.2)	0	(0.0)
Tinnitus	9	(1.9)	3	(0.6)
Vertigo	6	(1.2)	6	(1.2)
Vertigo positional	2	(0.4)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Endocrine disorders	**56**	**(11.6)**	**58**	**(11.9)**
Adrenal calcification	0	(0.0)	1	(0.2)
Adrenal disorder	0	(0.0)	1	(0.2)
Adrenal mass	0	(0.0)	1	(0.2)
Adrenomegaly	0	(0.0)	1	(0.2)
Androgen deficiency	1	(0.2)	1	(0.2)
Autoimmune thyroid disorder	0	(0.0)	1	(0.2)
Autoimmune thyroiditis	3	(0.6)	2	(0.4)
Basedow's disease	1	(0.2)	0	(0.0)
Central hypothyroidism	0	(0.0)	1	(0.2)
Cushing's syndrome	0	(0.0)	1	(0.2)
Goitre	2	(0.4)	9	(1.9)
Hyperparathyroidism	0	(0.0)	2	(0.4)
Hyperparathyroidism primary	1	(0.2)	0	(0.0)
Hyperthyroidism	6	(1.2)	8	(1.6)
Hypogonadism	1	(0.2)	1	(0.2)
Hypothyroidism	35	(7.2)	27	(5.6)
Myxoedema	1	(0.2)	0	(0.0)
Thyroid calcification	0	(0.0)	1	(0.2)
Thyroid cyst	0	(0.0)	2	(0.4)
Thyroid disorder	1	(0.2)	0	(0.0)
Thyroid dysfunction in pregnancy	1	(0.2)	0	(0.0)
Thyroid mass	6	(1.2)	8	(1.6)
Eye disorders	**41**	**(8.5)**	**42**	**(8.6)**
Age-related macular degeneration	1	(0.2)	0	(0.0)
Astigmatism	0	(0.0)	1	(0.2)
Blepharitis	0	(0.0)	1	(0.2)
Blepharospasm	1	(0.2)	0	(0.0)
Blindness	0	(0.0)	1	(0.2)
Cataract	14	(2.9)	12	(2.5)
Cataract nuclear	0	(0.0)	1	(0.2)
Chalazion	2	(0.4)	0	(0.0)
Diabetic retinopathy	3	(0.6)	2	(0.4)
Diplopia	0	(0.0)	1	(0.2)
Dry eye	3	(0.6)	2	(0.4)
Eye disorder	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Eye disorders	**41**	**(8.5)**	**42**	**(8.6)**
Eyelid function disorder	1	(0.2)	0	(0.0)
Eyelid margin crusting	1	(0.2)	0	(0.0)
Glaucoma	9	(1.9)	8	(1.6)
Hypermetropia	1	(0.2)	3	(0.6)
Keratoconus	1	(0.2)	0	(0.0)
Lacrimation decreased	0	(0.0)	1	(0.2)
Lacrimation increased	3	(0.6)	0	(0.0)
Maculopathy	1	(0.2)	0	(0.0)
Myopia	0	(0.0)	7	(1.4)
Ocular hypertension	0	(0.0)	1	(0.2)
Open angle glaucoma	0	(0.0)	1	(0.2)
Optic disc drusen	0	(0.0)	1	(0.2)
Photophobia	1	(0.2)	0	(0.0)
Presbyopia	0	(0.0)	1	(0.2)
Pterygium	1	(0.2)	0	(0.0)
Pupil fixed	0	(0.0)	1	(0.2)
Retinal detachment	2	(0.4)	3	(0.6)
Retinal haemorrhage	1	(0.2)	0	(0.0)
Retinal tear	0	(0.0)	2	(0.4)
Retinal vein thrombosis	1	(0.2)	0	(0.0)
Vision blurred	1	(0.2)	1	(0.2)
Visual impairment	1	(0.2)	1	(0.2)
Vitreous floaters	2	(0.4)	2	(0.4)
Xerophthalmia	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**137**	**(28.4)**	**112**	**(23.0)**
Abdominal hernia	2	(0.4)	3	(0.6)
Abdominal pain	1	(0.2)	1	(0.2)
Abdominal pain upper	5	(1.0)	2	(0.4)
Acid peptic disease	1	(0.2)	0	(0.0)
Anal fissure	1	(0.2)	0	(0.0)
Anal fistula	1	(0.2)	2	(0.4)
Anal incontinence	1	(0.2)	1	(0.2)
Angular cheilitis	0	(0.0)	1	(0.2)
Appendicolith	1	(0.2)	0	(0.0)
Ascites	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**137**	**(28.4)**	**112**	**(23.0)**
Barrett's oesophagus	1	(0.2)	3	(0.6)
Coeliac disease	1	(0.2)	1	(0.2)
Colitis	2	(0.4)	3	(0.6)
Colitis ulcerative	3	(0.6)	1	(0.2)
Colon dysplasia	0	(0.0)	1	(0.2)
Constipation	12	(2.5)	13	(2.7)
Dental caries	0	(0.0)	1	(0.2)
Diaphragmatic hernia	1	(0.2)	1	(0.2)
Diarrhoea	14	(2.9)	5	(1.0)
Diverticulum	6	(1.2)	6	(1.2)
Diverticulum intestinal	5	(1.0)	10	(2.1)
Dry mouth	2	(0.4)	3	(0.6)
Duodenal ulcer	1	(0.2)	1	(0.2)
Dyspepsia	7	(1.4)	10	(2.1)
Dysphagia	0	(0.0)	1	(0.2)
Faeces discoloured	1	(0.2)	0	(0.0)
Femoral hernia	0	(0.0)	1	(0.2)
Flatulence	1	(0.2)	0	(0.0)
Gastric disorder	1	(0.2)	0	(0.0)
Gastric ulcer	2	(0.4)	1	(0.2)
Gastritis	1	(0.2)	2	(0.4)
Gastritis erosive	1	(0.2)	0	(0.0)
Gastrointestinal disorder	0	(0.0)	1	(0.2)
Gastrooesophageal reflux disease	45	(9.3)	31	(6.4)
Gingival ulceration	1	(0.2)	0	(0.0)
Haemorrhoids	9	(1.9)	7	(1.4)
Hiatus hernia	12	(2.5)	12	(2.5)
Inguinal hernia	12	(2.5)	15	(3.1)
Intestinal obstruction	2	(0.4)	0	(0.0)
Intestinal polyp	1	(0.2)	0	(0.0)
Irritable bowel syndrome	5	(1.0)	2	(0.4)
Large intestine polyp	11	(2.3)	5	(1.0)
Lumbar hernia	1	(0.2)	0	(0.0)
Malpositioned teeth	0	(0.0)	1	(0.2)
Mesenteric panniculitis	2	(0.4)	0	(0.0)
Nausea	1	(0.2)	6	(1.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**137**	**(28.4)**	**112**	**(23.0)**
Oesophageal hypomotility	0	(0.0)	1	(0.2)
Oesophagitis	1	(0.2)	0	(0.0)
Pancreatic atrophy	1	(0.2)	0	(0.0)
Pancreatic cyst	0	(0.0)	1	(0.2)
Pancreatic disorder	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
Pancreatitis acute	3	(0.6)	0	(0.0)
Proctalgia	1	(0.2)	0	(0.0)
Pyloric sphincter insufficiency	0	(0.0)	1	(0.2)
Small intestinal obstruction	1	(0.2)	0	(0.0)
Stomatitis	1	(0.2)	0	(0.0)
Tongue ulceration	0	(0.0)	1	(0.2)
Umbilical hernia	6	(1.2)	6	(1.2)
Vomiting	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**49**	**(10.1)**	**44**	**(9.1)**
Asthenia	1	(0.2)	0	(0.0)
Axillary pain	2	(0.4)	1	(0.2)
Chest pain	1	(0.2)	0	(0.0)
Chronic fatigue syndrome	0	(0.0)	1	(0.2)
Cyst	2	(0.4)	1	(0.2)
Drug intolerance	3	(0.6)	1	(0.2)
Drug tolerance	1	(0.2)	0	(0.0)
Fat necrosis	1	(0.2)	0	(0.0)
Fatigue	15	(3.1)	15	(3.1)
Gait disturbance	3	(0.6)	1	(0.2)
Hernia	4	(0.8)	3	(0.6)
Inflammation	1	(0.2)	1	(0.2)
Influenza like illness	0	(0.0)	1	(0.2)
Localised oedema	2	(0.4)	0	(0.0)
Oedema	2	(0.4)	1	(0.2)
Oedema peripheral	9	(1.9)	7	(1.4)
Pain	4	(0.8)	12	(2.5)
Peripheral swelling	2	(0.4)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**49**	**(10.1)**	**44**	**(9.1)**
Retention cyst	0	(0.0)	1	(0.2)
Xerosis	1	(0.2)	1	(0.2)
Hepatobiliary disorders	**25**	**(5.2)**	**33**	**(6.8)**
Alcoholic liver disease	1	(0.2)	0	(0.0)
Bile duct stone	1	(0.2)	0	(0.0)
Biliary colic	1	(0.2)	0	(0.0)
Biliary cyst	0	(0.0)	1	(0.2)
Cholecystitis	0	(0.0)	2	(0.4)
Cholecystitis acute	1	(0.2)	0	(0.0)
Cholelithiasis	6	(1.2)	5	(1.0)
Drug-induced liver injury	0	(0.0)	1	(0.2)
Fatty liver alcoholic	1	(0.2)	0	(0.0)
Gallbladder disorder	0	(0.0)	1	(0.2)
Hepatic artery stenosis	0	(0.0)	1	(0.2)
Hepatic cirrhosis	0	(0.0)	1	(0.2)
Hepatic cyst	3	(0.6)	5	(1.0)
Hepatic cytolysis	0	(0.0)	1	(0.2)
Hepatic lesion	0	(0.0)	1	(0.2)
Hepatic steatosis	11	(2.3)	12	(2.5)
Hepatitis	1	(0.2)	1	(0.2)
Hepatomegaly	1	(0.2)	0	(0.0)
Hyperbilirubinaemia	0	(0.0)	2	(0.4)
Hypertransaminasaemia	1	(0.2)	0	(0.0)
Liver disorder	1	(0.2)	1	(0.2)
Sphincter of Oddi dysfunction	1	(0.2)	0	(0.0)
Immune system disorders	**69**	**(14.3)**	**74**	**(15.2)**
Allergy to animal	3	(0.6)	1	(0.2)
Allergy to arthropod sting	0	(0.0)	4	(0.8)
Allergy to metals	1	(0.2)	2	(0.4)
Allergy to plants	1	(0.2)	0	(0.0)
Allergy to vaccine	1	(0.2)	1	(0.2)
Contrast media allergy	5	(1.0)	5	(1.0)
Drug hypersensitivity	32	(6.6)	41	(8.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Immune system disorders	**69**	**(14.3)**	**74**	**(15.2)**
Dust allergy	1	(0.2)	4	(0.8)
Food allergy	4	(0.8)	4	(0.8)
Hypersensitivity	5	(1.0)	4	(0.8)
Iodine allergy	3	(0.6)	4	(0.8)
Mite allergy	1	(0.2)	1	(0.2)
Multiple allergies	0	(0.0)	1	(0.2)
Mycotic allergy	1	(0.2)	0	(0.0)
Reaction to food additive	0	(0.0)	1	(0.2)
Reaction to sweetener	0	(0.0)	1	(0.2)
Rubber sensitivity	1	(0.2)	2	(0.4)
Sarcoidosis	1	(0.2)	0	(0.0)
Seasonal allergy	23	(4.8)	23	(4.7)
Selective IgG subclass deficiency	0	(0.0)	1	(0.2)
Infections and infestations	**76**	**(15.7)**	**70**	**(14.4)**
Acute sinusitis	0	(0.0)	1	(0.2)
Anal abscess	1	(0.2)	0	(0.0)
Appendicitis	2	(0.4)	2	(0.4)
Arthritis infective	1	(0.2)	0	(0.0)
Bacterial disease carrier	0	(0.0)	1	(0.2)
Breast abscess	0	(0.0)	1	(0.2)
Bronchitis	6	(1.2)	1	(0.2)
Cellulitis	6	(1.2)	2	(0.4)
Chlamydial infection	1	(0.2)	0	(0.0)
Chorioretinitis	1	(0.2)	0	(0.0)
Chronic sinusitis	1	(0.2)	3	(0.6)
Coccidioidomycosis	0	(0.0)	1	(0.2)
Conjunctivitis	1	(0.2)	0	(0.0)
Cystitis	2	(0.4)	0	(0.0)
Dengue fever	0	(0.0)	1	(0.2)
Diverticulitis	5	(1.0)	1	(0.2)
Erysipelas	2	(0.4)	1	(0.2)
Eye infection	1	(0.2)	0	(0.0)
Folliculitis	2	(0.4)	0	(0.0)
Fungal foot infection	2	(0.4)	0	(0.0)
Fungal infection	0	(0.0)	4	(0.8)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**76**	**(15.7)**	**70**	**(14.4)**
Fungal skin infection	1	(0.2)	0	(0.0)
Gastroenteritis	0	(0.0)	1	(0.2)
Genital herpes	1	(0.2)	0	(0.0)
Groin abscess	0	(0.0)	1	(0.2)
Helicobacter gastritis	1	(0.2)	1	(0.2)
Hepatitis A	2	(0.4)	3	(0.6)
Hepatitis B	0	(0.0)	1	(0.2)
Herpes ophthalmic	0	(0.0)	1	(0.2)
Herpes simplex	1	(0.2)	1	(0.2)
Herpes virus infection	2	(0.4)	0	(0.0)
Herpes zoster	2	(0.4)	4	(0.8)
Hordeolum	0	(0.0)	1	(0.2)
Infectious mononucleosis	0	(0.0)	1	(0.2)
Infectious thyroiditis	1	(0.2)	0	(0.0)
Influenza	2	(0.4)	0	(0.0)
Labyrinthitis	2	(0.4)	2	(0.4)
Lyme disease	4	(0.8)	0	(0.0)
Meningitis	1	(0.2)	0	(0.0)
Meningitis viral	0	(0.0)	1	(0.2)
Mumps	1	(0.2)	0	(0.0)
Nasopharyngitis	1	(0.2)	2	(0.4)
Onychomycosis	0	(0.0)	2	(0.4)
Ophthalmic herpes zoster	1	(0.2)	0	(0.0)
Oral herpes	2	(0.4)	1	(0.2)
Osteomyelitis	0	(0.0)	1	(0.2)
Osteomyelitis chronic	1	(0.2)	0	(0.0)
Papilloma viral infection	2	(0.4)	0	(0.0)
Parotitis	0	(0.0)	1	(0.2)
Peritonitis	0	(0.0)	2	(0.4)
Peritonsillar abscess	0	(0.0)	1	(0.2)
Phlebitis infective	1	(0.2)	0	(0.0)
Pilonidal disease	1	(0.2)	0	(0.0)
Pneumonia	4	(0.8)	5	(1.0)
Post procedural infection	0	(0.0)	1	(0.2)
Postoperative wound infection	1	(0.2)	0	(0.0)
Pyelonephritis	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**76**	**(15.7)**	**70**	**(14.4)**
Q fever	1	(0.2)	0	(0.0)
Rhinitis	3	(0.6)	1	(0.2)
Rocky mountain spotted fever	0	(0.0)	1	(0.2)
Sinusitis	5	(1.0)	4	(0.8)
Skin infection	1	(0.2)	1	(0.2)
Subcutaneous abscess	1	(0.2)	1	(0.2)
Tinea infection	1	(0.2)	0	(0.0)
Tinea pedis	2	(0.4)	2	(0.4)
Tonsillitis	0	(0.0)	2	(0.4)
Tooth abscess	0	(0.0)	1	(0.2)
Tuberculosis	0	(0.0)	1	(0.2)
Typhoid fever	1	(0.2)	0	(0.0)
Upper respiratory tract infection	2	(0.4)	1	(0.2)
Urinary tract infection	5	(1.0)	4	(0.8)
Varicella	1	(0.2)	0	(0.0)
Varicella zoster virus infection	2	(0.4)	0	(0.0)
Vestibular neuronitis	1	(0.2)	0	(0.0)
Vibrio vulnificus infection	1	(0.2)	0	(0.0)
Viral upper respiratory tract infection	0	(0.0)	3	(0.6)
Wound infection	4	(0.8)	6	(1.2)
Wound infection staphylococcal	0	(0.0)	1	(0.2)
Injury, poisoning and procedural complications	**60**	**(12.4)**	**53**	**(10.9)**
Adrenal gland injury	0	(0.0)	1	(0.2)
Anaesthetic complication neurological	0	(0.0)	1	(0.2)
Ankle fracture	1	(0.2)	4	(0.8)
Arthropod bite	2	(0.4)	0	(0.0)
Arthropod sting	1	(0.2)	0	(0.0)
Axillary web syndrome	0	(0.0)	1	(0.2)
Bone contusion	1	(0.2)	0	(0.0)
Carcinogenicity	1	(0.2)	1	(0.2)
Clavicle fracture	0	(0.0)	2	(0.4)
Contusion	0	(0.0)	1	(0.2)
Coronary artery restenosis	1	(0.2)	0	(0.0)
Deafness traumatic	1	(0.2)	0	(0.0)
Epicondylitis	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**60**	**(12.4)**	**53**	**(10.9)**
Exposure to communicable disease	1	(0.2)	0	(0.0)
Facial bones fracture	1	(0.2)	0	(0.0)
Fall	0	(0.0)	1	(0.2)
Femur fracture	1	(0.2)	2	(0.4)
Fibula fracture	1	(0.2)	1	(0.2)
Forearm fracture	1	(0.2)	2	(0.4)
Foreign body	1	(0.2)	0	(0.0)
Fractured coccyx	0	(0.0)	1	(0.2)
Graft complication	0	(0.0)	1	(0.2)
Hand fracture	1	(0.2)	0	(0.0)
Head injury	1	(0.2)	1	(0.2)
Hip fracture	0	(0.0)	2	(0.4)
Humerus fracture	0	(0.0)	1	(0.2)
Iliotibial band syndrome	1	(0.2)	0	(0.0)
Incision site hypoaesthesia	3	(0.6)	1	(0.2)
Incision site pain	1	(0.2)	1	(0.2)
Incision site swelling	0	(0.0)	1	(0.2)
Incisional hernia	1	(0.2)	0	(0.0)
Injury	0	(0.0)	1	(0.2)
Intervertebral disc injury	1	(0.2)	0	(0.0)
Jaw fracture	0	(0.0)	1	(0.2)
Joint dislocation	1	(0.2)	0	(0.0)
Joint injury	1	(0.2)	1	(0.2)
Ligament rupture	2	(0.4)	3	(0.6)
Ligament sprain	1	(0.2)	0	(0.0)
Limb injury	1	(0.2)	0	(0.0)
Lower limb fracture	1	(0.2)	0	(0.0)
Lumbar vertebral fracture	0	(0.0)	1	(0.2)
Meniscus injury	0	(0.0)	1	(0.2)
Muscle injury	0	(0.0)	1	(0.2)
Muscle rupture	1	(0.2)	0	(0.0)
Patella fracture	0	(0.0)	1	(0.2)
Pelvic fracture	1	(0.2)	0	(0.0)
Post procedural complication	0	(0.0)	2	(0.4)
Post procedural discomfort	1	(0.2)	0	(0.0)
Procedural nausea	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**60**	**(12.4)**	**53**	**(10.9)**
Procedural pain	3	(0.6)	3	(0.6)
Procedural pneumothorax	1	(0.2)	0	(0.0)
Radius fracture	0	(0.0)	3	(0.6)
Rib fracture	1	(0.2)	3	(0.6)
Road traffic accident	1	(0.2)	0	(0.0)
Scar	5	(1.0)	3	(0.6)
Seroma	4	(0.8)	3	(0.6)
Skin laceration	2	(0.4)	0	(0.0)
Spinal column injury	0	(0.0)	1	(0.2)
Spinal compression fracture	1	(0.2)	0	(0.0)
Spinal fracture	2	(0.4)	0	(0.0)
Subdural haematoma	1	(0.2)	1	(0.2)
Sunburn	3	(0.6)	0	(0.0)
Tendon rupture	2	(0.4)	1	(0.2)
Thermal burn	0	(0.0)	1	(0.2)
Thoracic vertebral fracture	2	(0.4)	0	(0.0)
Tibia fracture	3	(0.6)	0	(0.0)
Traumatic haemothorax	1	(0.2)	0	(0.0)
Upper limb fracture	5	(1.0)	2	(0.4)
Wound complication	2	(0.4)	2	(0.4)
Wound secretion	1	(0.2)	0	(0.0)
Wrist fracture	4	(0.8)	2	(0.4)
Investigations	**95**	**(19.7)**	**74**	**(15.2)**
Alanine aminotransferase increased	10	(2.1)	11	(2.3)
Amylase increased	2	(0.4)	1	(0.2)
Arthroscopy	1	(0.2)	1	(0.2)
Aspartate aminotransferase increased	9	(1.9)	8	(1.6)
Bilirubin conjugated increased	1	(0.2)	1	(0.2)
Biopsy	0	(0.0)	1	(0.2)
Biopsy breast	1	(0.2)	0	(0.0)
Biopsy breast normal	0	(0.0)	1	(0.2)
Biopsy skin	1	(0.2)	3	(0.6)
Blood alkaline phosphatase increased	4	(0.8)	3	(0.6)
Blood bicarbonate increased	0	(0.0)	1	(0.2)
Blood bilirubin increased	9	(1.9)	7	(1.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**95**	**(19.7)**	**74**	**(15.2)**
Blood bilirubin unconjugated increased	0	(0.0)	1	(0.2)
Blood cholesterol increased	20	(4.1)	12	(2.5)
Blood creatine increased	2	(0.4)	1	(0.2)
Blood creatine phosphokinase increased	0	(0.0)	2	(0.4)
Blood creatinine increased	4	(0.8)	4	(0.8)
Blood glucose increased	3	(0.6)	2	(0.4)
Blood iron decreased	0	(0.0)	1	(0.2)
Blood iron increased	1	(0.2)	1	(0.2)
Blood lactate dehydrogenase increased	1	(0.2)	2	(0.4)
Blood magnesium increased	0	(0.0)	1	(0.2)
Blood phosphorus decreased	1	(0.2)	0	(0.0)
Blood potassium decreased	0	(0.0)	1	(0.2)
Blood pressure increased	0	(0.0)	1	(0.2)
Blood testosterone decreased	1	(0.2)	0	(0.0)
Blood thyroid stimulating hormone decreased	0	(0.0)	2	(0.4)
Blood thyroid stimulating hormone increased	4	(0.8)	1	(0.2)
Blood triglycerides increased	1	(0.2)	1	(0.2)
Blood urea increased	1	(0.2)	3	(0.6)
Blood uric acid increased	1	(0.2)	2	(0.4)
Blood urine present	1	(0.2)	0	(0.0)
Borrelia test positive	0	(0.0)	1	(0.2)
C-reactive protein increased	1	(0.2)	0	(0.0)
Cardiac murmur	4	(0.8)	3	(0.6)
Cardiac stress test	1	(0.2)	0	(0.0)
Catheterisation cardiac	2	(0.4)	0	(0.0)
Colonoscopy	5	(1.0)	1	(0.2)
Colposcopy	1	(0.2)	0	(0.0)
Diagnostic aspiration	1	(0.2)	0	(0.0)
Echocardiogram	1	(0.2)	0	(0.0)
Electrocardiogram QT prolonged	2	(0.4)	1	(0.2)
Electrocardiogram T wave abnormal	2	(0.4)	0	(0.0)
Endoscopy	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	5	(1.0)	7	(1.4)
Glomerular filtration rate decreased	3	(0.6)	1	(0.2)
Haemoglobin decreased	1	(0.2)	0	(0.0)
Heart rate irregular	2	(0.4)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**95**	**(19.7)**	**74**	**(15.2)**
Hepatic enzyme increased	0	(0.0)	1	(0.2)
Human papilloma virus test positive	0	(0.0)	1	(0.2)
Intraocular pressure increased	0	(0.0)	1	(0.2)
Lipase increased	3	(0.6)	4	(0.8)
Lipids abnormal	1	(0.2)	0	(0.0)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Lymphocyte count increased	1	(0.2)	0	(0.0)
Mammogram	1	(0.2)	0	(0.0)
Mycoplasma test positive	0	(0.0)	1	(0.2)
Panendoscopy	0	(0.0)	1	(0.2)
Platelet count decreased	0	(0.0)	4	(0.8)
Prostatic specific antigen increased	1	(0.2)	2	(0.4)
Serum ferritin increased	2	(0.4)	1	(0.2)
Sinus rhythm	1	(0.2)	0	(0.0)
Smear cervix abnormal	1	(0.2)	0	(0.0)
Thyroxine free decreased	1	(0.2)	0	(0.0)
Tri-iodothyronine free decreased	1	(0.2)	0	(0.0)
Tri-iodothyronine free increased	1	(0.2)	0	(0.0)
Ultrasound liver abnormal	1	(0.2)	0	(0.0)
Vitamin D decreased	1	(0.2)	0	(0.0)
Weight decreased	0	(0.0)	1	(0.2)
Weight increased	0	(0.0)	1	(0.2)
White blood cell count increased	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**174**	**(36.0)**	**183**	**(37.7)**
Decreased appetite	1	(0.2)	1	(0.2)
Diabetes mellitus	2	(0.4)	1	(0.2)
Dyslipidaemia	32	(6.6)	27	(5.6)
Fluid retention	0	(0.0)	1	(0.2)
Folate deficiency	0	(0.0)	1	(0.2)
Glucose tolerance impaired	4	(0.8)	3	(0.6)
Gluten sensitivity	0	(0.0)	1	(0.2)
Gout	10	(2.1)	11	(2.3)
Haemochromatosis	0	(0.0)	3	(0.6)
Hyperalbuminaemia	1	(0.2)	0	(0.0)
Hypercalcaemia	2	(0.4)	2	(0.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Metabolism and nutrition disorders	**174**	**(36.0)**	**183**	**(37.7)**
Hypercholesterolaemia	49	(10.1)	59	(12.1)
Hyperglycaemia	10	(2.1)	14	(2.9)
Hyperkalaemia	2	(0.4)	0	(0.0)
Hyperlipidaemia	28	(5.8)	28	(5.8)
Hypermagnesaemia	0	(0.0)	1	(0.2)
Hypertriglyceridaemia	4	(0.8)	2	(0.4)
Hyperuricaemia	9	(1.9)	13	(2.7)
Hypoalbuminaemia	1	(0.2)	0	(0.0)
Hypocalcaemia	0	(0.0)	1	(0.2)
Hypoglycaemia	1	(0.2)	0	(0.0)
Hypokalaemia	3	(0.6)	0	(0.0)
Hypomagnesaemia	1	(0.2)	3	(0.6)
Hyponatraemia	3	(0.6)	1	(0.2)
Hypophosphataemia	3	(0.6)	3	(0.6)
Hypovitaminosis	1	(0.2)	0	(0.0)
Impaired fasting glucose	0	(0.0)	1	(0.2)
Insulin resistance	1	(0.2)	3	(0.6)
Iron deficiency	1	(0.2)	1	(0.2)
Iron overload	1	(0.2)	0	(0.0)
Lactose intolerance	1	(0.2)	1	(0.2)
Lipid metabolism disorder	0	(0.0)	1	(0.2)
Metabolic syndrome	1	(0.2)	0	(0.0)
Obesity	23	(4.8)	16	(3.3)
Overweight	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	3	(0.6)	1	(0.2)
Type 2 diabetes mellitus	56	(11.6)	56	(11.5)
Vitamin B complex deficiency	0	(0.0)	1	(0.2)
Vitamin B12 deficiency	2	(0.4)	6	(1.2)
Vitamin D deficiency	5	(1.0)	10	(2.1)
Musculoskeletal and connective tissue disorders	**140**	**(29.0)**	**151**	**(31.1)**
Ankylosing spondylitis	1	(0.2)	2	(0.4)
Arthralgia	24	(5.0)	25	(5.1)
Arthritis	11	(2.3)	15	(3.1)
Arthropathy	1	(0.2)	0	(0.0)
Back pain	18	(3.7)	25	(5.1)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**140**	**(29.0)**	**151**	**(31.1)**
Bone cyst	1	(0.2)	0	(0.0)
Bone disorder	0	(0.0)	1	(0.2)
Bone pain	1	(0.2)	0	(0.0)
Bursitis	1	(0.2)	2	(0.4)
Cervical spinal stenosis	1	(0.2)	0	(0.0)
Dupuytren's contracture	3	(0.6)	1	(0.2)
Exostosis	0	(0.0)	1	(0.2)
Facet joint syndrome	1	(0.2)	0	(0.0)
Fibromyalgia	2	(0.4)	4	(0.8)
Foot deformity	3	(0.6)	2	(0.4)
Groin pain	2	(0.4)	0	(0.0)
Haemarthrosis	1	(0.2)	0	(0.0)
Hand deformity	2	(0.4)	0	(0.0)
Intervertebral disc degeneration	5	(1.0)	1	(0.2)
Intervertebral disc disorder	0	(0.0)	4	(0.8)
Intervertebral disc protrusion	5	(1.0)	12	(2.5)
Jaw clicking	0	(0.0)	1	(0.2)
Joint contracture	1	(0.2)	0	(0.0)
Joint effusion	0	(0.0)	1	(0.2)
Joint instability	0	(0.0)	1	(0.2)
Joint range of motion decreased	1	(0.2)	1	(0.2)
Joint swelling	0	(0.0)	1	(0.2)
Knee deformity	0	(0.0)	1	(0.2)
Kyphoscoliosis	0	(0.0)	1	(0.2)
Lumbar spinal stenosis	0	(0.0)	3	(0.6)
Meniscopathy	1	(0.2)	0	(0.0)
Mobility decreased	0	(0.0)	1	(0.2)
Muscle spasms	6	(1.2)	12	(2.5)
Muscle tightness	0	(0.0)	1	(0.2)
Muscular weakness	2	(0.4)	1	(0.2)
Musculoskeletal pain	1	(0.2)	0	(0.0)
Musculoskeletal stiffness	2	(0.4)	2	(0.4)
Myalgia	5	(1.0)	4	(0.8)
Myositis	1	(0.2)	0	(0.0)
Neck mass	0	(0.0)	1	(0.2)
Neck pain	9	(1.9)	7	(1.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**140**	**(29.0)**	**151**	**(31.1)**
Osteoarthritis	39	(8.1)	40	(8.2)
Osteopenia	8	(1.7)	2	(0.4)
Osteoporosis	14	(2.9)	9	(1.9)
Osteosclerosis	0	(0.0)	2	(0.4)
Pain in extremity	13	(2.7)	7	(1.4)
Plantar fasciitis	0	(0.0)	2	(0.4)
Polymyalgia rheumatica	0	(0.0)	1	(0.2)
Pseudarthrosis	0	(0.0)	1	(0.2)
Rheumatic disorder	1	(0.2)	0	(0.0)
Rheumatoid arthritis	1	(0.2)	1	(0.2)
Rotator cuff syndrome	2	(0.4)	6	(1.2)
Sacral pain	0	(0.0)	1	(0.2)
Scoliosis	2	(0.4)	2	(0.4)
Soft tissue mass	1	(0.2)	0	(0.0)
Spinal deformity	0	(0.0)	1	(0.2)
Spinal ligament ossification	1	(0.2)	0	(0.0)
Spinal osteoarthritis	7	(1.4)	13	(2.7)
Spinal pain	0	(0.0)	1	(0.2)
Spinal stenosis	3	(0.6)	1	(0.2)
Spondylitis	1	(0.2)	0	(0.0)
Spondylolisthesis	3	(0.6)	3	(0.6)
Spondylolysis	1	(0.2)	0	(0.0)
Synovial cyst	0	(0.0)	1	(0.2)
Temporomandibular joint syndrome	0	(0.0)	3	(0.6)
Tendon pain	0	(0.0)	1	(0.2)
Tendonitis	4	(0.8)	0	(0.0)
Tenosynovitis	1	(0.2)	1	(0.2)
Trigger finger	0	(0.0)	1	(0.2)
Vertebral foraminal stenosis	0	(0.0)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**128**	**(26.5)**	**125**	**(25.7)**
Acoustic neuroma	0	(0.0)	2	(0.4)
Acrochordon	1	(0.2)	1	(0.2)
Adenoma benign	0	(0.0)	2	(0.4)
Adrenal adenoma	1	(0.2)	2	(0.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**128**	**(26.5)**	**125**	**(25.7)**
Adrenal neoplasm	0	(0.0)	1	(0.2)
Anal cancer	0	(0.0)	1	(0.2)
Angiomyolipoma	0	(0.0)	1	(0.2)
Anogenital warts	0	(0.0)	1	(0.2)
Basal cell carcinoma	43	(8.9)	41	(8.4)
Basosquamous carcinoma of skin	0	(0.0)	1	(0.2)
Benign abdominal neoplasm	0	(0.0)	1	(0.2)
Benign breast neoplasm	0	(0.0)	1	(0.2)
Benign neoplasm of skin	1	(0.2)	0	(0.0)
Benign neoplasm of testis	0	(0.0)	1	(0.2)
Benign neoplasm of thyroid gland	0	(0.0)	2	(0.4)
Benign renal neoplasm	1	(0.2)	0	(0.0)
Bladder cancer	0	(0.0)	3	(0.6)
Bladder transitional cell carcinoma	1	(0.2)	1	(0.2)
Bowen's disease	3	(0.6)	2	(0.4)
Breast cancer	6	(1.2)	2	(0.4)
Breast cancer in situ	1	(0.2)	1	(0.2)
Breast neoplasm	0	(0.0)	1	(0.2)
Carcinoma in situ	1	(0.2)	1	(0.2)
Colon cancer	0	(0.0)	1	(0.2)
Colorectal adenocarcinoma	1	(0.2)	0	(0.0)
Colorectal adenoma	1	(0.2)	2	(0.4)
Dysplastic naevus	3	(0.6)	1	(0.2)
Enchondromatosis	0	(0.0)	1	(0.2)
Endometrial cancer	1	(0.2)	0	(0.0)
Eye naevus	1	(0.2)	0	(0.0)
Fibroadenoma of breast	0	(0.0)	1	(0.2)
Fibroma	1	(0.2)	2	(0.4)
Fibrous histiocytoma	3	(0.6)	1	(0.2)
Focal nodular hyperplasia	0	(0.0)	1	(0.2)
Follicular lymphoma	1	(0.2)	0	(0.0)
Gastrointestinal stromal tumour	0	(0.0)	1	(0.2)
Glioma	1	(0.2)	0	(0.0)
Haemangioma	0	(0.0)	4	(0.8)
Haemangioma of liver	3	(0.6)	9	(1.9)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**128**	**(26.5)**	**125**	**(25.7)**
Hairy cell leukaemia	1	(0.2)	0	(0.0)
Hypergammaglobulinaemia benign monoclonal	2	(0.4)	0	(0.0)
Intraductal papilloma of breast	1	(0.2)	0	(0.0)
Invasive ductal breast carcinoma	0	(0.0)	2	(0.4)
Keratoacanthoma	0	(0.0)	1	(0.2)
Lentigo maligna	1	(0.2)	2	(0.4)
Lipoma	8	(1.7)	2	(0.4)
Lipoma of breast	1	(0.2)	0	(0.0)
Lobular breast carcinoma in situ	0	(0.0)	1	(0.2)
Lung adenocarcinoma	1	(0.2)	0	(0.0)
Malignant melanoma	6	(1.2)	5	(1.0)
Malignant melanoma in situ	7	(1.4)	10	(2.1)
Melanocytic naevus	11	(2.3)	3	(0.6)
Meningioma	2	(0.4)	1	(0.2)
Meningioma benign	1	(0.2)	0	(0.0)
Monoclonal gammopathy	1	(0.2)	0	(0.0)
Myeloid leukaemia	0	(0.0)	1	(0.2)
Neoplasm	0	(0.0)	1	(0.2)
Osteoma	1	(0.2)	0	(0.0)
Ovarian cancer	0	(0.0)	1	(0.2)
Pancreatic cystadenoma	3	(0.6)	0	(0.0)
Pancreatic neuroendocrine tumour	1	(0.2)	0	(0.0)
Papillary thyroid cancer	1	(0.2)	0	(0.0)
Papilloma	1	(0.2)	0	(0.0)
Pituitary tumour benign	2	(0.4)	0	(0.0)
Pleomorphic adenoma	0	(0.0)	1	(0.2)
Prolactin-producing pituitary tumour	0	(0.0)	1	(0.2)
Prostate cancer	10	(2.1)	8	(1.6)
Prostatic adenoma	1	(0.2)	0	(0.0)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Renal neoplasm	0	(0.0)	1	(0.2)
Renal oncocytoma	0	(0.0)	1	(0.2)
Salivary gland adenoma	0	(0.0)	1	(0.2)
Seborrhoeic keratosis	10	(2.1)	10	(2.1)
Skin papilloma	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**128**	**(26.5)**	**125**	**(25.7)**
Squamous cell carcinoma	8	(1.7)	7	(1.4)
Squamous cell carcinoma of skin	7	(1.4)	8	(1.6)
Superficial spreading melanoma stage unspecified	1	(0.2)	1	(0.2)
Testicular neoplasm	0	(0.0)	2	(0.4)
Testis cancer	2	(0.4)	0	(0.0)
Thyroid cancer	1	(0.2)	1	(0.2)
Transitional cell carcinoma	0	(0.0)	2	(0.4)
Uterine leiomyoma	7	(1.4)	4	(0.8)
Nervous system disorders	**81**	**(16.8)**	**89**	**(18.3)**
Ageusia	1	(0.2)	1	(0.2)
Amnesia	1	(0.2)	0	(0.0)
Arachnoid cyst	0	(0.0)	1	(0.2)
Basal ganglia haemorrhage	0	(0.0)	1	(0.2)
Bell's palsy	3	(0.6)	2	(0.4)
Carotid arteriosclerosis	2	(0.4)	2	(0.4)
Carotid artery dissection	0	(0.0)	1	(0.2)
Carotid artery occlusion	0	(0.0)	1	(0.2)
Carotid artery stenosis	0	(0.0)	2	(0.4)
Carpal tunnel syndrome	4	(0.8)	2	(0.4)
Cerebral cyst	0	(0.0)	1	(0.2)
Cerebral disorder	0	(0.0)	1	(0.2)
Cerebrovascular accident	3	(0.6)	4	(0.8)
Cervical radiculopathy	1	(0.2)	1	(0.2)
Cervicobrachial syndrome	1	(0.2)	0	(0.0)
Cognitive disorder	0	(0.0)	1	(0.2)
Coma	1	(0.2)	0	(0.0)
Dementia	0	(0.0)	1	(0.2)
Dementia Alzheimer's type	0	(0.0)	1	(0.2)
Diabetic autonomic neuropathy	1	(0.2)	0	(0.0)
Diabetic neuropathy	2	(0.4)	3	(0.6)
Dizziness	4	(0.8)	5	(1.0)
Dysarthria	0	(0.0)	1	(0.2)
Dysgeusia	1	(0.2)	2	(0.4)
Dyskinesia	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**81**	**(16.8)**	**89**	**(18.3)**
Embolic stroke	0	(0.0)	1	(0.2)
Epilepsy	3	(0.6)	3	(0.6)
Essential tremor	1	(0.2)	3	(0.6)
Extrapyramidal disorder	0	(0.0)	1	(0.2)
Facial paralysis	1	(0.2)	1	(0.2)
Guillain-Barre syndrome	1	(0.2)	0	(0.0)
Headache	19	(3.9)	22	(4.5)
Hemiparesis	1	(0.2)	1	(0.2)
Hypoaesthesia	4	(0.8)	3	(0.6)
Hyposmia	0	(0.0)	1	(0.2)
Intracranial aneurysm	0	(0.0)	1	(0.2)
Ischaemic stroke	0	(0.0)	1	(0.2)
Lacunar stroke	0	(0.0)	1	(0.2)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Lumbosacral radiculopathy	1	(0.2)	1	(0.2)
Memory impairment	2	(0.4)	2	(0.4)
Migraine	6	(1.2)	10	(2.1)
Myelopathy	0	(0.0)	1	(0.2)
Narcolepsy	1	(0.2)	1	(0.2)
Nerve compression	0	(0.0)	1	(0.2)
Neuralgia	4	(0.8)	0	(0.0)
Neuropathy peripheral	6	(1.2)	9	(1.9)
Occipital neuralgia	1	(0.2)	0	(0.0)
Ophthalmic migraine	1	(0.2)	0	(0.0)
Paraesthesia	6	(1.2)	1	(0.2)
Parkinson's disease	3	(0.6)	3	(0.6)
Peripheral sensory neuropathy	2	(0.4)	1	(0.2)
Phrenic nerve paralysis	0	(0.0)	1	(0.2)
Polyneuropathy	2	(0.4)	1	(0.2)
Post herpetic neuralgia	1	(0.2)	0	(0.0)
Restless legs syndrome	2	(0.4)	1	(0.2)
Sciatica	4	(0.8)	1	(0.2)
Seizure	0	(0.0)	4	(0.8)
Sinus headache	0	(0.0)	1	(0.2)
Syncope	2	(0.4)	0	(0.0)
Tension headache	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**81**	**(16.8)**	**89**	**(18.3)**
Thoracic outlet syndrome	0	(0.0)	2	(0.4)
Transient ischaemic attack	4	(0.8)	2	(0.4)
Tremor	1	(0.2)	2	(0.4)
Trigeminal nerve disorder	0	(0.0)	1	(0.2)
Trigeminal neuralgia	0	(0.0)	1	(0.2)
Vascular encephalopathy	0	(0.0)	1	(0.2)
Vocal cord paresis	0	(0.0)	1	(0.2)
White matter lesion	1	(0.2)	0	(0.0)
Pregnancy, puerperium and perinatal conditions	**0**	**(0.0)**	**2**	**(0.4)**
Gestational diabetes	0	(0.0)	1	(0.2)
HELLP syndrome	0	(0.0)	1	(0.2)
Psychiatric disorders	**92**	**(19.0)**	**97**	**(20.0)**
Adjustment disorder	1	(0.2)	1	(0.2)
Agitation	1	(0.2)	1	(0.2)
Alcohol abuse	2	(0.4)	2	(0.4)
Alcohol use disorder	1	(0.2)	0	(0.0)
Alcoholism	1	(0.2)	2	(0.4)
Anxiety	35	(7.2)	38	(7.8)
Anxiety disorder	1	(0.2)	0	(0.0)
Attention deficit hyperactivity disorder	4	(0.8)	2	(0.4)
Bipolar I disorder	0	(0.0)	1	(0.2)
Bulimia nervosa	1	(0.2)	0	(0.0)
Claustrophobia	0	(0.0)	1	(0.2)
Confusional state	1	(0.2)	0	(0.0)
Depressed mood	1	(0.2)	1	(0.2)
Depression	33	(6.8)	37	(7.6)
Drug abuse	0	(0.0)	1	(0.2)
Drug dependence	0	(0.0)	1	(0.2)
Generalised anxiety disorder	1	(0.2)	1	(0.2)
Insomnia	30	(6.2)	24	(4.9)
Libido decreased	1	(0.2)	0	(0.0)
Major depression	1	(0.2)	1	(0.2)
Mixed anxiety and depressive disorder	0	(0.0)	2	(0.4)
Neurosis	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Psychiatric disorders	**92**	**(19.0)**	**97**	**(20.0)**
Nicotine dependence	0	(0.0)	1	(0.2)
Obsessive-compulsive disorder	0	(0.0)	1	(0.2)
Panic attack	1	(0.2)	0	(0.0)
Panic disorder	0	(0.0)	1	(0.2)
Personality disorder	1	(0.2)	0	(0.0)
Post-traumatic stress disorder	0	(0.0)	1	(0.2)
Premature ejaculation	0	(0.0)	1	(0.2)
Schizoaffective disorder	1	(0.2)	0	(0.0)
Sleep disorder	3	(0.6)	4	(0.8)
Sleep terror	1	(0.2)	0	(0.0)
Social anxiety disorder	0	(0.0)	1	(0.2)
Stress	1	(0.2)	0	(0.0)
Tobacco abuse	3	(0.6)	6	(1.2)
Renal and urinary disorders	**52**	**(10.8)**	**60**	**(12.3)**
Bladder diverticulum	0	(0.0)	1	(0.2)
Bladder hypertrophy	0	(0.0)	1	(0.2)
Bladder perforation	0	(0.0)	1	(0.2)
Bladder prolapse	0	(0.0)	3	(0.6)
Calculus urinary	2	(0.4)	1	(0.2)
Chronic kidney disease	2	(0.4)	7	(1.4)
Diabetic nephropathy	1	(0.2)	1	(0.2)
Glycosuria	1	(0.2)	0	(0.0)
Haematuria	3	(0.6)	3	(0.6)
Hydronephrosis	1	(0.2)	1	(0.2)
Hypercalciuria	1	(0.2)	0	(0.0)
Hypertonic bladder	0	(0.0)	1	(0.2)
Lower urinary tract symptoms	0	(0.0)	1	(0.2)
Microalbuminuria	0	(0.0)	1	(0.2)
Micturition disorder	0	(0.0)	1	(0.2)
Nephritis	0	(0.0)	2	(0.4)
Nephrolithiasis	16	(3.3)	7	(1.4)
Nephropathy	1	(0.2)	0	(0.0)
Nocturia	1	(0.2)	1	(0.2)
Pollakiuria	1	(0.2)	4	(0.8)
Polyuria	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Renal and urinary disorders	**52**	**(10.8)**	**60**	**(12.3)**
Proteinuria	2	(0.4)	4	(0.8)
Renal colic	1	(0.2)	1	(0.2)
Renal cyst	13	(2.7)	11	(2.3)
Renal disorder	0	(0.0)	1	(0.2)
Renal failure	3	(0.6)	3	(0.6)
Renal impairment	0	(0.0)	1	(0.2)
Renal infarct	1	(0.2)	0	(0.0)
Renal mass	0	(0.0)	1	(0.2)
Stress urinary incontinence	0	(0.0)	2	(0.4)
Ureteric stenosis	1	(0.2)	0	(0.0)
Ureterolithiasis	2	(0.4)	2	(0.4)
Urge incontinence	0	(0.0)	1	(0.2)
Urinary incontinence	1	(0.2)	4	(0.8)
Urinary retention	1	(0.2)	0	(0.0)
Urinary tract obstruction	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**60**	**(12.4)**	**80**	**(16.5)**
Asthenospermia	1	(0.2)	0	(0.0)
Atrophic vulvovaginitis	0	(0.0)	2	(0.4)
Benign prostatic hyperplasia	30	(6.2)	47	(9.7)
Breast calcifications	1	(0.2)	0	(0.0)
Breast cyst	3	(0.6)	2	(0.4)
Breast disorder	0	(0.0)	1	(0.2)
Breast mass	0	(0.0)	1	(0.2)
Breast swelling	0	(0.0)	1	(0.2)
Breast tenderness	0	(0.0)	1	(0.2)
Cervical dysplasia	0	(0.0)	1	(0.2)
Cystocele	0	(0.0)	1	(0.2)
Dysmenorrhoea	0	(0.0)	1	(0.2)
Endometriosis	0	(0.0)	2	(0.4)
Erectile dysfunction	3	(0.6)	8	(1.6)
Heavy menstrual bleeding	0	(0.0)	1	(0.2)
Oedema genital	1	(0.2)	0	(0.0)
Ovarian cyst	4	(0.8)	3	(0.6)
Pelvic pain	0	(0.0)	1	(0.2)
Penile dermatitis	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Reproductive system and breast disorders	**60**	**(12.4)**	**80**	**(16.5)**
Perineal disorder	1	(0.2)	0	(0.0)
Polycystic ovaries	1	(0.2)	0	(0.0)
Premenstrual dysphoric disorder	0	(0.0)	1	(0.2)
Premenstrual syndrome	1	(0.2)	0	(0.0)
Prostatic cyst	1	(0.2)	0	(0.0)
Prostatic disorder	0	(0.0)	2	(0.4)
Prostatism	2	(0.4)	0	(0.0)
Prostatitis	1	(0.2)	1	(0.2)
Prostatomegaly	2	(0.4)	3	(0.6)
Pruritus genital	0	(0.0)	1	(0.2)
Rectocele	1	(0.2)	1	(0.2)
Spermatocele	0	(0.0)	1	(0.2)
Testicular hypertrophy	1	(0.2)	0	(0.0)
Uterine cervical metaplasia	1	(0.2)	0	(0.0)
Uterine disorder	0	(0.0)	1	(0.2)
Uterine polyp	3	(0.6)	1	(0.2)
Uterine prolapse	2	(0.4)	1	(0.2)
Vaginal cyst	2	(0.4)	0	(0.0)
Vaginal haemorrhage	1	(0.2)	1	(0.2)
Vaginal lesion	0	(0.0)	1	(0.2)
Varicocele	0	(0.0)	1	(0.2)
Vulvovaginal dryness	2	(0.4)	0	(0.0)
Respiratory, tboracic and mediastinal disorders	**98**	**(20.3)**	**91**	**(18.7)**
Acquired diaphragmatic eventration	0	(0.0)	1	(0.2)
Allergic sinusitis	1	(0.2)	0	(0.0)
Asthma	25	(5.2)	22	(4.5)
Atelectasis	1	(0.2)	0	(0.0)
Bronchial hyperreactivity	1	(0.2)	2	(0.4)
Bronchial wall thickening	1	(0.2)	0	(0.0)
Bronchiectasis	0	(0.0)	1	(0.2)
Bronchitis chronic	2	(0.4)	0	(0.0)
Bronchospasm	1	(0.2)	0	(0.0)
Childhood asthma	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	3	(0.6)	10	(2.1)
Cough	8	(1.7)	10	(2.1)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**98**	**(20.3)**	**91**	**(18.7)**
Dyspnoea	5	(1.0)	4	(0.8)
Dyspnoea exertional	1	(0.2)	2	(0.4)
Emphysema	4	(0.8)	1	(0.2)
Epistaxis	1	(0.2)	1	(0.2)
Hypoxia	1	(0.2)	0	(0.0)
Laryngeal oedema	0	(0.0)	1	(0.2)
Lung disorder	0	(0.0)	2	(0.4)
Lung opacity	1	(0.2)	0	(0.0)
NSAID exacerbated respiratory disease	1	(0.2)	0	(0.0)
Nasal congestion	1	(0.2)	2	(0.4)
Nasal polyps	2	(0.4)	1	(0.2)
Nasal septum deviation	1	(0.2)	1	(0.2)
Obstructive sleep apnoea syndrome	10	(2.1)	8	(1.6)
Oropharyngeal pain	2	(0.4)	0	(0.0)
Pleural effusion	0	(0.0)	1	(0.2)
Pleurisy	0	(0.0)	2	(0.4)
Pneumothorax	1	(0.2)	0	(0.0)
Productive cough	2	(0.4)	1	(0.2)
Pulmonary embolism	10	(2.1)	5	(1.0)
Pulmonary fibrosis	0	(0.0)	1	(0.2)
Pulmonary granuloma	1	(0.2)	2	(0.4)
Pulmonary hilum mass	0	(0.0)	1	(0.2)
Pulmonary hypertension	2	(0.4)	0	(0.0)
Pulmonary infarction	1	(0.2)	0	(0.0)
Pulmonary mass	9	(1.9)	8	(1.6)
Pulmonary sarcoidosis	1	(0.2)	0	(0.0)
Reactive airways dysfunction syndrome	1	(0.2)	0	(0.0)
Respiratory failure	0	(0.0)	1	(0.2)
Rhinitis allergic	14	(2.9)	8	(1.6)
Rhinorrhoea	2	(0.4)	3	(0.6)
Sinus disorder	0	(0.0)	1	(0.2)
Sleep apnoea syndrome	14	(2.9)	10	(2.1)
Upper-airway cough syndrome	2	(0.4)	3	(0.6)
Skin and subcutaneous tissue disorders	**99**	**(20.5)**	**88**	**(18.1)**
Acne	3	(0.6)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**99**	**(20.5)**	**88**	**(18.1)**
Acne cystic	1	(0.2)	0	(0.0)
Actinic elastosis	4	(0.8)	0	(0.0)
Actinic keratosis	13	(2.7)	14	(2.9)
Alopecia	4	(0.8)	2	(0.4)
Blister	1	(0.2)	0	(0.0)
Cold urticaria	0	(0.0)	1	(0.2)
Dermal cyst	3	(0.6)	1	(0.2)
Dermatitis	2	(0.4)	2	(0.4)
Dermatitis acneiform	1	(0.2)	1	(0.2)
Dermatitis allergic	0	(0.0)	1	(0.2)
Dermatitis atopic	0	(0.0)	1	(0.2)
Dermatitis contact	3	(0.6)	2	(0.4)
Dermatitis exfoliative generalised	0	(0.0)	1	(0.2)
Diabetic foot	0	(0.0)	1	(0.2)
Drug eruption	1	(0.2)	0	(0.0)
Dry skin	11	(2.3)	7	(1.4)
Dyshidrotic eczema	2	(0.4)	0	(0.0)
Ecchymosis	1	(0.2)	0	(0.0)
Eczema	4	(0.8)	9	(1.9)
Erythema	2	(0.4)	1	(0.2)
Hangnail	1	(0.2)	0	(0.0)
Hidradenitis	3	(0.6)	0	(0.0)
Hirsutism	0	(0.0)	1	(0.2)
Hyperhidrosis	0	(0.0)	1	(0.2)
Hyperkeratosis	1	(0.2)	1	(0.2)
Ingrowing nail	1	(0.2)	0	(0.0)
Intertrigo	2	(0.4)	1	(0.2)
Lentigo	0	(0.0)	2	(0.4)
Lichen planus	1	(0.2)	1	(0.2)
Nail bed disorder	1	(0.2)	0	(0.0)
Neurodermatitis	0	(0.0)	1	(0.2)
Night sweats	1	(0.2)	0	(0.0)
Palmoplantar keratoderma	0	(0.0)	1	(0.2)
Photodermatosis	2	(0.4)	1	(0.2)
Pigmentation disorder	1	(0.2)	0	(0.0)
Polymorphic light eruption	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**99**	**(20.5)**	**88**	**(18.1)**
Pruritus	7	(1.4)	6	(1.2)
Psoriasis	8	(1.7)	6	(1.2)
Rash	14	(2.9)	7	(1.4)
Rash erythematous	0	(0.0)	1	(0.2)
Rash maculo-papular	3	(0.6)	0	(0.0)
Rash pruritic	1	(0.2)	1	(0.2)
Rosacea	6	(1.2)	4	(0.8)
Scab	2	(0.4)	0	(0.0)
Scar pain	2	(0.4)	2	(0.4)
Seborrhoea	0	(0.0)	1	(0.2)
Seborrhoeic dermatitis	0	(0.0)	2	(0.4)
Sensitive skin	0	(0.0)	1	(0.2)
Skin discolouration	1	(0.2)	0	(0.0)
Skin disorder	0	(0.0)	1	(0.2)
Skin erosion	1	(0.2)	0	(0.0)
Skin exfoliation	0	(0.0)	1	(0.2)
Skin fissures	1	(0.2)	0	(0.0)
Skin fragility	0	(0.0)	1	(0.2)
Skin hypopigmentation	0	(0.0)	1	(0.2)
Skin induration	0	(0.0)	1	(0.2)
Skin irritation	0	(0.0)	1	(0.2)
Skin lesion	3	(0.6)	1	(0.2)
Skin maceration	1	(0.2)	0	(0.0)
Skin mass	1	(0.2)	0	(0.0)
Skin ulcer	2	(0.4)	1	(0.2)
Solar dermatitis	1	(0.2)	0	(0.0)
Solar lentigo	4	(0.8)	1	(0.2)
Solar urticaria	1	(0.2)	0	(0.0)
Stasis dermatitis	2	(0.4)	0	(0.0)
Transient acantholytic dermatosis	2	(0.4)	0	(0.0)
Urticaria	2	(0.4)	2	(0.4)
Vitiligo	1	(0.2)	4	(0.8)
Xanthelasma	0	(0.0)	1	(0.2)
Xeroderma	1	(0.2)	1	(0.2)
Social circumstances	**22**	**(4.6)**	**28**	**(5.8)**

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Social circumstances	**22**	**(4.6)**	**28**	**(5.8)**
Alcohol use	2	(0.4)	0	(0.0)
Corrective lens user	0	(0.0)	1	(0.2)
Ex-alcoholic	0	(0.0)	1	(0.2)
Ex-tobacco user	4	(0.8)	8	(1.6)
Menopause	7	(1.4)	7	(1.4)
Postmenopause	2	(0.4)	1	(0.2)
Substance use	0	(0.0)	1	(0.2)
Tobacco user	8	(1.7)	12	(2.5)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Abdominal hernia repair	0	(0.0)	1	(0.2)
Acrochordon excision	1	(0.2)	0	(0.0)
Adenoidectomy	2	(0.4)	1	(0.2)
Adenotonsillectomy	1	(0.2)	1	(0.2)
Angioplasty	1	(0.2)	0	(0.0)
Aortic aneurysm repair	0	(0.0)	1	(0.2)
Aortic valve repair	0	(0.0)	1	(0.2)
Aortic valve replacement	3	(0.6)	0	(0.0)
Appendicectomy	25	(5.2)	26	(5.3)
Arthrodesis	0	(0.0)	1	(0.2)
Atrial appendage closure	1	(0.2)	0	(0.0)
Benign breast lump removal	1	(0.2)	0	(0.0)
Benign tumour excision	0	(0.0)	1	(0.2)
Bladder repair	0	(0.0)	1	(0.2)
Breast conserving surgery	1	(0.2)	1	(0.2)
Breast cyst excision	1	(0.2)	0	(0.0)
Breast tumour excision	0	(0.0)	2	(0.4)
Bunion operation	1	(0.2)	2	(0.4)
Bursal operation	0	(0.0)	1	(0.2)
Caesarean section	1	(0.2)	7	(1.4)
Cancer surgery	2	(0.4)	3	(0.6)
Cardiac ablation	1	(0.2)	1	(0.2)
Cardiac pacemaker insertion	1	(0.2)	3	(0.6)
Cardiac resynchronisation therapy	1	(0.2)	0	(0.0)
Carpal tunnel decompression	4	(0.8)	3	(0.6)
Cartilage operation	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Cataract operation	8	(1.7)	6	(1.2)
Cervical laser therapy	1	(0.2)	0	(0.0)
Cheilectomy	0	(0.0)	1	(0.2)
Cholecystectomy	16	(3.3)	20	(4.1)
Choledochectomy	1	(0.2)	0	(0.0)
Circumcision	1	(0.2)	0	(0.0)
Colectomy	5	(1.0)	0	(0.0)
Colorectostomy	1	(0.2)	0	(0.0)
Colostomy	1	(0.2)	1	(0.2)
Corneal transplant	1	(0.2)	0	(0.0)
Coronary angioplasty	0	(0.0)	3	(0.6)
Coronary arterial stent insertion	5	(1.0)	4	(0.8)
Coronary artery bypass	5	(1.0)	4	(0.8)
Cox-Maze procedure	1	(0.2)	0	(0.0)
Cryotherapy	2	(0.4)	1	(0.2)
Cyst drainage	1	(0.2)	0	(0.0)
Cyst removal	2	(0.4)	2	(0.4)
Dental care	1	(0.2)	0	(0.0)
Dental implantation	2	(0.4)	0	(0.0)
Dental operation	0	(0.0)	1	(0.2)
Ear tube insertion	1	(0.2)	0	(0.0)
Elbow operation	0	(0.0)	1	(0.2)
Endodontic procedure	1	(0.2)	0	(0.0)
Eye operation	1	(0.2)	2	(0.4)
Eye prosthesis insertion	1	(0.2)	0	(0.0)
Eyelid operation	0	(0.0)	1	(0.2)
Face lift	0	(0.0)	1	(0.2)
Female sterilisation	3	(0.6)	8	(1.6)
Finger amputation	2	(0.4)	1	(0.2)
Fistula repair	1	(0.2)	0	(0.0)
Foot amputation	0	(0.0)	1	(0.2)
Foot operation	0	(0.0)	1	(0.2)
Fracture reduction	0	(0.0)	1	(0.2)
Fracture treatment	2	(0.4)	2	(0.4)
Functional endoscopic sinus surgery	1	(0.2)	0	(0.0)
Gastrectomy	0	(0.0)	3	(0.6)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Gastric bypass	3	(0.6)	0	(0.0)
Haemorrhoid operation	4	(0.8)	4	(0.8)
Hearing aid therapy	0	(0.0)	1	(0.2)
Hernia hiatus repair	2	(0.4)	0	(0.0)
Hernia repair	4	(0.8)	5	(1.0)
Hip arthroplasty	6	(1.2)	8	(1.6)
Hip surgery	1	(0.2)	1	(0.2)
Hymenectomy	1	(0.2)	0	(0.0)
Hysterectomy	14	(2.9)	18	(3.7)
Hysterosalpingo-oophorectomy	3	(0.6)	3	(0.6)
Immune tolerance induction	0	(0.0)	1	(0.2)
Incisional hernia repair	1	(0.2)	0	(0.0)
Inguinal hernia repair	5	(1.0)	11	(2.3)
Internal fixation of fracture	0	(0.0)	1	(0.2)
Internal fixation of spine	0	(0.0)	1	(0.2)
Intervertebral disc operation	4	(0.8)	4	(0.8)
Intestinal polypectomy	1	(0.2)	0	(0.0)
Intestinal resection	1	(0.2)	0	(0.0)
Intraocular lens implant	1	(0.2)	1	(0.2)
Jaw operation	0	(0.0)	1	(0.2)
Joint arthroplasty	1	(0.2)	0	(0.0)
Keratomileusis	1	(0.2)	1	(0.2)
Knee arthroplasty	10	(2.1)	11	(2.3)
Knee operation	4	(0.8)	6	(1.2)
Large intestinal polypectomy	1	(0.2)	0	(0.0)
Lesion excision	0	(0.0)	1	(0.2)
Ligament operation	0	(0.0)	4	(0.8)
Limb operation	0	(0.0)	1	(0.2)
Lipoma excision	2	(0.4)	1	(0.2)
Lithotripsy	1	(0.2)	0	(0.0)
Loop electrosurgical excision procedure	1	(0.2)	0	(0.0)
Lung lobectomy	1	(0.2)	0	(0.0)
Lymphadenectomy	1	(0.2)	0	(0.0)
Mammoplasty	1	(0.2)	2	(0.4)
Mass excision	0	(0.0)	1	(0.2)
Mastectomy	0	(0.0)	2	(0.4)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Medical device implantation	1	(0.2)	0	(0.0)
Meniscus operation	1	(0.2)	2	(0.4)
Meniscus removal	3	(0.6)	2	(0.4)
Micrographic skin surgery	3	(0.6)	1	(0.2)
Mitral valve repair	1	(0.2)	0	(0.0)
Mole excision	1	(0.2)	0	(0.0)
Muscle operation	1	(0.2)	0	(0.0)
Myomectomy	2	(0.4)	0	(0.0)
Myopia correction	0	(0.0)	1	(0.2)
Nasal operation	1	(0.2)	0	(0.0)
Nasal polypectomy	1	(0.2)	0	(0.0)
Nasal septal operation	0	(0.0)	2	(0.4)
Neck dissection	0	(0.0)	1	(0.2)
Neck surgery	0	(0.0)	1	(0.2)
Nephrectomy	0	(0.0)	3	(0.6)
Nerve block	1	(0.2)	1	(0.2)
Oophorectomy	2	(0.4)	2	(0.4)
Oophorectomy bilateral	1	(0.2)	0	(0.0)
Open reduction of fracture	1	(0.2)	1	(0.2)
Oral surgery	1	(0.2)	0	(0.0)
Orchidectomy	1	(0.2)	0	(0.0)
Osteoporosis prophylaxis	0	(0.0)	1	(0.2)
Osteotomy	1	(0.2)	0	(0.0)
Ovarian cystectomy	0	(0.0)	3	(0.6)
Pancreaticoduodenectomy	0	(0.0)	1	(0.2)
Parathyroidectomy	0	(0.0)	2	(0.4)
Parotid cyst excision	0	(0.0)	1	(0.2)
Pelvic operation	1	(0.2)	0	(0.0)
Penile operation	1	(0.2)	0	(0.0)
Peripheral artery bypass	0	(0.0)	1	(0.2)
Peripheral nerve decompression	1	(0.2)	0	(0.0)
Phlebectomy	2	(0.4)	1	(0.2)
Plastic surgery	0	(0.0)	1	(0.2)
Plastic surgery to the face	1	(0.2)	0	(0.0)
Polypectomy	0	(0.0)	2	(0.4)
Positive airway pressure therapy	1	(0.2)	0	(0.0)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Proctectomy	1	(0.2)	0	(0.0)
Prostatectomy	3	(0.6)	3	(0.6)
Prostatic operation	0	(0.0)	1	(0.2)
Radical cystectomy	0	(0.0)	1	(0.2)
Rectal prolapse repair	0	(0.0)	1	(0.2)
Renal stone removal	2	(0.4)	2	(0.4)
Retinal operation	0	(0.0)	2	(0.4)
Rhinoplasty	1	(0.2)	2	(0.4)
Rotator cuff repair	1	(0.2)	3	(0.6)
Salivary gland calculus removal	1	(0.2)	0	(0.0)
Salpingectomy	0	(0.0)	2	(0.4)
Salpingo-oophorectomy	1	(0.2)	0	(0.0)
Salpingo-oophorectomy bilateral	0	(0.0)	1	(0.2)
Salpingoplasty	0	(0.0)	1	(0.2)
Shoulder arthroplasty	0	(0.0)	2	(0.4)
Shoulder operation	0	(0.0)	2	(0.4)
Sigmoidectomy	1	(0.2)	0	(0.0)
Sinus operation	2	(0.4)	1	(0.2)
Skin graft	4	(0.8)	5	(1.0)
Skin lesion removal	1	(0.2)	0	(0.0)
Skin neoplasm excision	12	(2.5)	12	(2.5)
Skin operation	0	(0.0)	1	(0.2)
Soft tissue flap operation	2	(0.4)	0	(0.0)
Spermatic cord operation	0	(0.0)	1	(0.2)
Spinal fusion surgery	0	(0.0)	1	(0.2)
Spinal laminectomy	2	(0.4)	1	(0.2)
Spinal nerve stimulator implantation	0	(0.0)	1	(0.2)
Spinal operation	2	(0.4)	2	(0.4)
Splenectomy	0	(0.0)	1	(0.2)
Stent placement	3	(0.6)	5	(1.0)
Sterilisation	0	(0.0)	1	(0.2)
Sterilisation reversal	0	(0.0)	1	(0.2)
Tendon operation	0	(0.0)	2	(0.4)
Tendon transfer	1	(0.2)	0	(0.0)
Tenoplasty	1	(0.2)	1	(0.2)
Testicular operation	0	(0.0)	1	(0.2)

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Surgical and medical procedures	**186**	**(38.5)**	**185**	**(38.1)**
Therapeutic aspiration	1	(0.2)	0	(0.0)
Thyroid adenoma removal	0	(0.0)	1	(0.2)
Thyroid operation	1	(0.2)	1	(0.2)
Thyroidectomy	7	(1.4)	6	(1.2)
Toe amputation	2	(0.4)	1	(0.2)
Toe operation	1	(0.2)	1	(0.2)
Tonsillectomy	11	(2.3)	20	(4.1)
Trabeculectomy	2	(0.4)	0	(0.0)
Trabeculoplasty	1	(0.2)	0	(0.0)
Transfusion	1	(0.2)	0	(0.0)
Transurethral bladder resection	0	(0.0)	4	(0.8)
Transurethral prostatectomy	4	(0.8)	3	(0.6)
Tumour excision	3	(0.6)	1	(0.2)
Tympanoplasty	0	(0.0)	1	(0.2)
Umbilical hernia repair	2	(0.4)	4	(0.8)
Ureteric repair	1	(0.2)	0	(0.0)
Urethral repair	1	(0.2)	0	(0.0)
Urinary bladder suspension	1	(0.2)	3	(0.6)
Urinary incontinence surgery	1	(0.2)	0	(0.0)
Uterine dilation and curettage	2	(0.4)	1	(0.2)
Uterine polypectomy	2	(0.4)	0	(0.0)
Uterine prolapse repair	1	(0.2)	0	(0.0)
Uvulopalatopharyngoplasty	0	(0.0)	1	(0.2)
Vaginal operation	0	(0.0)	2	(0.4)
Vagotomy	0	(0.0)	1	(0.2)
Varicocele repair	1	(0.2)	1	(0.2)
Varicose vein operation	5	(1.0)	3	(0.6)
Vascular graft	1	(0.2)	1	(0.2)
Vascular stent insertion	1	(0.2)	0	(0.0)
Vasectomy	5	(1.0)	8	(1.6)
Vitrectomy	1	(0.2)	1	(0.2)
Wisdom teeth removal	8	(1.7)	3	(0.6)
Wound treatment	1	(0.2)	0	(0.0)
Wrist surgery	1	(0.2)	1	(0.2)
Vascular disorders	**232**	**(48.0)**	**237**	**(48.8)**

Participants Medical History Conditions
(Incidence > 0% in One or More Treatment Group)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vascular disorders	**232**	**(48.0)**	**237**	**(48.8)**
Aortic aneurysm	4	(0.8)	4	(0.8)
Aortic arteriosclerosis	2	(0.4)	2	(0.4)
Aortic dilatation	1	(0.2)	2	(0.4)
Aortic stenosis	1	(0.2)	0	(0.0)
Aortic thrombosis	0	(0.0)	1	(0.2)
Arterial disorder	0	(0.0)	1	(0.2)
Arteriosclerosis	4	(0.8)	4	(0.8)
Deep vein thrombosis	8	(1.7)	5	(1.0)
Erythromelalgia	0	(0.0)	1	(0.2)
Essential hypertension	1	(0.2)	4	(0.8)
Haematoma	3	(0.6)	0	(0.0)
Hot flush	1	(0.2)	3	(0.6)
Hypertension	208	(43.1)	211	(43.4)
Hypertensive urgency	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)
Iliac artery stenosis	1	(0.2)	0	(0.0)
Lymphocele	3	(0.6)	3	(0.6)
Lymphoedema	5	(1.0)	4	(0.8)
Orthostatic hypotension	1	(0.2)	1	(0.2)
Peripheral arterial occlusive disease	0	(0.0)	4	(0.8)
Peripheral artery aneurysm	0	(0.0)	2	(0.4)
Peripheral artery dissection	0	(0.0)	1	(0.2)
Peripheral coldness	1	(0.2)	0	(0.0)
Peripheral vascular disorder	2	(0.4)	0	(0.0)
Peripheral venous disease	0	(0.0)	4	(0.8)
Phlebitis	2	(0.4)	3	(0.6)
Raynaud's phenomenon	0	(0.0)	1	(0.2)
Thrombosis	2	(0.4)	3	(0.6)
Varicose vein	11	(2.3)	5	(1.0)
Venous thrombosis limb	0	(0.0)	1	(0.2)
White coat hypertension	1	(0.2)	1	(0.2)

Every participant is counted a single time for each applicable specific condition. A participant with multiple conditions within a system organ class is counted a single time for that system organ class.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; admh]

Table 14.1-17
Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more concomitant medications	460	(95.2)	445	(91.6)
with no concomitant medication	23	(4.8)	41	(8.4)
ALIMENTARY TRACT AND METABOLISM				
ANABOLIC AGENTS FOR SYSTEMIC USE	**2**	**(0.4)**	**0**	**(0.0)**
PRASTERONE	2	(0.4)	0	(0.0)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	**238**	**(49.3)**	**108**	**(22.2)**
ALBUMIN TANNATE	1	(0.2)	0	(0.0)
AMPHOTERICIN B	4	(0.8)	1	(0.2)
ANTIDIARRHEAL MICROORGANISMS	0	(0.0)	1	(0.2)
ATROPINE SULFATE;DIPHENOXYLATE HYDROCHLORIDE	4	(0.8)	0	(0.0)
BACILLUS COAGULANS;INULIN	2	(0.4)	0	(0.0)
BACITRACIN	1	(0.2)	2	(0.4)
BACITRACIN;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
BECLOMETASONE DIPROPIONATE	5	(1.0)	4	(0.8)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE BUTYRATE PROPIONATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BIFIDOBACTERIUM BREVE;BIFIDOBACTERIUM INFANTIS;BIFIDOBACTERIUM LONGUM;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS BULGARICUS;LACTOBACILLUS PARACASEI;LACTOBACILLUS PLANTARUM;STREPTOCOCCUS THERMOPHILUS	1	(0.2)	0	(0.0)
BIFIDOBACTERIUM LACTIS;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS PARACASEI	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	**238**	**(49.3)**	**108**	**(22.2)**
BIFIDOBACTERIUM LONGUM;LACTOBACILLUS HELVETICUS;LACTOBACILLUS RHAMNOSUS	0	(0.0)	1	(0.2)
BISMUTH	1	(0.2)	0	(0.0)
BISMUTH SUBSALICYLATE	1	(0.2)	2	(0.4)
BUDESONIDE	9	(1.9)	6	(1.2)
CAMELLIA SINENSIS	1	(0.2)	0	(0.0)
CHARCOAL, ACTIVATED	0	(0.0)	2	(0.4)
CODEINE	2	(0.4)	4	(0.8)
COLESTYRAMINE	1	(0.2)	0	(0.0)
DIOSMECTITE	8	(1.7)	6	(1.2)
EUPATILIN	0	(0.0)	1	(0.2)
GLUCOSE MONOHYDRATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1	(0.2)	0	(0.0)
GLUCOSE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE BUTYRATE	3	(0.6)	0	(0.0)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
LACTOBACILLUS ACIDOPHILUS	0	(0.0)	3	(0.6)
LACTOBACILLUS NOS	1	(0.2)	1	(0.2)
LACTOBACILLUS RHAMNOSUS	1	(0.2)	0	(0.0)
LOPERAMIDE	14	(2.9)	9	(1.9)
LOPERAMIDE HYDROCHLORIDE	29	(6.0)	11	(2.3)
MACROGOL 4000;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE ANHYDROUS	1	(0.2)	0	(0.0)
MENTHOL	1	(0.2)	0	(0.0)
MESALAZINE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	**238**	**(49.3)**	**108**	**(22.2)**
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
NIFUROXAZIDE	1	(0.2)	0	(0.0)
NYSTATIN	13	(2.7)	4	(0.8)
PLANTAGO OVATA	4	(0.8)	2	(0.4)
PLANTAGO OVATA SEED	0	(0.0)	1	(0.2)
POVIDONE	0	(0.0)	1	(0.2)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PREDNISONE	99	(20.5)	29	(6.0)
PROBIOTICS NOS	2	(0.4)	8	(1.6)
PUNICA GRANATUM	0	(0.0)	1	(0.2)
RACECADOTRIL	7	(1.4)	7	(1.4)
RIFAXIMIN	1	(0.2)	2	(0.4)
SACCHAROMYCES BOULARDII	5	(1.0)	1	(0.2)
SILICON DIOXIDE, COLLOIDAL	1	(0.2)	0	(0.0)
TIXOCORTOL PIVALATE	1	(0.2)	1	(0.2)
VANCOMYCIN	2	(0.4)	4	(0.8)
VANCOMYCIN HYDROCHLORIDE	0	(0.0)	2	(0.4)
ANTIEMETICS AND ANTINAUSEANTS	**75**	**(15.5)**	**60**	**(12.3)**
ALIZAPRIDE	1	(0.2)	0	(0.0)
ALIZAPRIDE HYDROCHLORIDE	2	(0.4)	1	(0.2)
CANNABIS SATIVA	2	(0.4)	4	(0.8)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	2	(0.4)	0	(0.0)
DIFENIDOL HYDROCHLORIDE	1	(0.2)	0	(0.0)
DIMENHYDRINATE	1	(0.2)	1	(0.2)
DIPHENHYDRAMINE	4	(0.8)	2	(0.4)
DIPHENHYDRAMINE HYDROCHLORIDE	14	(2.9)	14	(2.9)
DOMPERIDONE	5	(1.0)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
ANTIEMETICS AND ANTINAUSEANTS	**75**	**(15.5)**	**60**	**(12.3)**
HYDROXYZINE	3	(0.6)	0	(0.0)
HYDROXYZINE HYDROCHLORIDE	5	(1.0)	6	(1.2)
HYOSCINE	2	(0.4)	0	(0.0)
MECLOZINE	1	(0.2)	2	(0.4)
METOCLOPRAMIDE	4	(0.8)	9	(1.9)
METOCLOPRAMIDE HYDROCHLORIDE	5	(1.0)	6	(1.2)
METOPIMAZINE	1	(0.2)	1	(0.2)
ONDANSETRON	14	(2.9)	16	(3.3)
ONDANSETRON HYDROCHLORIDE	11	(2.3)	4	(0.8)
PROCHLORPERAZINE	9	(1.9)	2	(0.4)
PROCHLORPERAZINE MALEATE	5	(1.0)	1	(0.2)
PROMETHAZINE	3	(0.6)	3	(0.6)
PROMETHAZINE HYDROCHLORIDE	3	(0.6)	2	(0.4)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS	**9**	**(1.9)**	**7**	**(1.4)**
ACETYLCARNITINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
AMFETAMINE ASPARTATE;AMFETAMINE SULFATE;DEXAMFETAMINE SACCHARATE;DEXAMFETAMINE SULFATE	0	(0.0)	1	(0.2)
BENZOCAINE	0	(0.0)	1	(0.2)
CAMELLIA SINENSIS	1	(0.2)	0	(0.0)
COLLAGEN	0	(0.0)	1	(0.2)
LIRAGLUTIDE	2	(0.4)	0	(0.0)
PLANTAGO OVATA	4	(0.8)	2	(0.4)
SEMAGLUTIDE	0	(0.0)	2	(0.4)
SPIRULINA SPP.	1	(0.2)	0	(0.0)
APPETITE STIMULANTS	**2**	**(0.4)**	**4**	**(0.8)**
CANNABIS SATIVA	2	(0.4)	4	(0.8)
BILE AND LIVER THERAPY	**25**	**(5.2)**	**17**	**(3.5)**
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
ANETHOLE TRITHIONE	1	(0.2)	0	(0.0)
BORNEOL;CAMPHENE;CINEOLE;MENTHOL; MENTHONE;PINENE	1	(0.2)	0	(0.0)
CURCUMA LONGA	8	(1.7)	5	(1.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
BILE AND LIVER THERAPY	**25**	**(5.2)**	**17**	**(3.5)**
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
LACTULOSE	7	(1.4)	4	(0.8)
LEVOGLUTAMIDE	0	(0.0)	1	(0.2)
RIFAXIMIN	1	(0.2)	2	(0.4)
ROSA CANINA	0	(0.0)	1	(0.2)
SILYBUM MARIANUM	1	(0.2)	0	(0.0)
DIGESTIVES, INCL. ENZYMES	**12**	**(2.5)**	**7**	**(1.4)**
ALPHA-AMYLASE SWINE PANCREAS	0	(0.0)	1	(0.2)
BROMELAINS	1	(0.2)	0	(0.0)
CALCIUM CARBONATE;CINNAMOMUM VERUM POWDER;COPTIS TRIFOLIA;DIASTASE, TAKA;FOENICULUM VULGARE;GLYCYRRHIZA GLABRA;MENTHOL;SIMALDRATE;SODIUM BICARBONATE;SYZYGIUM AROMATICUM FLOWER; ZANTHOXYLUM AMERICANUM BARK;ZINGIBER OFFICINALE RHIZOME	1	(0.2)	0	(0.0)
CETRARIA ISLANDICA	1	(0.2)	0	(0.0)
MONASCUS PURPUREUS	0	(0.0)	2	(0.4)
ORIGANUM VULGARE OIL	0	(0.0)	1	(0.2)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)
PANCREATIN	4	(0.8)	2	(0.4)
PRUNUS DOMESTICA	1	(0.2)	0	(0.0)
SILYBUM MARIANUM	1	(0.2)	0	(0.0)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
DRUGS FOR ACID RELATED DISORDERS	**162**	**(33.5)**	**113**	**(23.3)**
ALMAGATE	1	(0.2)	0	(0.0)
ALUMINIUM HYDROXIDE;MAGNESIUM CARBONATE	0	(0.0)	2	(0.4)
ALUMINIUM HYDROXIDE;MAGNESIUM CARBONATE;SIMETICONE	0	(0.0)	1	(0.2)
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE	3	(0.6)	2	(0.4)
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE;MAGNESIUM TRISILICATE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS FOR ACID RELATED DISORDERS	**162**	**(33.5)**	**113**	**(23.3)**
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE;SIMETICONE	1	(0.2)	0	(0.0)
BISMUTH	1	(0.2)	0	(0.0)
BISMUTH SUBCITRATE POTASSIUM;METRONIDAZOLE;TETRACYCLINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
BISMUTH SUBSALICYLATE	1	(0.2)	2	(0.4)
CALCIUM CARBONATE	11	(2.3)	7	(1.4)
CALCIUM CARBONATE;CALCIUM LACTATE GLUCONATE	0	(0.0)	1	(0.2)
CALCIUM CARBONATE;FAMOTIDINE;MAGNESIUM HYDROXIDE	1	(0.2)	0	(0.0)
CALCIUM CARBONATE;MAGNESIUM CARBONATE	0	(0.0)	1	(0.2)
CALCIUM CARBONATE;SODIUM ALGINATE;SODIUM BICARBONATE	5	(1.0)	3	(0.6)
CALCIUM;MAGNESIUM	1	(0.2)	1	(0.2)
DEXLANSOPRAZOLE	0	(0.0)	3	(0.6)
ESOMEPRAZOLE	8	(1.7)	6	(1.2)
ESOMEPRAZOLE MAGNESIUM	16	(3.3)	12	(2.5)
EUPATILIN	0	(0.0)	1	(0.2)
FAMOTIDINE	9	(1.9)	6	(1.2)
LANSOPRAZOLE	15	(3.1)	6	(1.2)
MAGALDRATE	1	(0.2)	0	(0.0)
MAGNESIUM CARBONATE	1	(0.2)	1	(0.2)
MAGNESIUM HYDROXIDE	0	(0.0)	2	(0.4)
MAGNESIUM OXIDE	3	(0.6)	3	(0.6)
OMEPRAZOLE	41	(8.5)	26	(5.3)
OMEPRAZOLE MAGNESIUM	1	(0.2)	0	(0.0)
PANTOPRAZOLE	43	(8.9)	31	(6.4)
PANTOPRAZOLE HEMIMAGNESIUM HYDRATE	1	(0.2)	0	(0.0)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	22	(4.6)	6	(1.2)
RABEPRAZOLE SODIUM	6	(1.2)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS FOR ACID RELATED DISORDERS	**162**	**(33.5)**	**113**	**(23.3)**
RANITIDINE	3	(0.6)	1	(0.2)
RANITIDINE HYDROCHLORIDE	3	(0.6)	3	(0.6)
SODIUM ALGINATE	0	(0.0)	2	(0.4)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SUCRALFATE	0	(0.0)	1	(0.2)
SULPIRIDE	1	(0.2)	0	(0.0)
TEPRENONE	1	(0.2)	0	(0.0)
DRUGS FOR CONSTIPATION	**68**	**(14.1)**	**67**	**(13.8)**
ALOE VERA	2	(0.4)	0	(0.0)
ALOIN;FRANGULA PURSHIANA;FRANGULA PURSHIANA BARK	1	(0.2)	0	(0.0)
BIFIDOBACTERIUM BIFIDUM;INULIN;LACTOBACILLUS ACIDOPHILUS;PLANTAGO OVATA HUSK	0	(0.0)	1	(0.2)
BISACODYL	4	(0.8)	3	(0.6)
CARMELLOSE SODIUM	2	(0.4)	1	(0.2)
CYAMOPSIS TETRAGONOLOBA GUM	0	(0.0)	1	(0.2)
DOCUSATE SODIUM	6	(1.2)	7	(1.4)
DOCUSATE SODIUM;SENNA ALEXANDRINA	2	(0.4)	1	(0.2)
DOCUSATE SODIUM;SENNOSIDE A+B	3	(0.6)	0	(0.0)
ELECTROLYTES NOS;MACROGOL 3350	1	(0.2)	0	(0.0)
FIBRE, DIETARY	0	(0.0)	1	(0.2)
FICUS CARICA FRUIT;SENNA ALEXANDRINA FRUIT;SENNOSIDE B	0	(0.0)	1	(0.2)
GLYCEROL	1	(0.2)	0	(0.0)
LACTULOSE	7	(1.4)	4	(0.8)
LINACLOTIDE	0	(0.0)	1	(0.2)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
MACROGOL	3	(0.6)	4	(0.8)
MACROGOL 3350	2	(0.4)	7	(1.4)
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	6	(1.2)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS FOR CONSTIPATION	**68**	**(14.1)**	**67**	**(13.8)**
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE ANHYDROUS	1	(0.2)	0	(0.0)
MACROGOL 4000;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE;SODIUM SULFATE ANHYDROUS	1	(0.2)	0	(0.0)
MAGNESIUM CARBONATE	1	(0.2)	1	(0.2)
MAGNESIUM CITRATE	0	(0.0)	4	(0.8)
MAGNESIUM HYDROXIDE	0	(0.0)	2	(0.4)
MAGNESIUM OXIDE	3	(0.6)	3	(0.6)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
METHYLCELLULOSE	0	(0.0)	1	(0.2)
PARAFFIN	1	(0.2)	1	(0.2)
PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
PLANTAGO OVATA	4	(0.8)	2	(0.4)
PLANTAGO OVATA HUSK	1	(0.2)	0	(0.0)
PLANTAGO OVATA SEED	0	(0.0)	1	(0.2)
PLANTAGO OVATA SEED HUSK	1	(0.2)	0	(0.0)
POLYCARBOPHIL CALCIUM	0	(0.0)	1	(0.2)
POTASSIUM BITARTRATE;SODIUM BICARBONATE	0	(0.0)	1	(0.2)
POTASSIUM PHOSPHATE DIBASIC	0	(0.0)	1	(0.2)
PROBIOTICS NOS	2	(0.4)	8	(1.6)
PRUNUS DOMESTICA	1	(0.2)	0	(0.0)
ROSA CANINA	0	(0.0)	1	(0.2)
SENNA ALEXANDRINA	4	(0.8)	3	(0.6)
SENNOSIDE A+B	2	(0.4)	4	(0.8)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
SODIUM PHOSPHATE DIBASIC	0	(0.0)	2	(0.4)
SODIUM PICOSULFATE	1	(0.2)	1	(0.2)
STERCULIA URENS GUM	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	**48**	**(9.9)**	**34**	**(7.0)**
ADIPHENINE HYDROCHLORIDE;METAMIZOLE SODIUM;PROMETHAZINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
ALIZAPRIDE	1	(0.2)	0	(0.0)
ALIZAPRIDE HYDROCHLORIDE	2	(0.4)	1	(0.2)
ALVERINE CITRATE;SIMETICONE	1	(0.2)	1	(0.2)
BOSWELLIA SACRA	0	(0.0)	1	(0.2)
CHLORDIAZEPOXIDE;CLIDINIUM BROMIDE	1	(0.2)	0	(0.0)
CLEBOPRIDE	1	(0.2)	0	(0.0)
CURCUMA LONGA	8	(1.7)	5	(1.0)
DEXPANTHENOL	4	(0.8)	0	(0.0)
DICYCLOVERINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
DIMETICONE;SILICON DIOXIDE	1	(0.2)	0	(0.0)
DOMPERIDONE	5	(1.0)	4	(0.8)
GLYCOPYRRONIUM BROMIDE	1	(0.2)	2	(0.4)
HYOSCINE	2	(0.4)	0	(0.0)
HYOSCINE BUTYLBROMIDE	2	(0.4)	2	(0.4)
ITOPRIDE HYDROCHLORIDE	1	(0.2)	0	(0.0)
MEBEVERINE	1	(0.2)	0	(0.0)
MENTHA X PIPERITA OIL	1	(0.2)	0	(0.0)
METOCLOPRAMIDE	4	(0.8)	9	(1.9)
METOCLOPRAMIDE HYDROCHLORIDE	5	(1.0)	6	(1.2)
OTILONIUM BROMIDE	1	(0.2)	0	(0.0)
PAPAVERINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
PHLOROGLUCINOL	1	(0.2)	0	(0.0)
PHLOROGLUCINOL;TRIMETHYLPHLOROGLUCINOL	4	(0.8)	3	(0.6)
SILICON DIOXIDE, COLLOIDAL	1	(0.2)	0	(0.0)
SIMETICONE	3	(0.6)	0	(0.0)
TRIMEBUTINE	3	(0.6)	2	(0.4)
TRIMEBUTINE MALEATE	1	(0.2)	1	(0.2)
TROSPIUM CHLORIDE	1	(0.2)	1	(0.2)
VALERIANA OFFICINALIS	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	**48**	**(9.9)**	**34**	**(7.0)**
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
DRUGS USED IN DIABETES	**67**	**(13.9)**	**66**	**(13.6)**
CANAGLIFLOZIN	0	(0.0)	1	(0.2)
CYAMOPSIS TETRAGONOLOBA GUM	0	(0.0)	1	(0.2)
DAPAGLIFLOZIN	1	(0.2)	0	(0.0)
DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE	2	(0.4)	4	(0.8)
DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE;METFORMIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE;SAXAGLIPTIN HYDROCHLORIDE	0	(0.0)	1	(0.2)
DULAGLUTIDE	3	(0.6)	4	(0.8)
EMPAGLIFLOZIN	4	(0.8)	6	(1.2)
EMPAGLIFLOZIN;METFORMIN HYDROCHLORIDE	1	(0.2)	1	(0.2)
GLICLAZIDE	5	(1.0)	8	(1.6)
GLIMEPIRIDE	4	(0.8)	5	(1.0)
GLIPIZIDE	1	(0.2)	0	(0.0)
INSULIN	3	(0.6)	6	(1.2)
INSULIN ASPART	7	(1.4)	5	(1.0)
INSULIN ASPART;INSULIN ASPART PROTAMINE (CRYSTALLINE)	1	(0.2)	1	(0.2)
INSULIN DEGLUDEC	3	(0.6)	5	(1.0)
INSULIN DEGLUDEC;LIRAGLUTIDE	0	(0.0)	1	(0.2)
INSULIN DETEMIR	1	(0.2)	1	(0.2)
INSULIN GLARGINE	12	(2.5)	8	(1.6)
INSULIN GLULISINE	0	(0.0)	1	(0.2)
INSULIN HUMAN	3	(0.6)	4	(0.8)
INSULIN HUMAN INJECTION, ISOPHANE	1	(0.2)	3	(0.6)
INSULIN HUMAN;INSULIN HUMAN INJECTION, ISOPHANE	0	(0.0)	1	(0.2)
INSULIN ISOPHANE PORCINE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
DRUGS USED IN DIABETES	**67**	**(13.9)**	**66**	**(13.6)**
INSULIN LISPRO	2	(0.4)	4	(0.8)
INSULIN LISPRO;INSULIN LISPRO PROTAMINE SUSPENSION	0	(0.0)	1	(0.2)
LINAGLIPTIN	0	(0.0)	1	(0.2)
LINAGLIPTIN;METFORMIN HYDROCHLORIDE	1	(0.2)	1	(0.2)
LIRAGLUTIDE	2	(0.4)	0	(0.0)
METFORMIN	32	(6.6)	31	(6.4)
METFORMIN HYDROCHLORIDE	20	(4.1)	18	(3.7)
METFORMIN HYDROCHLORIDE;PIOGLITAZONE HYDROCHLORIDE	0	(0.0)	1	(0.2)
METFORMIN HYDROCHLORIDE;SAXAGLIPTIN HYDROCHLORIDE	0	(0.0)	1	(0.2)
METFORMIN HYDROCHLORIDE;SITAGLIPTIN	1	(0.2)	1	(0.2)
METFORMIN HYDROCHLORIDE;SITAGLIPTIN PHOSPHATE MONOHYDRATE	3	(0.6)	4	(0.8)
METFORMIN HYDROCHLORIDE;VILDAGLIPTIN	1	(0.2)	1	(0.2)
PIOGLITAZONE	2	(0.4)	0	(0.0)
PIOGLITAZONE HYDROCHLORIDE	0	(0.0)	1	(0.2)
REPAGLINIDE	2	(0.4)	1	(0.2)
SAXAGLIPTIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
SEMAGLUTIDE	0	(0.0)	2	(0.4)
SITAGLIPTIN	4	(0.8)	2	(0.4)
SITAGLIPTIN PHOSPHATE	1	(0.2)	1	(0.2)
MINERAL SUPPLEMENTS	**85**	**(17.6)**	**85**	**(17.5)**
BORON	1	(0.2)	0	(0.0)
CALCIUM	2	(0.4)	8	(1.6)
CALCIUM ACETATE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
MINERAL SUPPLEMENTS	**85**	**(17.6)**	**85**	**(17.5)**
CALCIUM ASCORBATE DIHYDRATE;COLECALCIFEROL;MAGNESIUM OXIDE;MAGNESIUM PHOSPHATE PENTAHYDRATE;MANGANESE AMINO ACID CHELATE;PYRIDOXINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CALCIUM CARBONATE	11	(2.3)	7	(1.4)
CALCIUM CARBONATE;CALCIUM LACTATE GLUCONATE	0	(0.0)	1	(0.2)
CALCIUM CARBONATE;COLECALCIFEROL	9	(1.9)	5	(1.0)
CALCIUM CARBONATE;COLECALCIFEROL;PHYTOMENADIONE	1	(0.2)	1	(0.2)
CALCIUM CARBONATE;ERGOCALCIFEROL	0	(0.0)	1	(0.2)
CALCIUM CARBONATE;MAGNESIUM CARBONATE	0	(0.0)	1	(0.2)
CALCIUM CARBONATE;MAGNESIUM CHLORIDE	0	(0.0)	1	(0.2)
CALCIUM CITRATE	2	(0.4)	0	(0.0)
CALCIUM PHOSPHATE MONOBASIC;MAGNESIUM GLYCEROPHOSPHATE;PHOSPHORIC ACID;SODIUM PHOSPHATE DIBASIC	1	(0.2)	0	(0.0)
CALCIUM;COLECALCIFEROL	2	(0.4)	0	(0.0)
CALCIUM;MAGNESIUM	1	(0.2)	1	(0.2)
CALCIUM;VITAMIN D NOS	2	(0.4)	0	(0.0)
DL-ALPHA TOCOPHERYL ACETATE;MAGNESIUM HYDROXIDE;PYRIDOXINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MAGNESIUM	14	(2.9)	15	(3.1)
MAGNESIUM ASPARTATE	1	(0.2)	0	(0.0)
MAGNESIUM ASPARTATE HYDROCHLORIDE	1	(0.2)	1	(0.2)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
MINERAL SUPPLEMENTS	**85**	**(17.6)**	**85**	**(17.5)**
MAGNESIUM CARBONATE	1	(0.2)	1	(0.2)
MAGNESIUM CITRATE	0	(0.0)	4	(0.8)
MAGNESIUM GLUTAMATE	0	(0.0)	1	(0.2)
MAGNESIUM HYDROXIDE	0	(0.0)	2	(0.4)
MAGNESIUM OXIDE	3	(0.6)	3	(0.6)
MAGNESIUM PHOSPHATE;POTASSIUM PHOSPHATE DIBASIC;SODIUM SULFATE ANHYDROUS	0	(0.0)	1	(0.2)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
OTHER MINERAL PRODUCTS	0	(0.0)	2	(0.4)
POTASSIUM	0	(0.0)	4	(0.8)
POTASSIUM BICARBONATE;SODIUM BICARBONATE;SODIUM PHOSPHATE MONOBASIC (ANHYDROUS)	0	(0.0)	1	(0.2)
POTASSIUM CHLORIDE	16	(3.3)	9	(1.9)
POTASSIUM GLUCONATE	2	(0.4)	0	(0.0)
POTASSIUM PHOSPHATE DIBASIC	0	(0.0)	1	(0.2)
POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC;SODIUM PHOSPHATE DIBASIC;SODIUM PHOSPHATE MONOBASIC	2	(0.4)	2	(0.4)
POTASSIUM PHOSPHATE MONOBASIC	0	(0.0)	1	(0.2)
POTASSIUM PHOSPHATE MONOBASIC;SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
SELENIUM	4	(0.8)	0	(0.0)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM FLUORIDE	2	(0.4)	0	(0.0)
SODIUM FLUOROPHOSPHATE	0	(0.0)	1	(0.2)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
SODIUM PHOSPHATE DIBASIC	0	(0.0)	2	(0.4)
ZINC	1	(0.2)	5	(1.0)
ZINC CITRATE	0	(0.0)	1	(0.2)
ZINC OXIDE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	**25**	**(5.2)**	**29**	**(6.0)**
ACETYLCARNITINE;CITICOLINE;PANTOTHENIC ACID;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIOCTIC ACID;VITAMIN B1 NOS;VITAMIN B12 NOS	0	(0.0)	1	(0.2)
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
ANETHOLE TRITHIONE	1	(0.2)	0	(0.0)
ASTAXANTHIN	0	(0.0)	1	(0.2)
BIFIDOBACTERIUM NOS;LACTOBACILLUS ACIDOPHILUS;LACTOBACILLUS PARACASEI;STREPTOCOCCUS THERMOPHILUS	0	(0.0)	1	(0.2)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;POTASSIUM PHOSPHATE DIBASIC;POTASSIUM PHOSPHATE MONOBASIC;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;PROTEINS NOS;VITAMINS NOS	1	(0.2)	0	(0.0)
FIBRE, DIETARY	0	(0.0)	1	(0.2)
LEVOCARNITINE	0	(0.0)	1	(0.2)
LEVOGLUTAMIDE	0	(0.0)	1	(0.2)
LYSINE	0	(0.0)	2	(0.4)
LYSINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
PROBIOTICS NOS	2	(0.4)	8	(1.6)
QUERCETIN	1	(0.2)	0	(0.0)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SUCRALFATE	0	(0.0)	1	(0.2)
THIOCTIC ACID	1	(0.2)	0	(0.0)
UBIDECARENONE	6	(1.2)	3	(0.6)
UBIQUINOL	1	(0.2)	0	(0.0)
VARIOUS ALIMENTARY TRACT AND METABOLISM PRODUCTS	3	(0.6)	3	(0.6)
ZINC	1	(0.2)	5	(1.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
STOMATOLOGICAL PREPARATIONS	**256**	**(53.0)**	**211**	**(43.4)**
ACETYLSALICYLIC ACID	59	(12.2)	83	(17.1)
ALOE VERA	2	(0.4)	0	(0.0)
ALOE VERA;CELLULOSE MICROCRYSTALLINE;LACTOFERRIN;PANTHENOL;PROPYLENE GLYCOL;XYLITOL	2	(0.4)	0	(0.0)
AMPHOTERICIN B	4	(0.8)	1	(0.2)
ANTIINFECTIVES AND ANTISEPTICS FOR LOCAL ORAL TREATMENT	0	(0.0)	1	(0.2)
BENZOCAINE	0	(0.0)	1	(0.2)
BENZYDAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
BENZYDAMINE HYDROCHLORIDE;CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
BETAMETHASONE	13	(2.7)	3	(0.6)
BOTULINUM TOXIN TYPE A	1	(0.2)	1	(0.2)
CALCIUM CHLORIDE DIHYDRATE;CARMELLOSE SODIUM;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;POTASSIUM PHOSPHATE DIBASIC;SODIUM CHLORIDE;SORBITOL	2	(0.4)	0	(0.0)
CARBOMER	1	(0.2)	0	(0.0)
CETRARIA ISLANDICA	1	(0.2)	0	(0.0)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CETYLPYRIDINIUM CHLORIDE;CHLORHEXIDINE GLUCONATE	1	(0.2)	0	(0.0)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CHLORHEXIDINE GLUCONATE;CHLOROBUTANOL	0	(0.0)	1	(0.2)
CHLORHEXIDINE GLUCONATE;LIDOCAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLOBETASOL PROPIONATE	19	(3.9)	8	(1.6)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
STOMATOLOGICAL PREPARATIONS	**256**	**(53.0)**	**211**	**(43.4)**
CURCUMA LONGA	8	(1.7)	5	(1.0)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC EPOLAMINE	1	(0.2)	0	(0.0)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
DOXYCYCLINE	19	(3.9)	5	(1.0)
DOXYCYCLINE HYCLATE	1	(0.2)	0	(0.0)
ELECTROLYTES NOS	7	(1.4)	2	(0.4)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
FLURBIPROFEN	0	(0.0)	1	(0.2)
FLURBIPROFEN SODIUM	1	(0.2)	0	(0.0)
GLUCOSE OXIDASE;LACTOFERRIN;LACTOPEROXIDASE; LYSOZYME	3	(0.6)	2	(0.4)
GLUCOSE OXIDASE;LACTOFERRIN;LACTOPEROXIDASE; LYSOZYME HYDROCHLORIDE	1	(0.2)	0	(0.0)
GLYCEROL	1	(0.2)	0	(0.0)
GLYCOPYRRONIUM BROMIDE	1	(0.2)	2	(0.4)
HEXETIDINE	2	(0.4)	0	(0.0)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
IODINE	0	(0.0)	1	(0.2)
KETOPROFEN	8	(1.7)	4	(0.8)
KETOPROFEN LYSINE	1	(0.2)	0	(0.0)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
LIDOCAINE;PRILOCAINE	0	(0.0)	3	(0.6)
MENTHA X PIPERITA OIL	1	(0.2)	0	(0.0)
METRONIDAZOLE	6	(1.2)	11	(2.3)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
STOMATOLOGICAL PREPARATIONS	**256**	**(53.0)**	**211**	**(43.4)**
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
MINOCYCLINE	2	(0.4)	0	(0.0)
MINOCYCLINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
NAPROXEN	7	(1.4)	12	(2.5)
NIMESULIDE	3	(0.6)	1	(0.2)
NYSTATIN	13	(2.7)	4	(0.8)
OTHER AGENTS FOR LOCAL ORAL TREATMENT	1	(0.2)	0	(0.0)
OXYGEN	4	(0.8)	6	(1.2)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)
PHENOL	0	(0.0)	1	(0.2)
POTASSIUM	0	(0.0)	4	(0.8)
POVIDONE	0	(0.0)	1	(0.2)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SODIUM BICARBONATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM FLUORIDE	2	(0.4)	0	(0.0)
SODIUM FLUORIDE;VITAMINS NOS	0	(0.0)	1	(0.2)
SODIUM FLUOROPHOSPHATE	0	(0.0)	1	(0.2)
SUCRALFATE	0	(0.0)	1	(0.2)
TINIDAZOLE	1	(0.2)	0	(0.0)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
TRIESTER GLYCEROL OXIDE	0	(0.0)	1	(0.2)
XYLITOL	0	(0.0)	1	(0.2)
ZINC	1	(0.2)	5	(1.0)
TONICS	**14**	**(2.9)**	**12**	**(2.5)**
ALLIUM SATIVUM	0	(0.0)	1	(0.2)
ARGININE ASPARTATE;ASCORBIC ACID	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
TONICS	**14**	**(2.9)**	**12**	**(2.5)**
ASCORBIC ACID;COLECALCIFEROL;CURCUMA LONGA;ZINGIBER OFFICINALE	1	(0.2)	0	(0.0)
ASCORBIC ACID;LEUCINE;LYSINE HYDROCHLORIDE;MAGNESIUM ASPARTATE;PHENYLALANINE;VALINE	1	(0.2)	0	(0.0)
CURCUMA LONGA	8	(1.7)	5	(1.0)
CURCUMIN	1	(0.2)	0	(0.0)
DIETARY SUPPLEMENT	0	(0.0)	2	(0.4)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
PUNICA GRANATUM	0	(0.0)	1	(0.2)
SPIRULINA SPP.	1	(0.2)	0	(0.0)
TOCOPHEROL	1	(0.2)	5	(1.0)
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
AMINO ACIDS NOS;HERBAL NOS;MINERALS NOS;VITAMINS NOS	1	(0.2)	0	(0.0)
ARGININE ASPARTATE;ASCORBIC ACID	1	(0.2)	0	(0.0)
ASCORBIC ACID	13	(2.7)	13	(2.7)
ASCORBIC ACID;BETA VULGARIS;ECHINACEA PURPUREA;FORSYTHIA SUSPENSA;ISATIS SPP.;LEVOGLUTAMIDE;LONICERA JAPONICA;LYSINE;MAGNESIUM;MANGANESE ;RETINOL;SCHIZONEPETA SPP.;SELENIUM;VITAMIN E NOS;VITEX NEGUNDO; ZINC;ZINGIBER OFFICINALE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
ASCORBIC ACID;BETACAROTENE;BIOTIN;CALCIUM;CHROMIUM;COLECALCIFEROL;COPPER;FOLIC ACID;IODINE;IRON;LYCOPENE;MAGNESIUM;MANGANESE;NICOTINAMIDE;PANTOTHENIC ACID;PHOSPHORUS;PHYTOMENADIONE;POTASSIUM; PYRIDOXINE HYDROCHLORIDE;RETINOL;RIBOFLAVIN;SELENIUM;VITAMIN B1 NOS;VITAMIN B12 NOS;VITAMIN E NOS;XANTOFYL;ZINC	1	(0.2)	1	(0.2)
ASCORBIC ACID;BETACAROTENE;CUPRIC OXIDE;SODIUM SELENATE;TOCOPHERYL ACETATE;XANTOFYL;ZINC OXIDE	1	(0.2)	0	(0.0)
ASCORBIC ACID;BETACAROTENE;CUPRIC OXIDE;TOCOPHERYL ACETATE;ZINC OXIDE	1	(0.2)	0	(0.0)
ASCORBIC ACID;BIOTIN;CALCIUM;CALCIUM PANTOTHENATE;CYANOCOBALAMIN;NICOTINIC ACID;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
ASCORBIC ACID;CALCIUM CARBONATE;CALCIUM PANTOTHENATE;CALCIUM PHOSPHATE;CHROMIUM;CYANOCOBALAMIN;FOLIC ACID;MAGNESIUM CARBONATE;MAGNESIUM HYDROXIDE;MANGANESE GLUCONATE;NICOTINIC ACID; POTASSIUM BICARBONATE;POTASSIUM CARBONATE;POTASSIUM PHOSPHATE DIBASIC;PYRIDOXINE HYDROCHLORIDE;QUERCETIN;RIBOFLAVIN SODIUM PHOSPHATE;SODIUM BICARBONATE;SODIUM PHOSPHATE;THIAMINE HYDROCHLORIDE;	2	(0.4)	1	(0.2)
ASCORBIC ACID;CHROMIUM;COPPER;CYANOCOBALAMIN;FOLIC ACID;IODINE;MAGNESIUM;MANGANESE;MOLYBDENUM;NICOTINIC ACID;PANTOTHENIC ACID;POTASSIUM;PYRIDOXINE HYDROCHLORIDE;RETINOL;RIBOFLAVIN;SELENIUM;THIAMINE; TOCOPHEROL;VITAMIN D NOS;ZINC	1	(0.2)	0	(0.0)
ASCORBIC ACID;COLECALCIFEROL;ZINC	0	(0.0)	1	(0.2)
ASCORBIC ACID;CUPRIC OXIDE;TOCOPHERYL ACID SUCCINATE;ZINC OXIDE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
ASCORBIC ACID;DL-ALPHA TOCOPHERYL ACETATE;ECHINACEA PURPUREA;FORSYTHIA SUSPENSA FRUIT;ISATIS TINCTORIA ROOT;LEVOGLUTAMIDE;LONICERA JAPONICA FLOWER;LYSINE HYDROCHLORIDE;MAGNESIUM OXIDE; MAGNESIUM SULFATE;MANGANESE GLUCONATE;POTASSIUM BICARBONATE;RETINOL ACETATE;SCHIZONEPETA TENUIFOLIA;SELENIUM AMINO ACID CHELATE;SODIUM BICARBONATE;VITEX TRIFOLIA FRUIT;ZINC SULFATE;	1	(0.2)	0	(0.0)
ASCORBIC ACID;FOLIC ACID;VITAMIN B COMPLEX	0	(0.0)	1	(0.2)
ASCORBIC ACID;VITAMIN B COMPLEX	1	(0.2)	1	(0.2)
BETACAROTENE	0	(0.0)	1	(0.2)
BIOTIN	1	(0.2)	2	(0.4)
BIOTIN;CALCIUM PANTOTHENATE;CYANOCOBALAMIN;NICOTINAMIDE;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
CALCIFEDIOL	3	(0.6)	1	(0.2)
CALCITRIOL	1	(0.2)	0	(0.0)
CALCIUM ASCORBATE	0	(0.0)	1	(0.2)
CALCIUM ASCORBATE DIHYDRATE;COLECALCIFEROL;MAGNESIUM OXIDE;MAGNESIUM PHOSPHATE PENTAHYDRATE;MANGANESE AMINO ACID CHELATE;PYRIDOXINE HYDROCHLORIDE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
CALCIUM LEVOMEFOLATE;CYANOCOBALAMIN;MAGNESIUM;MAGNESIUM GLYCEROPHOSPHATE;PYRIDOXINE HYDROCHLORIDE;TAURINE	0	(0.0)	1	(0.2)
CALCIUM PANTOTHENATE;CYANOCOBALAMIN;FOLIC ACID;NICOTINAMIDE;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
COLECALCIFEROL	40	(8.3)	32	(6.6)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	2	(0.4)	0	(0.0)
DEXPANTHENOL	4	(0.8)	0	(0.0)
ERGOCALCIFEROL	2	(0.4)	1	(0.2)
IRON;MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
MAGNESIUM PHOSPHATE;MANGANESE AMINO ACID CHELATE;PYRIDOXINE HYDROCHLORIDE;RETINOL ACETATE;ZINC AMINO ACID CHELATE	0	(0.0)	1	(0.2)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
MINERALS NOS;VITAMINS NOS;XANTOFYL	0	(0.0)	1	(0.2)
NICOTINAMIDE	2	(0.4)	2	(0.4)
NICOTINIC ACID	1	(0.2)	1	(0.2)
PYRIDOXINE	1	(0.2)	0	(0.0)
RETINOL	0	(0.0)	1	(0.2)
RIBOFLAVIN	1	(0.2)	0	(0.0)
ROSA CANINA	0	(0.0)	1	(0.2)
SODIUM FLUORIDE;VITAMINS NOS	0	(0.0)	1	(0.2)
SULBUTIAMINE	1	(0.2)	0	(0.0)
THIAMINE	1	(0.2)	1	(0.2)
THIAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
TOCOPHEROL	1	(0.2)	5	(1.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ALIMENTARY TRACT AND METABOLISM				
VITAMINS	**101**	**(20.9)**	**89**	**(18.3)**
VITAMIN B COMPLEX	4	(0.8)	4	(0.8)
VITAMIN B NOS	0	(0.0)	1	(0.2)
VITAMIN D NOS	15	(3.1)	16	(3.3)
VITAMINS NOS	25	(5.2)	24	(4.9)
VITAMINS, OTHER COMBINATIONS	3	(0.6)	3	(0.6)
ANTIINFECTIVES FOR SYSTEMIC USE				
ANTIBACTERIALS FOR SYSTEMIC USE	**162**	**(33.5)**	**142**	**(29.2)**
ALLIUM SATIVUM	0	(0.0)	1	(0.2)
ALLIUM SATIVUM OIL	1	(0.2)	0	(0.0)
AMIKACIN	0	(0.0)	1	(0.2)
AMIKACIN SULFATE	0	(0.0)	1	(0.2)
AMOXICILLIN	27	(5.6)	18	(3.7)
AMOXICILLIN TRIHYDRATE	1	(0.2)	3	(0.6)
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	25	(5.2)	25	(5.1)
AMOXICILLIN;CLAVULANATE POTASSIUM	1	(0.2)	4	(0.8)
AMPICILLIN	2	(0.4)	0	(0.0)
AMPICILLIN SODIUM	0	(0.0)	1	(0.2)
AMPICILLIN SODIUM;SULBACTAM SODIUM	1	(0.2)	0	(0.0)
ANTIBACTERIALS FOR SYSTEMIC USE	3	(0.6)	1	(0.2)
AZITHROMYCIN	18	(3.7)	8	(1.6)
BACITRACIN	1	(0.2)	2	(0.4)
BENZATHINE BENZYLPENICILLIN	1	(0.2)	0	(0.0)
BENZYLPENICILLIN	1	(0.2)	0	(0.0)
CEFADROXIL	3	(0.6)	2	(0.4)
CEFALEXIN	11	(2.3)	19	(3.9)
CEFALEXIN MONOHYDRATE	0	(0.0)	1	(0.2)
CEFAZOLIN	5	(1.0)	7	(1.4)
CEFAZOLIN SODIUM	1	(0.2)	3	(0.6)
CEFAZOLIN SODIUM;GLUCOSE	1	(0.2)	0	(0.0)
CEFCAPENE PIVOXIL HYDROCHLORIDE	1	(0.2)	0	(0.0)
CEFDINIR	3	(0.6)	1	(0.2)
CEFDITOREN PIVOXIL	1	(0.2)	0	(0.0)
CEFEPIME	1	(0.2)	1	(0.2)

Participants With Specific Concomitant Medications
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTIINFECTIVES FOR SYSTEMIC USE				
ANTIBACTERIALS FOR SYSTEMIC USE	**162**	**(33.5)**	**142**	**(29.2)**
CEFIXIME	1	(0.2)	1	(0.2)
CEFOTAXIME SODIUM	0	(0.0)	1	(0.2)
CEFPODOXIME PROXETIL	0	(0.0)	2	(0.4)
CEFTRIAXONE	8	(1.7)	2	(0.4)
CEFTRIAXONE SODIUM	2	(0.4)	3	(0.6)
CEFUROXIME	1	(0.2)	6	(1.2)
CEFUROXIME AXETIL	0	(0.0)	1	(0.2)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)
CLARITHROMYCIN	2	(0.4)	5	(1.0)
CLARITHROMYCIN LACTOBIONATE	1	(0.2)	0	(0.0)
CLAVULANIC ACID	5	(1.0)	1	(0.2)
CLINDAMYCIN	5	(1.0)	1	(0.2)
CLINDAMYCIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLINDAMYCIN PHOSPHATE	1	(0.2)	0	(0.0)
COMBINATIONS OF ANTIBACTERIALS	1	(0.2)	0	(0.0)
D-MANNOSE	0	(0.0)	1	(0.2)
DOXYCYCLINE	19	(3.9)	5	(1.0)
DOXYCYCLINE HYCLATE	1	(0.2)	0	(0.0)
ERYTHROMYCIN	2	(0.4)	2	(0.4)
FLUCLOXACILLIN	3	(0.6)	2	(0.4)
FLUCLOXACILLIN SODIUM	1	(0.2)	0	(0.0)
FOSFOMYCIN	4	(0.8)	11	(2.3)
FOSFOMYCIN TROMETAMOL	1	(0.2)	2	(0.4)
FURAZIDIN	0	(0.0)	2	(0.4)
FUSIDATE SODIUM	1	(0.2)	2	(0.4)
FUSIDIC ACID	11	(2.3)	7	(1.4)
GENTAMICIN	2	(0.4)	1	(0.2)
GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
IMIPENEM	1	(0.2)	0	(0.0)
LEVOFLOXACIN	9	(1.9)	6	(1.2)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
LYMECYCLINE	1	(0.2)	0	(0.0)
MEROPENEM	1	(0.2)	1	(0.2)

Participants With Specific Concomitant Medications
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTIINFECTIVES FOR SYSTEMIC USE				
ANTIBACTERIALS FOR SYSTEMIC USE	**162**	**(33.5)**	**142**	**(29.2)**
METHENAMINE HIPPURATE	1	(0.2)	0	(0.0)
METRONIDAZOLE	6	(1.2)	11	(2.3)
MINOCYCLINE	2	(0.4)	0	(0.0)
MINOCYCLINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MOXIFLOXACIN	4	(0.8)	2	(0.4)
MOXIFLOXACIN HYDROCHLORIDE	3	(0.6)	0	(0.0)
NITROFURANTOIN	3	(0.6)	7	(1.4)
NITROFURANTOIN;PYRIDOXINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
NORFLOXACIN	1	(0.2)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
PENICILLIN NOS	1	(0.2)	0	(0.0)
PHENOXYMETHYLPENICILLIN	1	(0.2)	0	(0.0)
PHENOXYMETHYLPENICILLIN POTASSIUM	0	(0.0)	2	(0.4)
PIPERACILLIN	0	(0.0)	1	(0.2)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	5	(1.0)	2	(0.4)
PIVMECILLINAM	0	(0.0)	1	(0.2)
PRISTINAMYCIN	0	(0.0)	2	(0.4)
ROXITHROMYCIN	1	(0.2)	2	(0.4)
SPIRAMYCIN	0	(0.0)	2	(0.4)
SULFAMETHOXAZOLE;TRIMETHOPRIM	18	(3.7)	6	(1.2)
TAZOBACTAM	0	(0.0)	1	(0.2)
TINIDAZOLE	1	(0.2)	0	(0.0)
TOBRAMYCIN	2	(0.4)	1	(0.2)
TRIMETHOPRIM	1	(0.2)	0	(0.0)
VACCINIUM MACROCARPON	0	(0.0)	1	(0.2)
VANCOMYCIN	2	(0.4)	4	(0.8)
VANCOMYCIN HYDROCHLORIDE	0	(0.0)	2	(0.4)
ANTIMYCOBACTERIALS	**1**	**(0.2)**	**0**	**(0.0)**
DAPSONE	1	(0.2)	0	(0.0)
ANTIMYCOTICS FOR SYSTEMIC USE	**31**	**(6.4)**	**16**	**(3.3)**
AMPHOTERICIN B	4	(0.8)	1	(0.2)
DAPSONE	1	(0.2)	0	(0.0)
FLUCONAZOLE	9	(1.9)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTIINFECTIVES FOR SYSTEMIC USE				
ANTIMYCOTICS FOR SYSTEMIC USE	**31**	**(6.4)**	**16**	**(3.3)**
KETOCONAZOLE	6	(1.2)	6	(1.2)
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
NYSTATIN	13	(2.7)	4	(0.8)
PENTAMIDINE ISETHIONATE	1	(0.2)	0	(0.0)
ANTIVIRALS FOR SYSTEMIC USE	**16**	**(3.3)**	**11**	**(2.3)**
ACICLOVIR	3	(0.6)	4	(0.8)
AMANTADINE	0	(0.0)	1	(0.2)
BRIVUDINE	1	(0.2)	0	(0.0)
EMTRICITABINE	1	(0.2)	0	(0.0)
EMTRICITABINE;TENOFOVIR DISOPROXIL FUMARATE	1	(0.2)	0	(0.0)
ENTECAVIR	0	(0.0)	1	(0.2)
LOPINAVIR	1	(0.2)	0	(0.0)
OSELTAMIVIR PHOSPHATE	3	(0.6)	1	(0.2)
PENCICLOVIR	1	(0.2)	0	(0.0)
TENOFOVIR	1	(0.2)	1	(0.2)
VALACICLOVIR HYDROCHLORIDE	7	(1.4)	3	(0.6)
IMMUNE SERA AND IMMUNOGLOBULINS	**5**	**(1.0)**	**0**	**(0.0)**
IMMUNOGLOBULIN HUMAN NORMAL	5	(1.0)	0	(0.0)
VACCINES	**87**	**(18.0)**	**92**	**(18.9)**
COVID-19 VACCINE	2	(0.4)	2	(0.4)
COVID-19 VACCINE INACT (VERO) CZ02	4	(0.8)	3	(0.6)
COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19)	12	(2.5)	10	(2.1)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR 5-COMPONENT;POLIO VACCINE INACT 3V (VERO);TETANUS VACCINE TOXOID	1	(0.2)	0	(0.0)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR 5-COMPONENT;TETANUS VACCINE TOXOID	0	(0.0)	1	(0.2)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR;TETANUS VACCINE TOXOID	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTIINFECTIVES FOR SYSTEMIC USE				
VACCINES	**87**	**(18.0)**	**92**	**(18.9)**
DIPHTHERIA VACCINE TOXOID;TETANUS VACCINE TOXOID	0	(0.0)	3	(0.6)
ELASOMERAN	10	(2.1)	11	(2.3)
INFLUENZA VACCINE	26	(5.4)	17	(3.5)
INFLUENZA VACCINE INACT	1	(0.2)	2	(0.4)
INFLUENZA VACCINE INACT SAG 3V	0	(0.0)	3	(0.6)
INFLUENZA VACCINE INACT SAG 4V	4	(0.8)	5	(1.0)
INFLUENZA VACCINE INACT SPLIT 3V	1	(0.2)	1	(0.2)
INFLUENZA VACCINE INACT SPLIT 4V	6	(1.2)	2	(0.4)
INFLUENZA VACCINE RHA 4V (BACULOVIRUS)	0	(0.0)	1	(0.2)
PNEUMOCOCCAL VACCINE	4	(0.8)	3	(0.6)
PNEUMOCOCCAL VACCINE CONJ	0	(0.0)	1	(0.2)
PNEUMOCOCCAL VACCINE CONJ 13V (CRM197)	1	(0.2)	0	(0.0)
PNEUMOCOCCAL VACCINE POLYSACCH 23V	1	(0.2)	0	(0.0)
TICK-BORNE ENCEPHALITIS VACCINE	1	(0.2)	1	(0.2)
TOZINAMERAN	32	(6.6)	46	(9.5)
VARICELLA ZOSTER VACCINE	1	(0.2)	0	(0.0)
VARICELLA ZOSTER VACCINE RGE (CHO)	3	(0.6)	0	(0.0)
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS				
ANTINEOPLASTIC AGENTS	**34**	**(7.0)**	**22**	**(4.5)**
AFLIBERCEPT	1	(0.2)	0	(0.0)
CARBOPLATIN	1	(0.2)	0	(0.0)
CELECOXIB	10	(2.1)	7	(1.4)
CYCLOPHOSPHAMIDE	2	(0.4)	0	(0.0)
DOXORUBICIN	1	(0.2)	0	(0.0)
EPIRUBICIN	1	(0.2)	0	(0.0)
FLUOROURACIL	2	(0.4)	7	(1.4)
FLUOROURACIL;SALICYLIC ACID	0	(0.0)	1	(0.2)
IMIQUIMOD	1	(0.2)	1	(0.2)
IMPATIENS BALSAMINA	1	(0.2)	0	(0.0)
METHOTREXATE	5	(1.0)	0	(0.0)
METHOTREXATE SODIUM	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS				
ANTINEOPLASTIC AGENTS	**34**	**(7.0)**	**22**	**(4.5)**
MITOMYCIN	0	(0.0)	1	(0.2)
PACLITAXEL	1	(0.2)	0	(0.0)
PROPRANOLOL	7	(1.4)	4	(0.8)
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
SR 9009	0	(0.0)	1	(0.2)
TRETINOIN	1	(0.2)	1	(0.2)
VINCRISTINE	1	(0.2)	0	(0.0)
ENDOCRINE THERAPY	**9**	**(1.9)**	**7**	**(1.4)**
BICALUTAMIDE	0	(0.0)	1	(0.2)
ESTRADIOL	6	(1.2)	4	(0.8)
ESTRADIOL VALERATE	1	(0.2)	0	(0.0)
ESTROGENS	0	(0.0)	1	(0.2)
ETHINYLESTRADIOL	1	(0.2)	0	(0.0)
LETROZOLE	1	(0.2)	0	(0.0)
LEUPRORELIN ACETATE	0	(0.0)	1	(0.2)
MEDROXYPROGESTERONE ACETATE	0	(0.0)	1	(0.2)
NORETHISTERONE ACETATE	0	(0.0)	1	(0.2)
IMMUNOSTIMULANTS	**0**	**(0.0)**	**1**	**(0.2)**
ECHINACEA PURPUREA	0	(0.0)	1	(0.2)
IMMUNOSUPPRESSANTS	**26**	**(5.4)**	**5**	**(1.0)**
AZATHIOPRINE	1	(0.2)	0	(0.0)
CICLOSPORIN	1	(0.2)	0	(0.0)
COLCHICINE	4	(0.8)	3	(0.6)
HYDROXYCHLOROQUINE SULFATE	4	(0.8)	1	(0.2)
INFLIXIMAB	2	(0.4)	0	(0.0)
INFLIXIMAB ABDA	1	(0.2)	0	(0.0)
LEFLUNOMIDE	1	(0.2)	0	(0.0)
METHOTREXATE	5	(1.0)	0	(0.0)
METHOTREXATE SODIUM	2	(0.4)	0	(0.0)
MYCOPHENOLATE MOFETIL	3	(0.6)	0	(0.0)
TACROLIMUS	1	(0.2)	0	(0.0)
TACROLIMUS MONOHYDRATE	2	(0.4)	1	(0.2)
TOCILIZUMAB	1	(0.2)	0	(0.0)
VEDOLIZUMAB	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS				
ANTHELMINTICS	**7**	**(1.4)**	**3**	**(0.6)**
ALBENDAZOLE	1	(0.2)	0	(0.0)
CUCURBITA PEPO OIL	0	(0.0)	1	(0.2)
IVERMECTIN	6	(1.2)	2	(0.4)
PYRANTEL EMBONATE	1	(0.2)	0	(0.0)
ANTIPROTOZOALS	**27**	**(5.6)**	**22**	**(4.5)**
ATOVAQUONE	1	(0.2)	0	(0.0)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)
HYDROXYCHLOROQUINE SULFATE	4	(0.8)	1	(0.2)
METRONIDAZOLE	6	(1.2)	11	(2.3)
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
NITAZOXANIDE	2	(0.4)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
OXICONAZOLE NITRATE	0	(0.0)	1	(0.2)
PENTAMIDINE ISETHIONATE	1	(0.2)	0	(0.0)
TINIDAZOLE	1	(0.2)	0	(0.0)
ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS	**6**	**(1.2)**	**3**	**(0.6)**
DIMETICONE;PARAFFIN, LIQUID	0	(0.0)	1	(0.2)
IVERMECTIN	6	(1.2)	2	(0.4)
BLOOD AND BLOOD FORMING ORGANS				
ANTIANEMIC PREPARATIONS	**34**	**(7.0)**	**35**	**(7.2)**
ASCORBIC ACID;FERROUS FUMARATE	1	(0.2)	0	(0.0)
ASCORBIC ACID;FERROUS SULFATE	0	(0.0)	1	(0.2)
CALCIUM FOLINATE	1	(0.2)	0	(0.0)
CYANOCOBALAMIN	10	(2.1)	17	(3.5)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	2	(0.4)	0	(0.0)
FERRIC CARBOXYMALTOSE	1	(0.2)	0	(0.0)
FERRIC DERISOMALTOSE	1	(0.2)	1	(0.2)
FERRIC HYDROXIDE POLYMALTOSE COMPLEX	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
BLOOD AND BLOOD FORMING ORGANS				
ANTIANEMIC PREPARATIONS	**34**	**(7.0)**	**35**	**(7.2)**
FERRIC HYDROXIDE POLYMALTOSE COMPLEX;FOLIC ACID	1	(0.2)	0	(0.0)
FERROGLYCINATE CHELATE	1	(0.2)	0	(0.0)
FERROUS ASCORBATE	0	(0.0)	1	(0.2)
FERROUS FUMARATE	1	(0.2)	2	(0.4)
FERROUS PHOSPHATE	0	(0.0)	1	(0.2)
FERROUS SULFATE	4	(0.8)	3	(0.6)
FOLIC ACID	8	(1.7)	2	(0.4)
FOLIC ACID;SACCHARATED IRON OXIDE	0	(0.0)	1	(0.2)
HYDROXOCOBALAMIN	1	(0.2)	0	(0.0)
HYDROXOCOBALAMIN ACETATE	1	(0.2)	1	(0.2)
IRON	3	(0.6)	6	(1.2)
MECOBALAMIN	1	(0.2)	0	(0.0)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
SACCHARATED IRON OXIDE	1	(0.2)	0	(0.0)
VITAMIN B NOS	0	(0.0)	1	(0.2)
ANTIHEMORRHAGICS	**2**	**(0.4)**	**4**	**(0.8)**
COLLAGEN	0	(0.0)	1	(0.2)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MENATETRENONE	1	(0.2)	0	(0.0)
PHYTOMENADIONE	0	(0.0)	1	(0.2)
ANTITHROMBOTIC AGENTS	**121**	**(25.1)**	**123**	**(25.3)**
ACENOCOUMAROL	1	(0.2)	1	(0.2)
ACETYLSALICYLATE LYSINE	4	(0.8)	2	(0.4)
ACETYLSALICYLIC ACID	59	(12.2)	83	(17.1)
ACETYLSALICYLIC ACID;CLOPIDOGREL BISULFATE	2	(0.4)	0	(0.0)
ACETYLSALICYLIC ACID;GLYCINE	1	(0.2)	0	(0.0)
APIXABAN	15	(3.1)	5	(1.0)
CLOPIDOGREL	6	(1.2)	4	(0.8)
CLOPIDOGREL BISULFATE	2	(0.4)	4	(0.8)
DABIGATRAN	1	(0.2)	0	(0.0)
DABIGATRAN ETEXILATE MESILATE	1	(0.2)	2	(0.4)
DALTEPARIN SODIUM	2	(0.4)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
BLOOD AND BLOOD FORMING ORGANS				
ANTITHROMBOTIC AGENTS	**121**	**(25.1)**	**123**	**(25.3)**
ENOXAPARIN SODIUM	19	(3.9)	20	(4.1)
HEPARIN	2	(0.4)	4	(0.8)
HEPARIN SODIUM	0	(0.0)	2	(0.4)
HEPARINOID	1	(0.2)	0	(0.0)
NADROPARIN CALCIUM	1	(0.2)	1	(0.2)
PHENPROCOUMON	2	(0.4)	2	(0.4)
RIVAROXABAN	13	(2.7)	11	(2.3)
TICAGRELOR	1	(0.2)	4	(0.8)
TINZAPARIN SODIUM	3	(0.6)	2	(0.4)
WARFARIN	1	(0.2)	1	(0.2)
WARFARIN SODIUM	1	(0.2)	2	(0.4)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	**89**	**(18.4)**	**77**	**(15.8)**
BLOOD PLASMA	1	(0.2)	0	(0.0)
BLOOD, CALF, DEPROT., LMW PORTION	1	(0.2)	0	(0.0)
CALCIUM CHLORIDE DIHYDRATE;GLUCOSE 1-PHOSPHATE DISODIUM;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE;SODIUM CITRATE DIHYDRATE	1	(0.2)	0	(0.0)
CALCIUM CHLORIDE DIHYDRATE;MALTOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1	(0.2)	0	(0.0)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
BLOOD AND BLOOD FORMING ORGANS				
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	**89**	**(18.4)**	**77**	**(15.8)**
CALCIUM;MAGNESIUM;POTASSIUM;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;PROTEIN;VITAMINS NOS	0	(0.0)	1	(0.2)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
ELECTROLYTES NOS	7	(1.4)	2	(0.4)
ELECTROLYTES NOS;SODIUM LACTATE	3	(0.6)	4	(0.8)
GLUCONATE SODIUM;MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
GLUCOSE	1	(0.2)	0	(0.0)
GLUCOSE MONOHYDRATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
GLUCOSE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1	(0.2)	0	(0.0)
GLUCOSE;SODIUM BICARBONATE	1	(0.2)	0	(0.0)
GLUCOSE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
GLYCEROL	1	(0.2)	0	(0.0)
LYSINE	0	(0.0)	2	(0.4)
LYSINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MAGNESIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
MAGNESIUM CITRATE	0	(0.0)	4	(0.8)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
NUTRIENTS NOS	1	(0.2)	1	(0.2)
POTASSIUM	0	(0.0)	4	(0.8)
POTASSIUM CHLORIDE	16	(3.3)	9	(1.9)
POTASSIUM CHLORIDE;SODIUM CHLORIDE	2	(0.4)	0	(0.0)
POTASSIUM PHOSPHATE DIBASIC	0	(0.0)	1	(0.2)
POTASSIUM PHOSPHATE MONOBASIC	0	(0.0)	1	(0.2)
POVIDONE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
BLOOD AND BLOOD FORMING ORGANS				
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	**89**	**(18.4)**	**77**	**(15.8)**
RED BLOOD CELLS	0	(0.0)	1	(0.2)
SELENIUM	4	(0.8)	0	(0.0)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SODIUM BICARBONATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
SODIUM PHOSPHATE DIBASIC	0	(0.0)	2	(0.4)
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	1	(0.2)	0	(0.0)
UREA	10	(2.1)	3	(0.6)
VITAMINS NOS	25	(5.2)	24	(4.9)
XYLITOL	0	(0.0)	1	(0.2)
ZINC	1	(0.2)	5	(1.0)
OTHER HEMATOLOGICAL AGENTS	**1**	**(0.2)**	**1**	**(0.2)**
BROMELAINS	1	(0.2)	0	(0.0)
LEVOGLUTAMIDE	0	(0.0)	1	(0.2)
CARDIOVASCULAR SYSTEM				
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	**175**	**(36.2)**	**182**	**(37.4)**
ALISKIREN FUMARATE	0	(0.0)	1	(0.2)
AMLODIPINE BESILATE;BENAZEPRIL HYDROCHLORIDE	0	(0.0)	2	(0.4)
AMLODIPINE BESILATE;HYDROCHLOROTHIAZIDE;OLMESARTAN MEDOXOMIL	1	(0.2)	1	(0.2)
AMLODIPINE BESILATE;HYDROCHLOROTHIAZIDE;VALSARTAN	3	(0.6)	1	(0.2)
AMLODIPINE BESILATE;INDAPAMIDE;PERINDOPRIL ARGININE	0	(0.0)	2	(0.4)
AMLODIPINE BESILATE;OLMESARTAN MEDOXOMIL	1	(0.2)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	**175**	**(36.2)**	**182**	**(37.4)**
AMLODIPINE BESILATE;PERINDOPRIL ARGININE	2	(0.4)	4	(0.8)
AMLODIPINE BESILATE;PERINDOPRIL TOSILATE	0	(0.0)	1	(0.2)
AMLODIPINE BESILATE;RAMIPRIL	1	(0.2)	1	(0.2)
AMLODIPINE BESILATE;VALSARTAN	3	(0.6)	5	(1.0)
BENAZEPRIL HYDROCHLORIDE	0	(0.0)	2	(0.4)
BENAZEPRIL HYDROCHLORIDE;HYDROCHLOROTHIAZIDE	0	(0.0)	1	(0.2)
CANDESARTAN	13	(2.7)	13	(2.7)
CANDESARTAN CILEXETIL	3	(0.6)	8	(1.6)
CANDESARTAN CILEXETIL;HYDROCHLOROTHIAZIDE	1	(0.2)	1	(0.2)
CANDESARTAN;HYDROCHLOROTHIAZIDE	0	(0.0)	1	(0.2)
CAPTOPRIL	6	(1.2)	7	(1.4)
ENALAPRIL	9	(1.9)	12	(2.5)
ENALAPRIL MALEATE	3	(0.6)	1	(0.2)
ENALAPRIL MALEATE;HYDROCHLOROTHIAZIDE	0	(0.0)	1	(0.2)
ENALAPRIL MALEATE;LERCANIDIPINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
EPROSARTAN	0	(0.0)	1	(0.2)
HYDROCHLOROTHIAZIDE;IRBESARTAN	3	(0.6)	1	(0.2)
HYDROCHLOROTHIAZIDE;LISINOPRIL	5	(1.0)	2	(0.4)
HYDROCHLOROTHIAZIDE;LISINOPRIL DIHYDRATE	1	(0.2)	0	(0.0)
HYDROCHLOROTHIAZIDE;LOSARTAN POTASSIUM	5	(1.0)	3	(0.6)
HYDROCHLOROTHIAZIDE;OLMESARTAN MEDOXOMIL	3	(0.6)	1	(0.2)
HYDROCHLOROTHIAZIDE;RAMIPRIL	3	(0.6)	1	(0.2)
HYDROCHLOROTHIAZIDE;TELMISARTAN	1	(0.2)	2	(0.4)
HYDROCHLOROTHIAZIDE;VALSARTAN	3	(0.6)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	**175**	**(36.2)**	**182**	**(37.4)**
HYDROCHLOROTHIAZIDE;ZOFENOPRIL CALCIUM	0	(0.0)	1	(0.2)
INDAPAMIDE;PERINDOPRIL	3	(0.6)	0	(0.0)
INDAPAMIDE;PERINDOPRIL ARGININE	1	(0.2)	3	(0.6)
INDAPAMIDE;PERINDOPRIL ERBUMINE	2	(0.4)	2	(0.4)
IRBESARTAN	7	(1.4)	8	(1.6)
LISINOPRIL	19	(3.9)	17	(3.5)
LOSARTAN	23	(4.8)	16	(3.3)
LOSARTAN POTASSIUM	7	(1.4)	7	(1.4)
OLMESARTAN MEDOXOMIL	9	(1.9)	11	(2.3)
PERINDOPRIL	11	(2.3)	6	(1.2)
PERINDOPRIL ARGININE	5	(1.0)	7	(1.4)
PERINDOPRIL ERBUMINE	2	(0.4)	5	(1.0)
RAMIPRIL	25	(5.2)	28	(5.8)
TELMISARTAN	8	(1.7)	8	(1.6)
VALSARTAN	6	(1.2)	8	(1.6)
ZOFENOPRIL CALCIUM	1	(0.2)	0	(0.0)
ANTIHYPERTENSIVES	**27**	**(5.6)**	**31**	**(6.4)**
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
DOXAZOSIN	3	(0.6)	5	(1.0)
DOXAZOSIN MESILATE	3	(0.6)	4	(0.8)
HYDRALAZINE	2	(0.4)	1	(0.2)
HYDRALAZINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
MINOXIDIL	0	(0.0)	1	(0.2)
MOXONIDINE	3	(0.6)	2	(0.4)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
RILMENIDINE PHOSPHATE	1	(0.2)	0	(0.0)
SILDENAFIL CITRATE	5	(1.0)	4	(0.8)
TADALAFIL	3	(0.6)	5	(1.0)
TERAZOSIN	1	(0.2)	1	(0.2)
URAPIDIL	1	(0.2)	1	(0.2)
VARDENAFIL HYDROCHLORIDE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
BETA BLOCKING AGENTS	**102**	**(21.1)**	**92**	**(18.9)**
ACEBUTOLOL	1	(0.2)	0	(0.0)
ACEBUTOLOL HYDROCHLORIDE	0	(0.0)	1	(0.2)
ATENOLOL	17	(3.5)	5	(1.0)
ATENOLOL;CHLORTALIDONE	2	(0.4)	0	(0.0)
BISOPROLOL	21	(4.3)	21	(4.3)
BISOPROLOL FUMARATE	12	(2.5)	13	(2.7)
BISOPROLOL FUMARATE;HYDROCHLOROTHIAZIDE	0	(0.0)	1	(0.2)
CARTEOLOL HYDROCHLORIDE	1	(0.2)	0	(0.0)
CARVEDILOL	5	(1.0)	4	(0.8)
LABETALOL	1	(0.2)	1	(0.2)
METOPROLOL	9	(1.9)	13	(2.7)
METOPROLOL SUCCINATE	7	(1.4)	11	(2.3)
METOPROLOL TARTRATE	7	(1.4)	5	(1.0)
NADOLOL	0	(0.0)	1	(0.2)
NEBIVOLOL	8	(1.7)	6	(1.2)
NEBIVOLOL HYDROCHLORIDE	4	(0.8)	7	(1.4)
PROPRANOLOL	7	(1.4)	4	(0.8)
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
SOTALOL	2	(0.4)	1	(0.2)
TIMOLOL	0	(0.0)	1	(0.2)
TIMOLOL MALEATE	0	(0.0)	3	(0.6)
CALCIUM CHANNEL BLOCKERS	**76**	**(15.7)**	**67**	**(13.8)**
AMLODIPINE	43	(8.9)	35	(7.2)
AMLODIPINE BESILATE	14	(2.9)	9	(1.9)
AMLODIPINE MALEATE	0	(0.0)	2	(0.4)
DILTIAZEM	5	(1.0)	1	(0.2)
DILTIAZEM HYDROCHLORIDE	4	(0.8)	1	(0.2)
FELODIPINE	1	(0.2)	2	(0.4)
LACIDIPINE	1	(0.2)	2	(0.4)
LERCANIDIPINE	5	(1.0)	6	(1.2)
LERCANIDIPINE HYDROCHLORIDE	2	(0.4)	4	(0.8)
MANIDIPINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
NICARDIPINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
NIFEDIPINE	3	(0.6)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
CALCIUM CHANNEL BLOCKERS	**76**	**(15.7)**	**67**	**(13.8)**
NITRENDIPINE	2	(0.4)	4	(0.8)
VERAPAMIL	0	(0.0)	1	(0.2)
VERAPAMIL HYDROCHLORIDE	0	(0.0)	2	(0.4)
CARDIAC THERAPY	**126**	**(26.1)**	**107**	**(22.0)**
AMIODARONE	3	(0.6)	1	(0.2)
AMIODARONE HYDROCHLORIDE	2	(0.4)	0	(0.0)
CAMPHOR	1	(0.2)	0	(0.0)
CRATAEGUS SPP. DRY EXTRACT;VALERIANA OFFICINALIS DRY EXTRACT	1	(0.2)	0	(0.0)
DIGITOXIN	0	(0.0)	1	(0.2)
DIGOXIN	1	(0.2)	1	(0.2)
EMPAGLIFLOZIN	4	(0.8)	6	(1.2)
EPHEDRINE	1	(0.2)	1	(0.2)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
FLECAINIDE	2	(0.4)	0	(0.0)
FLECAINIDE ACETATE	3	(0.6)	3	(0.6)
GLYCERYL TRINITRATE	3	(0.6)	6	(1.2)
IBUPROFEN	86	(17.8)	61	(12.6)
IBUPROFEN ARGININE	1	(0.2)	1	(0.2)
IBUPROFEN LYSINATE	0	(0.0)	1	(0.2)
INDOMETACIN	0	(0.0)	1	(0.2)
IPRATROPIUM BROMIDE	2	(0.4)	6	(1.2)
ISOSORBIDE DINITRATE	1	(0.2)	0	(0.0)
ISOSORBIDE MONONITRATE	0	(0.0)	1	(0.2)
LEVOCARNITINE	0	(0.0)	1	(0.2)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
MAGNESIUM ASPARTATE;POTASSIUM ASPARTATE	1	(0.2)	0	(0.0)
MIDODRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
NICOTINAMIDE	2	(0.4)	2	(0.4)
NOREPINEPHRINE	0	(0.0)	1	(0.2)
PACLITAXEL	1	(0.2)	0	(0.0)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
CARDIAC THERAPY	**126**	**(26.1)**	**107**	**(22.0)**
PHENYLEPHRINE	1	(0.2)	3	(0.6)
PHENYLEPHRINE HYDROCHLORIDE	2	(0.4)	2	(0.4)
PROPAFENONE HYDROCHLORIDE	1	(0.2)	1	(0.2)
RACECADOTRIL	7	(1.4)	7	(1.4)
RANOLAZINE	2	(0.4)	0	(0.0)
RANOLAZINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
SODIUM ALGINATE	0	(0.0)	2	(0.4)
TRIMETAZIDINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
UBIDECARENONE	6	(1.2)	3	(0.6)
UBIQUINOL	1	(0.2)	0	(0.0)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
DIURETICS	**63**	**(13.0)**	**67**	**(13.8)**
ACETAZOLAMIDE	1	(0.2)	0	(0.0)
ALTIZIDE;SPIRONOLACTONE	1	(0.2)	0	(0.0)
AMILORIDE	0	(0.0)	2	(0.4)
AMILORIDE HYDROCHLORIDE;BENDROFLUMETHIAZIDE	0	(0.0)	1	(0.2)
AMILORIDE HYDROCHLORIDE;HYDROCHLOROTHIAZIDE	0	(0.0)	2	(0.4)
BUMETANIDE	1	(0.2)	2	(0.4)
CANRENONE	0	(0.0)	1	(0.2)
CHLORTALIDONE	3	(0.6)	6	(1.2)
CLOPAMIDE	0	(0.0)	1	(0.2)
DIURETICS	1	(0.2)	0	(0.0)
EPLERENONE	1	(0.2)	3	(0.6)
FUROSEMIDE	19	(3.9)	18	(3.7)
FUROSEMIDE SODIUM	0	(0.0)	1	(0.2)
HYDROCHLOROTHIAZIDE	24	(5.0)	22	(4.5)
HYDROCHLOROTHIAZIDE;TRIAMTERENE	1	(0.2)	1	(0.2)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
INDAPAMIDE	7	(1.4)	7	(1.4)
PIRETANIDE	0	(0.0)	1	(0.2)
ROSA CANINA	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
DIURETICS	**63**	**(13.0)**	**67**	**(13.8)**
SPIRONOLACTONE	2	(0.4)	2	(0.4)
TORASEMIDE	8	(1.7)	12	(2.5)
TRICHLORMETHIAZIDE	1	(0.2)	0	(0.0)
XIPAMIDE	1	(0.2)	0	(0.0)
LIPID MODIFYING AGENTS	**139**	**(28.8)**	**140**	**(28.8)**
ALLIUM SATIVUM	0	(0.0)	1	(0.2)
ALLIUM SATIVUM OIL	1	(0.2)	0	(0.0)
AMLODIPINE BESILATE;ATORVASTATIN CALCIUM	0	(0.0)	1	(0.2)
ASTAXANTHIN;FOLIC ACID;MONASCUS PURPUREUS;POLICOSANOL;UBIDECARENONE	1	(0.2)	1	(0.2)
ATORVASTATIN	24	(5.0)	43	(8.8)
ATORVASTATIN CALCIUM	29	(6.0)	20	(4.1)
ATORVASTATIN CALCIUM;EZETIMIBE	0	(0.0)	3	(0.6)
BEZAFIBRATE	0	(0.0)	1	(0.2)
CIPROFIBRATE	1	(0.2)	1	(0.2)
COLESTIPOL HYDROCHLORIDE	1	(0.2)	1	(0.2)
COLESTYRAMINE	1	(0.2)	0	(0.0)
CURCUMA LONGA	8	(1.7)	5	(1.0)
CYAMOPSIS TETRAGONOLOBA GUM	0	(0.0)	1	(0.2)
EICOSAPENTAENOIC ACID ETHYL ESTER	1	(0.2)	0	(0.0)
EZETIMIBE	7	(1.4)	3	(0.6)
EZETIMIBE;SIMVASTATIN	2	(0.4)	1	(0.2)
FENOFIBRATE	5	(1.0)	4	(0.8)
FISH OIL	5	(1.0)	9	(1.9)
FISH OIL;TOCOPHEROL	0	(0.0)	1	(0.2)
FLUVASTATIN SODIUM	0	(0.0)	1	(0.2)
KRILL OIL	1	(0.2)	1	(0.2)
LINOLENIC ACID	1	(0.2)	0	(0.0)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
LOVASTATIN	2	(0.4)	1	(0.2)
MONASCUS PURPUREUS	0	(0.0)	2	(0.4)
NICOTINIC ACID	1	(0.2)	1	(0.2)
OMEGA-3 MARINE TRIGLYCERIDES	10	(2.1)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
LIPID MODIFYING AGENTS	**139**	**(28.8)**	**140**	**(28.8)**
OMEGA-3 TRIGLYCERIDES	1	(0.2)	1	(0.2)
OMEGA-3-ACID ETHYL ESTER	1	(0.2)	0	(0.0)
PITAVASTATIN CALCIUM	1	(0.2)	1	(0.2)
POLICOSANOL	1	(0.2)	0	(0.0)
PRAVASTATIN	8	(1.7)	4	(0.8)
PRAVASTATIN SODIUM	0	(0.0)	3	(0.6)
ROSUVASTATIN	17	(3.5)	13	(2.7)
ROSUVASTATIN CALCIUM	19	(3.9)	15	(3.1)
SIMVASTATIN	18	(3.7)	18	(3.7)
OTHER	**0**	**(0.0)**	**1**	**(0.2)**
ALLIUM SATIVUM	0	(0.0)	1	(0.2)
PERIPHERAL VASODILATORS	**6**	**(1.2)**	**10**	**(2.1)**
BETAHISTINE	0	(0.0)	3	(0.6)
BETAHISTINE HYDROCHLORIDE	2	(0.4)	1	(0.2)
DIHYDROERGOCRISTINE MESILATE	0	(0.0)	1	(0.2)
DIHYDROERGOCRISTINE MESILATE;FLUNARIZINE DIHYDROCHLORIDE	0	(0.0)	1	(0.2)
FLUNARIZINE DIHYDROCHLORIDE	0	(0.0)	1	(0.2)
GINKGO BILOBA	1	(0.2)	3	(0.6)
GINKGO BILOBA EXTRACT	1	(0.2)	0	(0.0)
NICOTINIC ACID	1	(0.2)	1	(0.2)
PAPAVERINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
VASOPROTECTIVES	**181**	**(37.5)**	**101**	**(20.8)**
AMYLOCAINE HYDROCHLORIDE;BENZALKONIUM CHLORIDE;BENZOCAINE;ESCULOSIDE;HYDROCORTISONE ACETATE	1	(0.2)	0	(0.0)
ARNICA MONTANA	1	(0.2)	0	(0.0)
BECLOMETASONE DIPROPIONATE	5	(1.0)	4	(0.8)
BENZOCAINE	0	(0.0)	1	(0.2)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE BUTYRATE PROPIONATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
VASOPROTECTIVES	**181**	**(37.5)**	**101**	**(20.8)**
BISMUTH	1	(0.2)	0	(0.0)
BISMUTH OXIDE;MYROXYLON BALSAMUM BALSAM;ZINC OXIDE	0	(0.0)	1	(0.2)
CARBOMER	1	(0.2)	0	(0.0)
CHONDRUS CRISPUS EXTRACT;TITANIUM DIOXIDE;ZINC OXIDE	1	(0.2)	1	(0.2)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DICLOFENAC EPOLAMINE;HEPARIN SODIUM	0	(0.0)	1	(0.2)
DILTIAZEM	5	(1.0)	1	(0.2)
DILTIAZEM HYDROCHLORIDE	4	(0.8)	1	(0.2)
DIOSMIN	1	(0.2)	0	(0.0)
DIOSMIN;HESPERIDIN	1	(0.2)	1	(0.2)
EUPATILIN	0	(0.0)	1	(0.2)
FLUOCINOLONE ACETONIDE	1	(0.2)	2	(0.4)
FLUOCINONIDE	1	(0.2)	0	(0.0)
FLUOROMETHOLONE	1	(0.2)	1	(0.2)
GLUCOSE MONOHYDRATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
GLUCOSE;SODIUM CHLORIDE	1	(0.2)	0	(0.0)
GLYCERYL TRINITRATE	3	(0.6)	6	(1.2)
HEPARIN	2	(0.4)	4	(0.8)
HEPARIN SODIUM	0	(0.0)	2	(0.4)
HEPARINOID	1	(0.2)	0	(0.0)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
IODINE	0	(0.0)	1	(0.2)
ISOSORBIDE DINITRATE	1	(0.2)	0	(0.0)
LAUROMACROGOL 400	1	(0.2)	1	(0.2)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
NIFEDIPINE	3	(0.6)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
CARDIOVASCULAR SYSTEM				
VASOPROTECTIVES	**181**	**(37.5)**	**101**	**(20.8)**
OLEA EUROPAEA	1	(0.2)	1	(0.2)
PHENOL	0	(0.0)	1	(0.2)
PHENYLEPHRINE	1	(0.2)	3	(0.6)
PHENYLEPHRINE HYDROCHLORIDE	2	(0.4)	2	(0.4)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PYCNOGENOL	1	(0.2)	0	(0.0)
QUERCETIN	1	(0.2)	0	(0.0)
SODIUM ALGINATE	0	(0.0)	2	(0.4)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
ZINC	1	(0.2)	5	(1.0)
DERMATOLOGICALS				
ANTI-ACNE PREPARATIONS	**161**	**(33.3)**	**103**	**(21.2)**
AZELAIC ACID	2	(0.4)	0	(0.0)
AZITHROMYCIN	18	(3.7)	8	(1.6)
BENZOYL PEROXIDE	1	(0.2)	0	(0.0)
BENZOYL PEROXIDE;CLINDAMYCIN PHOSPHATE	0	(0.0)	1	(0.2)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CLINDAMYCIN	5	(1.0)	1	(0.2)
CLINDAMYCIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLINDAMYCIN PHOSPHATE	1	(0.2)	0	(0.0)
CYPROTERONE ACETATE;ETHINYLESTRADIOL	1	(0.2)	0	(0.0)
DAPSONE	1	(0.2)	0	(0.0)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DIENOGEST;ETHINYLESTRADIOL	0	(0.0)	2	(0.4)
DOXYCYCLINE	19	(3.9)	5	(1.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
ANTI-ACNE PREPARATIONS	**161**	**(33.3)**	**103**	**(21.2)**
ERYTHROMYCIN	2	(0.4)	2	(0.4)
ETHINYLESTRADIOL;NORETHISTERONE	1	(0.2)	0	(0.0)
ETHINYLESTRADIOL;NORETHISTERONE ACETATE	1	(0.2)	0	(0.0)
ETHINYLESTRADIOL;NORGESTIMATE	1	(0.2)	0	(0.0)
FLUOROMETHOLONE	1	(0.2)	1	(0.2)
IBUPROFEN	86	(17.8)	61	(12.6)
ISOTRETINOIN	1	(0.2)	0	(0.0)
METHYLPREDNISOLONE	43	(8.9)	7	(1.4)
METHYLPREDNISOLONE ACETATE	2	(0.4)	1	(0.2)
METHYLPREDNISOLONE SODIUM SUCCINATE	12	(2.5)	4	(0.8)
MINOCYCLINE	2	(0.4)	0	(0.0)
MINOCYCLINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
NICOTINAMIDE	2	(0.4)	2	(0.4)
RETINOL	0	(0.0)	1	(0.2)
SALICYLIC ACID	4	(0.8)	0	(0.0)
TRETINOIN	1	(0.2)	1	(0.2)
TRICLOSAN	1	(0.2)	1	(0.2)
ZINC	1	(0.2)	5	(1.0)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	**89**	**(18.4)**	**65**	**(13.4)**
ACICLOVIR	3	(0.6)	4	(0.8)
AMIKACIN	0	(0.0)	1	(0.2)
AMIKACIN SULFATE	0	(0.0)	1	(0.2)
BACITRACIN	1	(0.2)	2	(0.4)
BACITRACIN ZINC;POLYMYXIN B SULFATE	0	(0.0)	1	(0.2)
BACITRACIN;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
BACITRACIN;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
BENZOYL PEROXIDE	1	(0.2)	0	(0.0)
BENZYLPENICILLIN	1	(0.2)	0	(0.0)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	**89**	**(18.4)**	**65**	**(13.4)**
CLARITHROMYCIN	2	(0.4)	5	(1.0)
DOXYCYCLINE	19	(3.9)	5	(1.0)
ERYTHROMYCIN	2	(0.4)	2	(0.4)
FUSIDATE SODIUM	1	(0.2)	2	(0.4)
FUSIDIC ACID	11	(2.3)	7	(1.4)
GENTAMICIN	2	(0.4)	1	(0.2)
GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
GRAMICIDIN;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
HYALURONATE SODIUM;SULFADIAZINE SILVER	1	(0.2)	0	(0.0)
IMIQUIMOD	1	(0.2)	1	(0.2)
INGENOL MEBUTATE	0	(0.0)	1	(0.2)
LEVOFLOXACIN	9	(1.9)	6	(1.2)
METRONIDAZOLE	6	(1.2)	11	(2.3)
MINOCYCLINE	2	(0.4)	0	(0.0)
MINOCYCLINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MOXIFLOXACIN	4	(0.8)	2	(0.4)
MUPIROCIN	5	(1.0)	5	(1.0)
MUPIROCIN CALCIUM	0	(0.0)	1	(0.2)
NORFLOXACIN	1	(0.2)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
PENCICLOVIR	1	(0.2)	0	(0.0)
RIFAXIMIN	1	(0.2)	2	(0.4)
SULFADIAZINE SILVER	1	(0.2)	0	(0.0)
ANTIFUNGALS FOR DERMATOLOGICAL USE	**64**	**(13.3)**	**39**	**(8.0)**
AMOROLFINE	3	(0.6)	0	(0.0)
AMPHOTERICIN B	4	(0.8)	1	(0.2)
BETAMETHASONE DIPROPIONATE;CLOTRIMAZOLE	1	(0.2)	1	(0.2)
BIFONAZOLE	1	(0.2)	0	(0.0)
CALCIUM UNDECENOATE	1	(0.2)	0	(0.0)
CICLOPIROX	5	(1.0)	3	(0.6)
CICLOPIROX OLAMINE	6	(1.2)	3	(0.6)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
ANTIFUNGALS FOR DERMATOLOGICAL USE	**64**	**(13.3)**	**39**	**(8.0)**
CLOTRIMAZOLE;HYDROCORTISONE	0	(0.0)	1	(0.2)
CLOTRIMAZOLE;HYDROCORTISONE ACETATE	0	(0.0)	1	(0.2)
ECONAZOLE	2	(0.4)	2	(0.4)
ECONAZOLE NITRATE	0	(0.0)	3	(0.6)
FLUCONAZOLE	9	(1.9)	6	(1.2)
FLUPREDNIDENE ACETATE;MICONAZOLE NITRATE	1	(0.2)	3	(0.6)
HEXETIDINE	2	(0.4)	0	(0.0)
HYDROCORTISONE;NYSTATIN;ZINC OXIDE	1	(0.2)	0	(0.0)
KELUAMID	2	(0.4)	0	(0.0)
KETOCONAZOLE	6	(1.2)	6	(1.2)
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
NYSTATIN	13	(2.7)	4	(0.8)
NYSTATIN;ZINC OXIDE	0	(0.0)	1	(0.2)
OXICONAZOLE NITRATE	0	(0.0)	1	(0.2)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SELENIUM SULFIDE	0	(0.0)	1	(0.2)
TERBINAFINE	4	(0.8)	0	(0.0)
TERBINAFINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
TOLNAFTATE	1	(0.2)	0	(0.0)
UREA	10	(2.1)	3	(0.6)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	**134**	**(27.7)**	**84**	**(17.3)**
ANTIHISTAMINES FOR TOPICAL USE	1	(0.2)	0	(0.0)
ARNICA MONTANA	1	(0.2)	0	(0.0)
BENZOCAINE	0	(0.0)	1	(0.2)
BILASTINE	6	(1.2)	0	(0.0)
CALAMINE;ZINC OXIDE	2	(0.4)	0	(0.0)
CAMPHOR	1	(0.2)	0	(0.0)
CAMPHOR;EUCALYPTUS GLOBULUS OIL;MENTHOL	1	(0.2)	0	(0.0)
CETIRIZINE HYDROCHLORIDE	30	(6.2)	25	(5.1)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	**134**	**(27.7)**	**84**	**(17.3)**
CHLORHEXIDINE GLUCONATE;LIDOCAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CHLORPHENAMINE	3	(0.6)	2	(0.4)
CHLORPHENAMINE MALEATE	2	(0.4)	1	(0.2)
CLEMASTINE	0	(0.0)	1	(0.2)
CLEMASTINE FUMARATE	2	(0.4)	1	(0.2)
DESLORATADINE	15	(3.1)	6	(1.2)
DEXCHLORPHENIRAMINE MALEATE	2	(0.4)	2	(0.4)
DIMETINDENE MALEATE	1	(0.2)	1	(0.2)
DIPHENHYDRAMINE	4	(0.8)	2	(0.4)
DIPHENHYDRAMINE HYDROCHLORIDE	14	(2.9)	14	(2.9)
DOXEPIN HYDROCHLORIDE	2	(0.4)	1	(0.2)
EBASTINE	4	(0.8)	3	(0.6)
FEXOFENADINE HYDROCHLORIDE	15	(3.1)	8	(1.6)
HYDROXYZINE	3	(0.6)	0	(0.0)
HYDROXYZINE HYDROCHLORIDE	5	(1.0)	6	(1.2)
KETOTIFEN FUMARATE	0	(0.0)	1	(0.2)
LAUROMACROGOL 400	1	(0.2)	1	(0.2)
LEVOCETIRIZINE	2	(0.4)	2	(0.4)
LEVOCETIRIZINE DIHYDROCHLORIDE	2	(0.4)	1	(0.2)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
LIDOCAINE;PRILOCAINE	0	(0.0)	3	(0.6)
LORATADINE	34	(7.0)	11	(2.3)
MENTHA X PIPERITA OIL	1	(0.2)	0	(0.0)
MENTHOL	1	(0.2)	0	(0.0)
MENTHOL;PARAFFIN, LIQUID;PETROLATUM	1	(0.2)	0	(0.0)
OLOPATADINE HYDROCHLORIDE	1	(0.2)	2	(0.4)
PROMETHAZINE	3	(0.6)	3	(0.6)
PROMETHAZINE HYDROCHLORIDE	3	(0.6)	2	(0.4)
RUPATADINE	0	(0.0)	1	(0.2)
UREA-CRESOL-SULFONATE SODIUM	1	(0.2)	0	(0.0)
ANTIPSORIATICS	**6**	**(1.2)**	**3**	**(0.6)**
ACITRETIN	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
ANTIPSORIATICS	**6**	**(1.2)**	**3**	**(0.6)**
ALLANTOIN;ALOE VERA;NICOTINAMIDE;SALICYLIC ACID;UREA	0	(0.0)	1	(0.2)
BETAMETHASONE DIPROPIONATE;CALCIPOTRIOL	1	(0.2)	1	(0.2)
BETAMETHASONE DIPROPIONATE;CALCIPOTRIOL MONOHYDRATE	0	(0.0)	1	(0.2)
CALCIPOTRIOL	2	(0.4)	0	(0.0)
CALCITRIOL	1	(0.2)	0	(0.0)
TRETINOIN	1	(0.2)	1	(0.2)
ANTISEPTICS AND DISINFECTANTS	**10**	**(2.1)**	**10**	**(2.1)**
ALLANTOIN;OCTENIDINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
BISMUTH	1	(0.2)	0	(0.0)
BORIC ACID;SODIUM BORATE	0	(0.0)	1	(0.2)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
IODINE	0	(0.0)	1	(0.2)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	1	(0.2)	0	(0.0)
PHENOL	0	(0.0)	1	(0.2)
POVIDONE	0	(0.0)	1	(0.2)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
SILVER OXIDE	1	(0.2)	0	(0.0)
TRICLOSAN	1	(0.2)	1	(0.2)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	**271**	**(56.1)**	**129**	**(26.5)**
BECLOMETASONE DIPROPIONATE	5	(1.0)	4	(0.8)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE ACETATE;BETAMETHASONE SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
BETAMETHASONE BUTYRATE PROPIONATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	**271**	**(56.1)**	**129**	**(26.5)**
BETAMETHASONE DIPROPIONATE;BETAMETHASONE SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE;CLOTRIMAZOLE;GENTAMICIN SULFATE	2	(0.4)	1	(0.2)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE;KETOCONAZOLE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
BETAMETHASONE DIPROPIONATE;SALICYLIC ACID	3	(0.6)	1	(0.2)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BETAMETHASONE VALERATE;FUSIDIC ACID	3	(0.6)	1	(0.2)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	1	(0.2)	2	(0.4)
BETAMETHASONE;FUSIDIC ACID	0	(0.0)	1	(0.2)
BETAMETHASONE;SALICYLIC ACID	0	(0.0)	1	(0.2)
BUDESONIDE	9	(1.9)	6	(1.2)
CIPROFLOXACIN HYDROCHLORIDE;FLUOCINOLONE ACETONIDE	1	(0.2)	0	(0.0)
CLOBETASOL PROPIONATE	19	(3.9)	8	(1.6)
CLOBETASONE BUTYRATE	1	(0.2)	1	(0.2)
CORTICOSTEROIDS, WEAK, COMBINATIONS WITH ANTISEPTICS	1	(0.2)	0	(0.0)
DESONIDE	1	(0.2)	0	(0.0)
DESOXIMETASONE	2	(0.4)	0	(0.0)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
DIFLUCORTOLONE VALERATE	7	(1.4)	2	(0.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	**271**	**(56.1)**	**129**	**(26.5)**
DIFLUPREDNATE	1	(0.2)	0	(0.0)
FLUDROCORTISONE	2	(0.4)	0	(0.0)
FLUDROCORTISONE ACETATE	1	(0.2)	0	(0.0)
FLUMETASONE PIVALATE;TRICLOSAN	0	(0.0)	1	(0.2)
FLUOCINOLONE ACETONIDE	1	(0.2)	2	(0.4)
FLUOCINONIDE	1	(0.2)	0	(0.0)
FLUOROMETHOLONE	1	(0.2)	1	(0.2)
FLUTICASONE	3	(0.6)	0	(0.0)
FLUTICASONE PROPIONATE	10	(2.1)	12	(2.5)
FUSIDIC ACID;HYDROCORTISONE ACETATE	1	(0.2)	0	(0.0)
GENTAMICIN SULFATE;PREDNISOLONE	2	(0.4)	0	(0.0)
GRAMICIDIN;NEOMYCIN SULFATE;NYSTATIN;TRIAMCINOLONE ACETONIDE	1	(0.2)	1	(0.2)
HALOMETASONE MONOHYDRATE;TRICLOSAN	0	(0.0)	1	(0.2)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
HYDROCORTISONE BUTYRATE	3	(0.6)	0	(0.0)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
HYDROCORTISONE;NATAMYCIN;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
HYDROCORTISONE;OXYTETRACYCLINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
HYDROCORTISONE;UREA	1	(0.2)	0	(0.0)
METHYLPREDNISOLONE	43	(8.9)	7	(1.4)
METHYLPREDNISOLONE ACEPONATE	6	(1.2)	5	(1.0)
METHYLPREDNISOLONE ACETATE	2	(0.4)	1	(0.2)
METHYLPREDNISOLONE SODIUM SUCCINATE	12	(2.5)	4	(0.8)
MOMETASONE FUROATE	30	(6.2)	10	(2.1)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	**271**	**(56.1)**	**129**	**(26.5)**
NEOMYCIN SULFATE;NYSTATIN;TRIAMCINOLONE ACETONIDE	0	(0.0)	1	(0.2)
OCTENIDINE;PREDNICARBATE	1	(0.2)	0	(0.0)
PREDNICARBATE	1	(0.2)	0	(0.0)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PREDNISONE	99	(20.5)	29	(6.0)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
EMOLLIENTS AND PROTECTIVES	**54**	**(11.2)**	**26**	**(5.3)**
ALOE VERA	2	(0.4)	0	(0.0)
ALOE VERA;ASCORBIC ACID;SIMMONDSIA CHINENSIS OIL;VITAMIN E NOS	0	(0.0)	1	(0.2)
ALUM;COPPER;ZINC SULFATE	0	(0.0)	1	(0.2)
BEESWAX;CETYL PALMITATE;PARAFFIN, LIQUID	0	(0.0)	1	(0.2)
BENZALKONIUM CHLORIDE;CHLORHEXIDINE HYDROCHLORIDE;ISOPROPYL MYRISTATE;PARAFFIN, LIQUID	1	(0.2)	1	(0.2)
BETACAROTENE	0	(0.0)	1	(0.2)
CALAMINE;ZINC OXIDE	2	(0.4)	0	(0.0)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1	(0.2)	0	(0.0)
CAMPHOR;MENTHOL;PHENOL	1	(0.2)	0	(0.0)
CARBAMIDE PRODUCTS	1	(0.2)	1	(0.2)
CETOSTEARYL ALCOHOL;GLYCEROL	1	(0.2)	0	(0.0)
CETOSTEARYL ALCOHOL;SODIUM LAURYL SULFATE	1	(0.2)	0	(0.0)
CETYL ALCOHOL;PROPYLENE GLYCOL;SODIUM LAURYL SULFATE;STEARYL ALCOHOL	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
EMOLLIENTS AND PROTECTIVES	**54**	**(11.2)**	**26**	**(5.3)**
COPPER SULFATE;SUCRALFATE;ZINC OXIDE;ZINC SULFATE	1	(0.2)	0	(0.0)
DEXPANTHENOL;RETINOL;TOCOPHEROL	1	(0.2)	0	(0.0)
DIMETICONE;SILICON DIOXIDE	1	(0.2)	0	(0.0)
EMOLLIENTS AND PROTECTIVES	1	(0.2)	0	(0.0)
GLYCEROL	1	(0.2)	0	(0.0)
GLYCEROL;PARAFFIN, LIQUID;WHITE SOFT PARAFFIN	11	(2.3)	2	(0.4)
HEPARINOID	1	(0.2)	0	(0.0)
ISOPROPYL MYRISTATE;PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
LACTIC ACID	2	(0.4)	1	(0.2)
LACTIC ACID;SALICYLIC ACID;UREA	1	(0.2)	0	(0.0)
LACTIC ACID;UREA	0	(0.0)	1	(0.2)
LAUROMACROGOL 400;UREA	1	(0.2)	1	(0.2)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
OTHER EMOLLIENTS AND PROTECTIVES	6	(1.2)	2	(0.4)
PARAFFIN	1	(0.2)	1	(0.2)
PARAFFIN SOFT	1	(0.2)	1	(0.2)
PARAFFIN SOFT;PARAFFIN, LIQUID;WOOL FAT	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID;PETROLATUM;WOOL FAT	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID;WHITE SOFT PARAFFIN	3	(0.6)	1	(0.2)
PRUNUS AMYGDALUS OIL	2	(0.4)	0	(0.0)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SIMMONDSIA CHINENSIS OIL	0	(0.0)	1	(0.2)
THIOCTIC ACID	1	(0.2)	0	(0.0)
TITANIUM DIOXIDE	1	(0.2)	0	(0.0)
TOCOPHEROL	1	(0.2)	5	(1.0)
UREA	10	(2.1)	3	(0.6)
ZINC	1	(0.2)	5	(1.0)
ZINC OXIDE	1	(0.2)	0	(0.0)
MEDICATED DRESSINGS	**49**	**(10.1)**	**45**	**(9.3)**
CALAMINE;ZINC OXIDE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
MEDICATED DRESSINGS	**49**	**(10.1)**	**45**	**(9.3)**
CALCIUM ALGINATE;GLUCOSE OXIDASE;LACTOPEROXIDASE;SODIUM ALGINATE	1	(0.2)	0	(0.0)
CARMELLOSE SODIUM	2	(0.4)	1	(0.2)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
FUSIDATE SODIUM	1	(0.2)	2	(0.4)
FUSIDIC ACID	11	(2.3)	7	(1.4)
PARAFFIN	1	(0.2)	1	(0.2)
PARAFFIN SOFT	1	(0.2)	1	(0.2)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
SODIUM ALGINATE	0	(0.0)	2	(0.4)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
TRICLOSAN	1	(0.2)	1	(0.2)
ZINC	1	(0.2)	5	(1.0)
ZINC OXIDE	1	(0.2)	0	(0.0)
OTHER	**8**	**(1.7)**	**6**	**(1.2)**
DIOSMECTITE	8	(1.7)	6	(1.2)
OTHER DERMATOLOGICAL PREPARATIONS	**156**	**(32.3)**	**121**	**(24.9)**
ASCORBIC ACID	13	(2.7)	13	(2.7)
BETACAROTENE;BIOTIN;CALCIUM PANTOTHENATE;COPPER GLUCONATE;FERROUS GLUCONATE;FOLIC ACID;KERATIN;NICOTINIC ACID;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;SACCHAROMYCES CEREVISIAE;SODIUM ASCORBATE;THIAMINE HYDROCHLORIDE;TOCOPHERYL ACID SUCCINATE;ZINC GLUCONATE	0	(0.0)	1	(0.2)
BIMATOPROST	2	(0.4)	1	(0.2)
BIOTIN;PANTOTHENIC ACID;PYRIDOXINE HYDROCHLORIDE;RIBOFLAVIN;SETARIA SPHACELATA OIL;THIAMINE;VITAMIN E NOS;ZINC	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
OTHER DERMATOLOGICAL PREPARATIONS	**156**	**(32.3)**	**121**	**(24.9)**
BOTULINUM TOXIN TYPE A	1	(0.2)	1	(0.2)
BRIMONIDINE TARTRATE	1	(0.2)	1	(0.2)
CAMPHOR;MENTHOL;PHENOL	1	(0.2)	0	(0.0)
COLLAGEN	0	(0.0)	1	(0.2)
DAPSONE	1	(0.2)	0	(0.0)
DEXPANTHENOL	4	(0.8)	0	(0.0)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
DIMETHYL SULFOXIDE;FLUOROURACIL;SALICYLIC ACID	1	(0.2)	0	(0.0)
DISODIUM UNDECYLENAMIDE SULFOSUCCINATE;LAUROMACROGOL 400	1	(0.2)	0	(0.0)
DUTASTERIDE	0	(0.0)	3	(0.6)
ESTRADIOL	6	(1.2)	4	(0.8)
FATTY ACIDS NOS	1	(0.2)	1	(0.2)
FINASTERIDE	5	(1.0)	7	(1.4)
FLUOROURACIL;SALICYLIC ACID	0	(0.0)	1	(0.2)
GLYCOPYRRONIUM BROMIDE	1	(0.2)	2	(0.4)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
IBUPROFEN	86	(17.8)	61	(12.6)
ICTASOL;JUNIPERUS OXYCEDRUS;OLEA EUROPAEA FRUIT OIL;PINUS PALUSTRIS OIL	0	(0.0)	1	(0.2)
IVERMECTIN	6	(1.2)	2	(0.4)
LACTIC ACID	2	(0.4)	1	(0.2)
LITHIUM GLUCONATE	1	(0.2)	0	(0.0)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
MINOXIDIL	0	(0.0)	1	(0.2)
OTHER DERMATOLOGICALS	11	(2.3)	3	(0.6)
OXYGEN	4	(0.8)	6	(1.2)
OXYMETAZOLINE HYDROCHLORIDE	3	(0.6)	0	(0.0)
PHYTOMENADIONE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
OTHER DERMATOLOGICAL PREPARATIONS	**156**	**(32.3)**	**121**	**(24.9)**
PIMECROLIMUS	2	(0.4)	0	(0.0)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
PYRIDOXINE	1	(0.2)	0	(0.0)
PYRITHIONE ZINC;UNDECYLENIC ACID MONOETHANOLAMIDE;UREA	1	(0.2)	0	(0.0)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SELENIUM	4	(0.8)	0	(0.0)
SELENIUM SULFIDE	0	(0.0)	1	(0.2)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SODIUM HYDROXIDE	0	(0.0)	1	(0.2)
SUCRALFATE	0	(0.0)	1	(0.2)
TACROLIMUS	1	(0.2)	0	(0.0)
TACROLIMUS MONOHYDRATE	2	(0.4)	1	(0.2)
TRETINOIN	1	(0.2)	1	(0.2)
UBIDECARENONE	6	(1.2)	3	(0.6)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	**47**	**(9.7)**	**43**	**(8.8)**
ARNICA MONTANA	1	(0.2)	0	(0.0)
BOSWELLIA SACRA	0	(0.0)	1	(0.2)
BROMELAINS	1	(0.2)	0	(0.0)
CARMELLOSE SODIUM	2	(0.4)	1	(0.2)
COPPER GLUCONATE;HYALURONATE SODIUM;MADECASSOSIDE;MANGANESE GLUCONATE;ZINC GLUCONATE	2	(0.4)	0	(0.0)
DEXPANTHENOL	4	(0.8)	0	(0.0)
DIMETICONE;SILICON DIOXIDE	1	(0.2)	0	(0.0)
FISH OIL	5	(1.0)	9	(1.9)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONATE SODIUM;SULFADIAZINE SILVER	1	(0.2)	0	(0.0)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
LYSINE	0	(0.0)	2	(0.4)
LYSINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
DERMATOLOGICALS				
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	**47**	**(9.7)**	**43**	**(8.8)**
TOCOPHEROL	1	(0.2)	5	(1.0)
GENITO URINARY SYSTEM AND SEX HORMONES				
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	**95**	**(19.7)**	**72**	**(14.8)**
AMPHOTERICIN B	4	(0.8)	1	(0.2)
ASCORBIC ACID	13	(2.7)	13	(2.7)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CICLOPIROX	5	(1.0)	3	(0.6)
CICLOPIROX OLAMINE	6	(1.2)	3	(0.6)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)
CLINDAMYCIN	5	(1.0)	1	(0.2)
CLINDAMYCIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLINDAMYCIN PHOSPHATE	1	(0.2)	0	(0.0)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)
CLOTRIMAZOLE;HYALURONIC ACID;METRONIDAZOLE	1	(0.2)	0	(0.0)
CLOTRIMAZOLE;METRONIDAZOLE	1	(0.2)	0	(0.0)
DEXAMETHASONE;METRONIDAZOLE	1	(0.2)	0	(0.0)
ECONAZOLE	2	(0.4)	2	(0.4)
ECONAZOLE NITRATE	0	(0.0)	3	(0.6)
HEXETIDINE	2	(0.4)	0	(0.0)
HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
KETOCONAZOLE	6	(1.2)	6	(1.2)
LACTIC ACID	2	(0.4)	1	(0.2)
LACTOBACILLUS ACIDOPHILUS	0	(0.0)	3	(0.6)
LACTOBACILLUS NOS	1	(0.2)	1	(0.2)
LACTOBACILLUS RHAMNOSUS	1	(0.2)	0	(0.0)
METRONIDAZOLE	6	(1.2)	11	(2.3)
METRONIDAZOLE;MICONAZOLE NITRATE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
GENITO URINARY SYSTEM AND SEX HORMONES				
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	**95**	**(19.7)**	**72**	**(14.8)**
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
NORFLOXACIN	1	(0.2)	0	(0.0)
NYSTATIN	13	(2.7)	4	(0.8)
OCTENIDINE HYDROCHLORIDE;PHENOXYETHANOL	1	(0.2)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
OXICONAZOLE NITRATE	0	(0.0)	1	(0.2)
POTASSIUM	0	(0.0)	4	(0.8)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
TERBINAFINE	4	(0.8)	0	(0.0)
TERBINAFINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
TINIDAZOLE	1	(0.2)	0	(0.0)
OTHER GYNECOLOGICALS	**127**	**(26.3)**	**114**	**(23.5)**
BENZYDAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
CARBOMER	1	(0.2)	0	(0.0)
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
COLLAGEN	0	(0.0)	1	(0.2)
ETHINYLESTRADIOL;ETONOGESTREL	1	(0.2)	1	(0.2)
GLYCEROL	1	(0.2)	0	(0.0)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
IBUPROFEN	86	(17.8)	61	(12.6)
IBUPROFEN ARGININE	1	(0.2)	1	(0.2)
IBUPROFEN LYSINATE	0	(0.0)	1	(0.2)
LEVONORGESTREL	4	(0.8)	2	(0.4)
METHOTREXATE	5	(1.0)	0	(0.0)
METHOTREXATE SODIUM	2	(0.4)	0	(0.0)
NAPROXEN	7	(1.4)	12	(2.5)
NAPROXEN SODIUM	4	(0.8)	11	(2.3)
NIFEDIPINE	3	(0.6)	6	(1.2)
PAROXETINE	2	(0.4)	2	(0.4)
PAROXETINE HYDROCHLORIDE	1	(0.2)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
GENITO URINARY SYSTEM AND SEX HORMONES				
OTHER GYNECOLOGICALS	**127**	**(26.3)**	**114**	**(23.5)**
PAROXETINE MESILATE	0	(0.0)	1	(0.2)
PROGESTERONE	1	(0.2)	0	(0.0)
SALBUTAMOL	17	(3.5)	13	(2.7)
SALBUTAMOL SULFATE	9	(1.9)	4	(0.8)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
TERBUTALINE SULFATE	0	(0.0)	1	(0.2)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	**26**	**(5.4)**	**28**	**(5.8)**
BAZEDOXIFENE ACETATE;ESTROGENS CONJUGATED	0	(0.0)	1	(0.2)
CYPROTERONE ACETATE;ETHINYLESTRADIOL	1	(0.2)	0	(0.0)
DESOGESTREL	0	(0.0)	3	(0.6)
DIENOGEST	0	(0.0)	1	(0.2)
DIENOGEST;ESTRADIOL VALERATE	1	(0.2)	1	(0.2)
DIENOGEST;ETHINYLESTRADIOL	0	(0.0)	2	(0.4)
DROSPIRENONE	1	(0.2)	0	(0.0)
DROSPIRENONE;ETHINYLESTRADIOL	1	(0.2)	1	(0.2)
DROSPIRENONE;ETHINYLESTRADIOL BETADEX CLATHRATE	0	(0.0)	1	(0.2)
ESTRADIOL	6	(1.2)	4	(0.8)
ESTRADIOL VALERATE	1	(0.2)	0	(0.0)
ESTRADIOL;NORETHISTERONE ACETATE	0	(0.0)	1	(0.2)
ESTRIOL	1	(0.2)	0	(0.0)
ESTROGENS	0	(0.0)	1	(0.2)
ETHINYLESTRADIOL	1	(0.2)	0	(0.0)
ETHINYLESTRADIOL;FERROUS FUMARATE;NORETHISTERONE ACETATE	0	(0.0)	1	(0.2)
ETHINYLESTRADIOL;GESTODENE	1	(0.2)	2	(0.4)
ETHINYLESTRADIOL;LEVONORGESTREL	1	(0.2)	2	(0.4)
ETHINYLESTRADIOL;NORELGESTROMIN	0	(0.0)	1	(0.2)
ETHINYLESTRADIOL;NORETHISTERONE	1	(0.2)	0	(0.0)
ETHINYLESTRADIOL;NORETHISTERONE ACETATE	1	(0.2)	0	(0.0)
ETHINYLESTRADIOL;NORGESTIMATE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
GENITO URINARY SYSTEM AND SEX HORMONES				
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	**26**	**(5.4)**	**28**	**(5.8)**
HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE	0	(0.0)	1	(0.2)
LEVONORGESTREL	4	(0.8)	2	(0.4)
MEDROXYPROGESTERONE ACETATE	0	(0.0)	1	(0.2)
NORETHISTERONE ACETATE	0	(0.0)	1	(0.2)
NORETHISTERONE ENANTATE	1	(0.2)	0	(0.0)
PRASTERONE	2	(0.4)	0	(0.0)
PROGESTERONE	1	(0.2)	0	(0.0)
PROMESTRIENE	1	(0.2)	0	(0.0)
TESTOSTERONE	0	(0.0)	2	(0.4)
TESTOSTERONE CIPIONATE	2	(0.4)	0	(0.0)
TESTOSTERONE UNDECANOATE	0	(0.0)	1	(0.2)
UROLOGICALS	**90**	**(18.6)**	**89**	**(18.3)**
ALFUZOSIN HYDROCHLORIDE	2	(0.4)	5	(1.0)
AMITRIPTYLINE HYDROCHLORIDE	7	(1.4)	7	(1.4)
BENZOCAINE	0	(0.0)	1	(0.2)
BOTULINUM TOXIN TYPE A	1	(0.2)	1	(0.2)
BUDESONIDE	9	(1.9)	6	(1.2)
CHONDROITIN	1	(0.2)	0	(0.0)
CHONDROITIN SULFATE SODIUM	2	(0.4)	2	(0.4)
CLOMIPRAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
COLLAGEN	0	(0.0)	1	(0.2)
CUCURBITA PEPO OIL	0	(0.0)	1	(0.2)
DOXAZOSIN	3	(0.6)	5	(1.0)
DOXAZOSIN MESILATE	3	(0.6)	4	(0.8)
DULOXETINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
DUTASTERIDE	0	(0.0)	3	(0.6)
DUTASTERIDE;TAMSULOSIN HYDROCHLORIDE	2	(0.4)	4	(0.8)
EPILOBIUM PARVIFLORUM;SELENOMETHIONINE;SERENOA REPENS FRUIT;SOLANUM LYCOPERSICUM;ZINC GLUCONATE	1	(0.2)	0	(0.0)
FINASTERIDE	5	(1.0)	7	(1.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
GENITO URINARY SYSTEM AND SEX HORMONES				
UROLOGICALS	**90**	**(18.6)**	**89**	**(18.3)**
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
LIDOCAINE;PRILOCAINE	0	(0.0)	3	(0.6)
MAGNESIUM CITRATE	0	(0.0)	4	(0.8)
MAGNESIUM HYDROXIDE	0	(0.0)	2	(0.4)
MIRABEGRON	1	(0.2)	2	(0.4)
OXYBUTYNIN	2	(0.4)	0	(0.0)
PAPAVERINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
PHENAZOPYRIDINE HYDROCHLORIDE	2	(0.4)	2	(0.4)
POTASSIUM PHOSPHATE MONOBASIC	0	(0.0)	1	(0.2)
POTASSIUM PHOSPHATE MONOBASIC;SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
PRUNUS AFRICANA	1	(0.2)	0	(0.0)
PRUNUS AFRICANA EXTRACT	1	(0.2)	0	(0.0)
SERENOA REPENS	2	(0.4)	2	(0.4)
SERENOA REPENS EXTRACT	1	(0.2)	1	(0.2)
SILDENAFIL CITRATE	5	(1.0)	4	(0.8)
SILODOSIN	1	(0.2)	1	(0.2)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SOLIFENACIN SUCCINATE	1	(0.2)	0	(0.0)
SOLIFENACIN SUCCINATE;TAMSULOSIN HYDROCHLORIDE	1	(0.2)	0	(0.0)
TADALAFIL	3	(0.6)	5	(1.0)
TAMSULOSIN HYDROCHLORIDE	20	(4.1)	19	(3.9)
TERAZOSIN	1	(0.2)	1	(0.2)
TOLTERODINE	0	(0.0)	1	(0.2)
TROSPIUM CHLORIDE	1	(0.2)	1	(0.2)
VARDENAFIL HYDROCHLORIDE	0	(0.0)	1	(0.2)
MUSCULO-SKELETAL SYSTEM				
ANTIGOUT PREPARATIONS	**19**	**(3.9)**	**27**	**(5.6)**
ALLOPURINOL	12	(2.5)	23	(4.7)
COLCHICINE	4	(0.8)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
MUSCULO-SKELETAL SYSTEM				
ANTIGOUT PREPARATIONS	**19**	**(3.9)**	**27**	**(5.6)**
COLCHICINE;PAPAVER SOMNIFERUM POWDER;TIEMONIUM METHYLSULPHATE	3	(0.6)	0	(0.0)
FEBUXOSTAT	4	(0.8)	3	(0.6)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	**155**	**(32.1)**	**139**	**(28.6)**
ACECLOFENAC	0	(0.0)	1	(0.2)
ACEMETACIN	2	(0.4)	0	(0.0)
ARNICA MONTANA	1	(0.2)	0	(0.0)
BENZYDAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
BOSWELLIA SACRA	0	(0.0)	1	(0.2)
BROMFENAC SODIUM	1	(0.2)	0	(0.0)
CELECOXIB	10	(2.1)	7	(1.4)
CHONDROITIN	1	(0.2)	0	(0.0)
CHONDROITIN SULFATE SODIUM	2	(0.4)	2	(0.4)
CHONDROITIN SULFATE;GLUCOSAMINE	1	(0.2)	0	(0.0)
CHONDROITIN;GLUCOSAMINE	2	(0.4)	5	(1.0)
CLONIXIN LYSINATE	0	(0.0)	1	(0.2)
COLLAGEN	0	(0.0)	1	(0.2)
CURCUMA LONGA	8	(1.7)	5	(1.0)
CURCUMIN	1	(0.2)	0	(0.0)
DEXKETOPROFEN	2	(0.4)	0	(0.0)
DEXKETOPROFEN TROMETAMOL	2	(0.4)	1	(0.2)
DIACEREIN	1	(0.2)	0	(0.0)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC DIETHYLAMINE	1	(0.2)	1	(0.2)
DICLOFENAC EPOLAMINE	1	(0.2)	0	(0.0)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
ESOMEPRAZOLE MAGNESIUM;NAPROXEN	1	(0.2)	0	(0.0)
ETORICOXIB	5	(1.0)	5	(1.0)
FISH OIL	5	(1.0)	9	(1.9)
FLURBIPROFEN	0	(0.0)	1	(0.2)
FLURBIPROFEN SODIUM	1	(0.2)	0	(0.0)
GLUCOSAMINE	6	(1.2)	0	(0.0)
GLUCOSAMINE SULFATE	0	(0.0)	1	(0.2)
HEPARINOID	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
MUSCULO-SKELETAL SYSTEM				
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	**155**	**(32.1)**	**139**	**(28.6)**
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
IBUPROFEN	86	(17.8)	61	(12.6)
IBUPROFEN ARGININE	1	(0.2)	1	(0.2)
IBUPROFEN LYSINATE	0	(0.0)	1	(0.2)
IMPATIENS BALSAMINA	1	(0.2)	0	(0.0)
INDOMETACIN	0	(0.0)	1	(0.2)
KETOPROFEN	8	(1.7)	4	(0.8)
KETOPROFEN LYSINE	1	(0.2)	0	(0.0)
KETOROLAC TROMETHAMINE	8	(1.7)	7	(1.4)
KRILL OIL	1	(0.2)	1	(0.2)
LOXOPROFEN SODIUM	1	(0.2)	0	(0.0)
MEFENAMIC ACID	1	(0.2)	1	(0.2)
MELOXICAM	6	(1.2)	9	(1.9)
METHYLSULFONYLMETHANE	0	(0.0)	1	(0.2)
NABUMETONE	1	(0.2)	0	(0.0)
NAPROXEN	7	(1.4)	12	(2.5)
NAPROXEN SODIUM	4	(0.8)	11	(2.3)
NIFLUMIC ACID	1	(0.2)	0	(0.0)
NIMESULIDE	3	(0.6)	1	(0.2)
PIROXICAM	0	(0.0)	1	(0.2)
ROSA CANINA	0	(0.0)	1	(0.2)
TIAPROFENIC ACID	0	(0.0)	1	(0.2)
VACCINIUM MACROCARPON	0	(0.0)	1	(0.2)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
DRUGS FOR TREATMENT OF BONE DISEASES	**10**	**(2.1)**	**8**	**(1.6)**
ALENDRONATE SODIUM	1	(0.2)	2	(0.4)
ALENDRONIC ACID	2	(0.4)	0	(0.0)
DENOSUMAB	2	(0.4)	3	(0.6)
IBANDRONATE SODIUM	1	(0.2)	0	(0.0)
IBANDRONIC ACID	0	(0.0)	2	(0.4)
RISEDRONATE SODIUM	2	(0.4)	0	(0.0)
ZOLEDRONIC ACID	2	(0.4)	0	(0.0)
ZOLEDRONIC ACID MONOHYDRATE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
MUSCULO-SKELETAL SYSTEM				
MUSCLE RELAXANTS	**22**	**(4.6)**	**26**	**(5.3)**
BACLOFEN	1	(0.2)	1	(0.2)
BOTULINUM TOXIN TYPE A	1	(0.2)	1	(0.2)
CAFFEINE;CARISOPRODOL;DICLOFENAC;PARACETAMOL	1	(0.2)	0	(0.0)
CAFFEINE;METAMIZOLE SODIUM;ORPHENADRINE CITRATE	1	(0.2)	0	(0.0)
CYCLOBENZAPRINE HYDROCHLORIDE	8	(1.7)	7	(1.4)
DIAZEPAM	4	(0.8)	9	(1.9)
EPERISONE HYDROCHLORIDE	1	(0.2)	0	(0.0)
METHOCARBAMOL	3	(0.6)	3	(0.6)
METHOCARBAMOL;PARACETAMOL	0	(0.0)	1	(0.2)
ORPHENADRINE	0	(0.0)	1	(0.2)
ROCURONIUM BROMIDE	2	(0.4)	0	(0.0)
SUXAMETHONIUM CHLORIDE	1	(0.2)	1	(0.2)
THIOCOLCHICOSIDE	2	(0.4)	1	(0.2)
TIZANIDINE HYDROCHLORIDE	0	(0.0)	3	(0.6)
TOLPERISONE HYDROCHLORIDE	0	(0.0)	1	(0.2)
VECURONIUM BROMIDE	1	(0.2)	0	(0.0)
OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM	**8**	**(1.7)**	**5**	**(1.0)**
BROMELAINS	1	(0.2)	0	(0.0)
CLOMIPRAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	**191**	**(39.5)**	**185**	**(38.1)**
ACECLOFENAC	0	(0.0)	1	(0.2)
ACETYLSALICYLIC ACID	59	(12.2)	83	(17.1)
ARNICA MONTANA	1	(0.2)	0	(0.0)
BENZYDAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
CAMPHOR	1	(0.2)	0	(0.0)
CAMPHOR;EUCALYPTUS GLOBULUS OIL;MENTHOL	1	(0.2)	0	(0.0)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1	(0.2)	0	(0.0)
CHONDROITIN	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
MUSCULO-SKELETAL SYSTEM				
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	**191**	**(39.5)**	**185**	**(38.1)**
CHONDROITIN SULFATE SODIUM	2	(0.4)	2	(0.4)
CHONDROITIN SULFATE;GLUCOSAMINE	1	(0.2)	0	(0.0)
CHONDROITIN;GLUCOSAMINE	2	(0.4)	5	(1.0)
DEXKETOPROFEN	2	(0.4)	0	(0.0)
DEXKETOPROFEN TROMETAMOL	2	(0.4)	1	(0.2)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC DIETHYLAMINE	1	(0.2)	1	(0.2)
DICLOFENAC EPOLAMINE	1	(0.2)	0	(0.0)
DICLOFENAC EPOLAMINE;HEPARIN SODIUM	0	(0.0)	1	(0.2)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
FLURBIPROFEN	0	(0.0)	1	(0.2)
FLURBIPROFEN SODIUM	1	(0.2)	0	(0.0)
FOLIC ACID	8	(1.7)	2	(0.4)
GLUCOSAMINE	6	(1.2)	0	(0.0)
GLUCOSAMINE SULFATE	0	(0.0)	1	(0.2)
HEPARINOID	1	(0.2)	0	(0.0)
IBUPROFEN	86	(17.8)	61	(12.6)
IBUPROFEN ARGININE	1	(0.2)	1	(0.2)
IBUPROFEN LYSINATE	0	(0.0)	1	(0.2)
INDOMETACIN	0	(0.0)	1	(0.2)
KETOPROFEN	8	(1.7)	4	(0.8)
KETOPROFEN LYSINE	1	(0.2)	0	(0.0)
KETOROLAC TROMETHAMINE	8	(1.7)	7	(1.4)
LOXOPROFEN SODIUM	1	(0.2)	0	(0.0)
MELOXICAM	6	(1.2)	9	(1.9)
MENTHOL	1	(0.2)	0	(0.0)
METHYLSULFONYLMETHANE	0	(0.0)	1	(0.2)
NAPROXEN	7	(1.4)	12	(2.5)
NAPROXEN SODIUM	4	(0.8)	11	(2.3)
NIFLUMIC ACID	1	(0.2)	0	(0.0)
NIMESULIDE	3	(0.6)	1	(0.2)
PIROXICAM	0	(0.0)	1	(0.2)
SALICYLIC ACID	4	(0.8)	0	(0.0)
TOLPERISONE HYDROCHLORIDE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
MUSCULO-SKELETAL SYSTEM				
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	**191**	**(39.5)**	**185**	**(38.1)**
VACCINIUM MACROCARPON	0	(0.0)	1	(0.2)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)
NERVOUS SYSTEM				
ANALGESICS	**269**	**(55.7)**	**243**	**(50.0)**
ACETYLSALICYLATE LYSINE	4	(0.8)	2	(0.4)
ACETYLSALICYLIC ACID	59	(12.2)	83	(17.1)
ACETYLSALICYLIC ACID;ASCORBIC ACID	1	(0.2)	0	(0.0)
ACETYLSALICYLIC ACID;CAFFEINE;CODEINE PHOSPHATE;PARACETAMOL	1	(0.2)	0	(0.0)
ACETYLSALICYLIC ACID;CAFFEINE;PARACETAMOL	3	(0.6)	2	(0.4)
ACETYLSALICYLIC ACID;CALCIUM CARBONATE	1	(0.2)	0	(0.0)
ACETYLSALICYLIC ACID;GLYCINE	1	(0.2)	0	(0.0)
ACETYLSALICYLIC ACID;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
ADIPHENINE HYDROCHLORIDE;METAMIZOLE SODIUM;PROMETHAZINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
AMITRIPTYLINE HYDROCHLORIDE	7	(1.4)	7	(1.4)
ASCORBIC ACID;RUTOSIDE;SALICYLAMIDE	1	(0.2)	0	(0.0)
BOTULINUM TOXIN TYPE A	1	(0.2)	1	(0.2)
CAFFEINE;CODEINE PHOSPHATE;MEPROBAMATE;PARACETAMOL	1	(0.2)	0	(0.0)
CAFFEINE;CODEINE;PARACETAMOL	1	(0.2)	0	(0.0)
CAFFEINE;ISOMETHEPTENE HYDROCHLORIDE;METAMIZOLE SODIUM	1	(0.2)	0	(0.0)
CAFFEINE;PAPAVER SOMNIFERUM LATEX;PARACETAMOL	1	(0.2)	1	(0.2)
CANNABIDIOL	0	(0.0)	1	(0.2)
CANNABIS SATIVA	2	(0.4)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
ANALGESICS	**269**	**(55.7)**	**243**	**(50.0)**
CARBAMAZEPINE	1	(0.2)	1	(0.2)
CHLORPHENAMINE MALEATE;DEXTROMETHORPHAN HYDROBROMIDE;PARACETAMOL;PHENYLEPHRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CHLORPHENAMINE MALEATE;PARACETAMOL	0	(0.0)	1	(0.2)
CHLORPHENAMINE MALEATE;PARACETAMOL;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLOMIPRAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
CODEINE	2	(0.4)	4	(0.8)
CODEINE PHOSPHATE	2	(0.4)	2	(0.4)
CODEINE PHOSPHATE HEMIHYDRATE;PARACETAMOL	1	(0.2)	0	(0.0)
CODEINE PHOSPHATE;DOXYLAMINE SUCCINATE;PARACETAMOL	0	(0.0)	1	(0.2)
CODEINE PHOSPHATE;IBUPROFEN;PARACETAMOL	2	(0.4)	0	(0.0)
CODEINE PHOSPHATE;PARACETAMOL	8	(1.7)	7	(1.4)
CODEINE;PARACETAMOL	1	(0.2)	1	(0.2)
DEXKETOPROFEN TROMETAMOL;TRAMADOL HYDROCHLORIDE	1	(0.2)	0	(0.0)
DEXTROMETHORPHAN HYDROBROMIDE;DOXYLAMINE SUCCINATE;PARACETAMOL	1	(0.2)	0	(0.0)
DEXTROMETHORPHAN HYDROBROMIDE;DOXYLAMINE SUCCINATE;PARACETAMOL;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
ANALGESICS	**269**	**(55.7)**	**243**	**(50.0)**
DEXTROMETHORPHAN HYDROBROMIDE;GUAIFENESIN;PARACETAMOL;PHENYLEPHRINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
DEXTROMETHORPHAN HYDROBROMIDE;PARACETAMOL;PSEUDOEPHEDRINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
DIHYDROCODEINE BITARTRATE	1	(0.2)	1	(0.2)
DIHYDROERGOCRISTINE MESILATE	0	(0.0)	1	(0.2)
DIPHENHYDRAMINE HYDROCHLORIDE;PARACETAMOL	1	(0.2)	0	(0.0)
DIPHENHYDRAMINE HYDROCHLORIDE;PARACETAMOL;PHENYLEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
DOXYLAMINE SUCCINATE;PARACETAMOL	1	(0.2)	0	(0.0)
DULOXETINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
ERENUMAB AOOE	0	(0.0)	1	(0.2)
FENTANYL	7	(1.4)	10	(2.1)
FENTANYL CITRATE	2	(0.4)	1	(0.2)
FLUNARIZINE DIHYDROCHLORIDE	0	(0.0)	1	(0.2)
GABAPENTIN	13	(2.7)	10	(2.1)
HYDROCODONE	1	(0.2)	0	(0.0)
HYDROCODONE BITARTRATE;PARACETAMOL	5	(1.0)	10	(2.1)
HYDROMORPHONE	1	(0.2)	3	(0.6)
HYDROMORPHONE HYDROCHLORIDE	2	(0.4)	2	(0.4)
IBUPROFEN;PARACETAMOL	1	(0.2)	2	(0.4)
IMPATIENS BALSAMINA	1	(0.2)	0	(0.0)
MENTHOL	1	(0.2)	0	(0.0)
METAMIZOLE MAGNESIUM	0	(0.0)	1	(0.2)
METAMIZOLE SODIUM	15	(3.1)	15	(3.1)
METAMIZOLE SODIUM MONOHYDRATE	0	(0.0)	2	(0.4)
METOPROLOL	9	(1.9)	13	(2.7)
METOPROLOL SUCCINATE	7	(1.4)	11	(2.3)
METOPROLOL TARTRATE	7	(1.4)	5	(1.0)
MORPHINE	3	(0.6)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
ANALGESICS	**269**	**(55.7)**	**243**	**(50.0)**
MORPHINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
MORPHINE SULFATE	1	(0.2)	1	(0.2)
MORPHINE SULFATE PENTAHYDRATE	0	(0.0)	1	(0.2)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	1	(0.2)	4	(0.8)
NALOXONE HYDROCHLORIDE;TILIDINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
NEFOPAM	2	(0.4)	0	(0.0)
OXYCODONE	8	(1.7)	6	(1.2)
OXYCODONE HYDROCHLORIDE	6	(1.2)	4	(0.8)
OXYCODONE HYDROCHLORIDE;PARACETAMOL	2	(0.4)	6	(1.2)
PAPAVER SOMNIFERUM;PARACETAMOL	1	(0.2)	3	(0.6)
PARACETAMOL	151	(31.3)	114	(23.5)
PARACETAMOL;PHENYLEPHRINE HYDROCHLORIDE	1	(0.2)	2	(0.4)
PARACETAMOL;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	1	(0.2)
PARACETAMOL;TRAMADOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
PETHIDINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
PREGABALIN	18	(3.7)	20	(4.1)
PROPRANOLOL	7	(1.4)	4	(0.8)
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
PRUNUS DOMESTICA	1	(0.2)	0	(0.0)
RIZATRIPTAN BENZOATE	0	(0.0)	1	(0.2)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SUMATRIPTAN	0	(0.0)	2	(0.4)
SUMATRIPTAN SUCCINATE	0	(0.0)	1	(0.2)
TAPENTADOL	2	(0.4)	2	(0.4)
TAPENTADOL HYDROCHLORIDE	1	(0.2)	0	(0.0)
TIMOLOL	0	(0.0)	1	(0.2)
TIMOLOL MALEATE	0	(0.0)	3	(0.6)
TOPIRAMATE	0	(0.0)	1	(0.2)
TRAMADOL HYDROCHLORIDE	22	(4.6)	22	(4.5)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
ANALGESICS	**269**	**(55.7)**	**243**	**(50.0)**
VALPROATE SODIUM	1	(0.2)	0	(0.0)
VENLAFAXINE HYDROCHLORIDE	5	(1.0)	3	(0.6)
VERAPAMIL	0	(0.0)	1	(0.2)
VERAPAMIL HYDROCHLORIDE	0	(0.0)	2	(0.4)
ZOLMITRIPTAN	0	(0.0)	1	(0.2)
ANESTHETICS	**26**	**(5.4)**	**29**	**(6.0)**
ANESTHETICS	1	(0.2)	2	(0.4)
BENZOCAINE	0	(0.0)	1	(0.2)
BUPIVACAINE	0	(0.0)	4	(0.8)
BUPIVACAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
BUPIVACAINE HYDROCHLORIDE;EPINEPHRINE BITARTRATE	1	(0.2)	0	(0.0)
BUPIVACAINE HYDROCHLORIDE;LIDOCAINE	0	(0.0)	1	(0.2)
CHLORHEXIDINE GLUCONATE;LIDOCAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
EPINEPHRINE;LIDOCAINE HYDROCHLORIDE	4	(0.8)	5	(1.0)
ETOMIDATE	0	(0.0)	1	(0.2)
FENTANYL	7	(1.4)	10	(2.1)
FENTANYL CITRATE	2	(0.4)	1	(0.2)
KETAMINE	1	(0.2)	0	(0.0)
KETAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
LIDOCAINE;PRILOCAINE	0	(0.0)	3	(0.6)
MEPIVACAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
PHENOL	0	(0.0)	1	(0.2)
PRILOCAINE	0	(0.0)	1	(0.2)
PRILOCAINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
PROPOFOL	3	(0.6)	9	(1.9)
REMIFENTANIL HYDROCHLORIDE	1	(0.2)	1	(0.2)
ANTI-PARKINSON DRUGS	**21**	**(4.3)**	**22**	**(4.5)**
AMANTADINE	0	(0.0)	1	(0.2)
BENSERAZIDE HYDROCHLORIDE;LEVODOPA	1	(0.2)	2	(0.4)
BIPERIDEN HYDROCHLORIDE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
ANTI-PARKINSON DRUGS	**21**	**(4.3)**	**22**	**(4.5)**
CARBIDOPA MONOHYDRATE;LEVODOPA	2	(0.4)	0	(0.0)
CARBIDOPA;LEVODOPA	1	(0.2)	1	(0.2)
DIPHENHYDRAMINE	4	(0.8)	2	(0.4)
DIPHENHYDRAMINE HYDROCHLORIDE	14	(2.9)	14	(2.9)
LEVODOPA	0	(0.0)	1	(0.2)
ORPHENADRINE	0	(0.0)	1	(0.2)
PRAMIPEXOLE	0	(0.0)	1	(0.2)
PRAMIPEXOLE DIHYDROCHLORIDE	0	(0.0)	2	(0.4)
RASAGILINE MESYLATE	0	(0.0)	2	(0.4)
ROPINIROLE HYDROCHLORIDE	2	(0.4)	1	(0.2)
ANTIEPILEPTICS	**59**	**(12.2)**	**65**	**(13.4)**
ACETAZOLAMIDE	1	(0.2)	0	(0.0)
CANNABIDIOL	0	(0.0)	1	(0.2)
CANNABIS SATIVA	2	(0.4)	4	(0.8)
CARBAMAZEPINE	1	(0.2)	1	(0.2)
CLONAZEPAM	7	(1.4)	8	(1.6)
DIAZEPAM	4	(0.8)	9	(1.9)
GABAPENTIN	13	(2.7)	10	(2.1)
LAMOTRIGINE	1	(0.2)	2	(0.4)
LEVETIRACETAM	2	(0.4)	4	(0.8)
LORAZEPAM	9	(1.9)	14	(2.9)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
MIDAZOLAM	3	(0.6)	3	(0.6)
MIDAZOLAM HYDROCHLORIDE	2	(0.4)	2	(0.4)
PHENYTOIN	0	(0.0)	1	(0.2)
PREGABALIN	18	(3.7)	20	(4.1)
PRIMIDONE	1	(0.2)	0	(0.0)
TOPIRAMATE	0	(0.0)	1	(0.2)
VALPROATE SODIUM	1	(0.2)	0	(0.0)
OTHER NERVOUS SYSTEM DRUGS	**52**	**(10.8)**	**58**	**(11.9)**
ACETYLCARNITINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
BACLOFEN	1	(0.2)	1	(0.2)
BETAHISTINE	0	(0.0)	3	(0.6)
BETAHISTINE HYDROCHLORIDE	2	(0.4)	1	(0.2)
BUPROPION	1	(0.2)	2	(0.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
OTHER NERVOUS SYSTEM DRUGS	**52**	**(10.8)**	**58**	**(11.9)**
BUPROPION HYDROCHLORIDE	1	(0.2)	2	(0.4)
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
CYANOCOBALAMIN	10	(2.1)	17	(3.5)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	2	(0.4)	0	(0.0)
CYTIDINE PHOSPHATE SODIUM;HYDROXOCOBALAMIN ACETATE;URIDINE TRIPHOSPHATE TRISODIUM	2	(0.4)	0	(0.0)
CYTISINICLINE	1	(0.2)	0	(0.0)
DIHYDROERGOCRISTINE MESILATE;FLUNARIZINE DIHYDROCHLORIDE	0	(0.0)	1	(0.2)
DIMENHYDRINATE	1	(0.2)	1	(0.2)
FLUNARIZINE DIHYDROCHLORIDE	0	(0.0)	1	(0.2)
FLUOXETINE	3	(0.6)	1	(0.2)
FLUOXETINE HYDROCHLORIDE	1	(0.2)	4	(0.8)
GABAPENTIN	13	(2.7)	10	(2.1)
GINKGO BILOBA	1	(0.2)	3	(0.6)
GINKGO BILOBA EXTRACT	1	(0.2)	0	(0.0)
HYDROXOCOBALAMIN	1	(0.2)	0	(0.0)
LYSINE	0	(0.0)	2	(0.4)
LYSINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MECLOZINE	1	(0.2)	2	(0.4)
MECOBALAMIN	1	(0.2)	0	(0.0)
NALMEFENE HYDROCHLORIDE DIHYDRATE	0	(0.0)	1	(0.2)
NALOXONE HYDROCHLORIDE;OXYCODONE HYDROCHLORIDE	1	(0.2)	4	(0.8)
NEOSTIGMINE METILSULFATE	1	(0.2)	0	(0.0)
NICOTINE	1	(0.2)	1	(0.2)
NICOTINE POLACRILEX	0	(0.0)	1	(0.2)
PILOCARPINE	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
OTHER NERVOUS SYSTEM DRUGS	**52**	**(10.8)**	**58**	**(11.9)**
PROPRANOLOL	7	(1.4)	4	(0.8)
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
PYRIDOSTIGMINE BROMIDE	1	(0.2)	0	(0.0)
THIOCTIC ACID	1	(0.2)	0	(0.0)
TRIMETAZIDINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
PSYCHOANALEPTICS	**60**	**(12.4)**	**78**	**(16.0)**
ACETYLCARNITINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
AGOMELATINE	1	(0.2)	0	(0.0)
AMFETAMINE ASPARTATE;AMFETAMINE SULFATE;DEXAMFETAMINE SACCHARATE;DEXAMFETAMINE SULFATE	0	(0.0)	1	(0.2)
AMITRIPTYLINE HYDROCHLORIDE	7	(1.4)	7	(1.4)
AMITRIPTYLINE HYDROCHLORIDE;PERPHENAZINE	1	(0.2)	0	(0.0)
ARGININE;GRIFFONIA SIMPLICIFOLIA;LYSINE;MELISSA OFFICINALIS;PEPTIDES NOS;PYRIDOXINE HYDROCHLORIDE;RHODIOLA ROSEA	0	(0.0)	1	(0.2)
BUPROPION	1	(0.2)	2	(0.4)
BUPROPION HYDROCHLORIDE	1	(0.2)	2	(0.4)
CAMELLIA SINENSIS	1	(0.2)	0	(0.0)
CITALOPRAM	4	(0.8)	4	(0.8)
CITALOPRAM HYDROBROMIDE	0	(0.0)	2	(0.4)
CLOMIPRAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
DESVENLAFAXINE	0	(0.0)	1	(0.2)
DESVENLAFAXINE SUCCINATE MONOHYDRATE	1	(0.2)	0	(0.0)
DEXAMFETAMINE SULFATE	1	(0.2)	0	(0.0)
DEXMETHYLPHENIDATE HYDROCHLORIDE	1	(0.2)	0	(0.0)
DONEPEZIL	1	(0.2)	0	(0.0)
DOXEPIN HYDROCHLORIDE	2	(0.4)	1	(0.2)
DULOXETINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
ESCITALOPRAM	4	(0.8)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
PSYCHOANALEPTICS	**60**	**(12.4)**	**78**	**(16.0)**
ESCITALOPRAM OXALATE	3	(0.6)	7	(1.4)
FLUOXETINE	3	(0.6)	1	(0.2)
FLUOXETINE HYDROCHLORIDE	1	(0.2)	4	(0.8)
FLUVOXAMINE MALEATE	0	(0.0)	1	(0.2)
GINKGO BILOBA	1	(0.2)	3	(0.6)
GINKGO BILOBA EXTRACT	1	(0.2)	0	(0.0)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
LAMOTRIGINE	1	(0.2)	2	(0.4)
LISDEXAMFETAMINE MESILATE	2	(0.4)	0	(0.0)
MEMANTINE	0	(0.0)	1	(0.2)
METHYLPHENIDATE	1	(0.2)	0	(0.0)
METHYLPHENIDATE HYDROCHLORIDE	2	(0.4)	2	(0.4)
MIRTAZAPINE	3	(0.6)	7	(1.4)
MODAFINIL	1	(0.2)	0	(0.0)
NORTRIPTYLINE	1	(0.2)	0	(0.0)
NORTRIPTYLINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
OPIPRAMOL HYDROCHLORIDE	0	(0.0)	2	(0.4)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)
PAROXETINE	2	(0.4)	2	(0.4)
PAROXETINE HYDROCHLORIDE	1	(0.2)	3	(0.6)
PAROXETINE MESILATE	0	(0.0)	1	(0.2)
PIRACETAM	0	(0.0)	2	(0.4)
REBOXETINE MESILATE	0	(0.0)	1	(0.2)
RIVASTIGMINE	0	(0.0)	1	(0.2)
SERTRALINE HYDROCHLORIDE	11	(2.3)	12	(2.5)
TRAZODONE HYDROCHLORIDE	2	(0.4)	5	(1.0)
VENLAFAXINE HYDROCHLORIDE	5	(1.0)	3	(0.6)
VINPOCETINE	1	(0.2)	2	(0.4)
VORTIOXETINE HYDROBROMIDE	0	(0.0)	1	(0.2)
PSYCHOLEPTICS	**137**	**(28.4)**	**129**	**(26.5)**
ALPRAZOLAM	14	(2.9)	8	(1.6)
AMISULPRIDE	1	(0.2)	0	(0.0)
AMITRIPTYLINE HYDROCHLORIDE	7	(1.4)	7	(1.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
PSYCHOLEPTICS	**137**	**(28.4)**	**129**	**(26.5)**
ANEMARRHENA ASPHODELOIDES;GLYCYRRHIZA GLABRA;HUMULUS LUPULUS;MAGNESIUM OROTATE;PORIA COCOS;VALERIANA OFFICINALIS	1	(0.2)	0	(0.0)
ARIPIPRAZOLE	1	(0.2)	3	(0.6)
BROMAZEPAM	6	(1.2)	4	(0.8)
BROTIZOLAM	1	(0.2)	1	(0.2)
BUSPIRONE HYDROCHLORIDE	1	(0.2)	2	(0.4)
BUTALBITAL	0	(0.0)	1	(0.2)
CANNABIDIOL	0	(0.0)	1	(0.2)
CANNABIS SATIVA	2	(0.4)	4	(0.8)
CARBAMAZEPINE	1	(0.2)	1	(0.2)
CLOMIPRAMINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CLONAZEPAM	7	(1.4)	8	(1.6)
CRATAEGUS SPP. DRY EXTRACT;VALERIANA OFFICINALIS DRY EXTRACT	1	(0.2)	0	(0.0)
CYAMEMAZINE	1	(0.2)	0	(0.0)
DELORAZEPAM	0	(0.0)	1	(0.2)
DIAZEPAM	4	(0.8)	9	(1.9)
DIPHENHYDRAMINE	4	(0.8)	2	(0.4)
DIPHENHYDRAMINE HYDROCHLORIDE	14	(2.9)	14	(2.9)
DIPHENHYDRAMINE HYDROCHLORIDE;PARACETAMOL	1	(0.2)	0	(0.0)
DOXEPIN HYDROCHLORIDE	2	(0.4)	1	(0.2)
DOXYLAMINE SUCCINATE	0	(0.0)	1	(0.2)
DULOXETINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
ESCHSCHOLZIA CALIFORNICA HERB;HUMULUS LUPULUS CONE;MELATONIN;MELISSA OFFICINALIS LEAF;PASSIFLORA INCARNATA HERB;PYRIDOXINE HYDROCHLORIDE;VALERIANA OFFICINALIS ROOT	1	(0.2)	0	(0.0)
ESCITALOPRAM	4	(0.8)	6	(1.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
PSYCHOLEPTICS	**137**	**(28.4)**	**129**	**(26.5)**
ESCITALOPRAM OXALATE	3	(0.6)	7	(1.4)
ESTAZOLAM	1	(0.2)	0	(0.0)
ESZOPICLONE	1	(0.2)	0	(0.0)
FLUNITRAZEPAM	1	(0.2)	0	(0.0)
FLUOXETINE	3	(0.6)	1	(0.2)
FLUOXETINE HYDROCHLORIDE	1	(0.2)	4	(0.8)
FLURAZEPAM	0	(0.0)	1	(0.2)
HALOPERIDOL	1	(0.2)	1	(0.2)
HALOPERIDOL LACTATE	1	(0.2)	0	(0.0)
HERBAL EXTRACT NOS;VALERIANA OFFICINALIS EXTRACT	0	(0.0)	1	(0.2)
HYDROXYZINE	3	(0.6)	0	(0.0)
HYDROXYZINE HYDROCHLORIDE	5	(1.0)	6	(1.2)
HYOSCINE	2	(0.4)	0	(0.0)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
LITHIUM GLUCONATE	1	(0.2)	0	(0.0)
LORAZEPAM	9	(1.9)	14	(2.9)
LORMETAZEPAM	1	(0.2)	2	(0.4)
LOXAPINE SUCCINATE	0	(0.0)	1	(0.2)
MELATONIN	9	(1.9)	13	(2.7)
MIDAZOLAM	3	(0.6)	3	(0.6)
MIDAZOLAM HYDROCHLORIDE	2	(0.4)	2	(0.4)
NITRAZEPAM	1	(0.2)	0	(0.0)
OLANZAPINE	1	(0.2)	1	(0.2)
OXAZEPAM	2	(0.4)	2	(0.4)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)
PAROXETINE	2	(0.4)	2	(0.4)
PAROXETINE HYDROCHLORIDE	1	(0.2)	3	(0.6)
PRAZEPAM	1	(0.2)	0	(0.0)
PREGABALIN	18	(3.7)	20	(4.1)
PROCHLORPERAZINE	9	(1.9)	2	(0.4)
PROCHLORPERAZINE MALEATE	5	(1.0)	1	(0.2)
PROMETHAZINE	3	(0.6)	3	(0.6)
PROMETHAZINE HYDROCHLORIDE	3	(0.6)	2	(0.4)
PROPRANOLOL	7	(1.4)	4	(0.8)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
NERVOUS SYSTEM				
PSYCHOLEPTICS	**137**	**(28.4)**	**129**	**(26.5)**
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
QUETIAPINE FUMARATE	4	(0.8)	4	(0.8)
RISPERIDONE	0	(0.0)	1	(0.2)
SERTRALINE HYDROCHLORIDE	11	(2.3)	12	(2.5)
SULPIRIDE	1	(0.2)	0	(0.0)
TEMAZEPAM	1	(0.2)	1	(0.2)
TRIAZOLAM	1	(0.2)	0	(0.0)
VALERIANA OFFICINALIS	0	(0.0)	1	(0.2)
VALPROATE SODIUM	1	(0.2)	0	(0.0)
VENLAFAXINE HYDROCHLORIDE	5	(1.0)	3	(0.6)
ZOLPIDEM	4	(0.8)	7	(1.4)
ZOLPIDEM TARTRATE	4	(0.8)	3	(0.6)
ZOPICLONE	5	(1.0)	4	(0.8)
OTHER				
OTHER	**2**	**(0.4)**	**2**	**(0.4)**
BEVACIZUMAB	0	(0.0)	1	(0.2)
PEMBROLIZUMAB	0	(0.0)	1	(0.2)
RITUXIMAB	2	(0.4)	0	(0.0)
RESPIRATORY SYSTEM				
ANTIHISTAMINES FOR SYSTEMIC USE	**123**	**(25.5)**	**75**	**(15.4)**
AZELASTINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
BILASTINE	6	(1.2)	0	(0.0)
CETIRIZINE HYDROCHLORIDE	30	(6.2)	25	(5.1)
CHLORPHENAMINE	3	(0.6)	2	(0.4)
CHLORPHENAMINE MALEATE	2	(0.4)	1	(0.2)
CLEMASTINE	0	(0.0)	1	(0.2)
CLEMASTINE FUMARATE	2	(0.4)	1	(0.2)
DESLORATADINE	15	(3.1)	6	(1.2)
DEXCHLORPHENIRAMINE MALEATE	2	(0.4)	2	(0.4)
DIMENHYDRINATE	1	(0.2)	1	(0.2)
DIMETINDENE MALEATE	1	(0.2)	1	(0.2)
DIPHENHYDRAMINE	4	(0.8)	2	(0.4)
DIPHENHYDRAMINE HYDROCHLORIDE	14	(2.9)	14	(2.9)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
ANTIHISTAMINES FOR SYSTEMIC USE	**123**	**(25.5)**	**75**	**(15.4)**
DOXYLAMINE SUCCINATE	0	(0.0)	1	(0.2)
EBASTINE	4	(0.8)	3	(0.6)
FEXOFENADINE HYDROCHLORIDE	15	(3.1)	8	(1.6)
FEXOFENADINE HYDROCHLORIDE;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
HYDROXYZINE	3	(0.6)	0	(0.0)
HYDROXYZINE HYDROCHLORIDE	5	(1.0)	6	(1.2)
KETOTIFEN FUMARATE	0	(0.0)	1	(0.2)
LEVOCETIRIZINE	2	(0.4)	2	(0.4)
LEVOCETIRIZINE DIHYDROCHLORIDE	2	(0.4)	1	(0.2)
LORATADINE	34	(7.0)	11	(2.3)
MECLOZINE	1	(0.2)	2	(0.4)
OLOPATADINE HYDROCHLORIDE	1	(0.2)	2	(0.4)
PROMETHAZINE	3	(0.6)	3	(0.6)
PROMETHAZINE HYDROCHLORIDE	3	(0.6)	2	(0.4)
QUERCETIN	1	(0.2)	0	(0.0)
RUPATADINE	0	(0.0)	1	(0.2)
THIETHYLPERAZINE	0	(0.0)	1	(0.2)
COUGH AND COLD PREPARATIONS	**66**	**(13.7)**	**58**	**(11.9)**
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
ADENOPHORA SPP. ROOT;CITRUS MAXIMA PEEL;ERIOBOTRYA JAPONICA LEAF;FRITILLARIA CIRRHOSA BULB;GLYCYRRHIZA URALENSIS ROOT;HONEY;MENTHOL;PINELLIA TERNATA RHIZOME;PLATYCODON GRANDIFLORUS ROOT; POLYGALA SPP. ROOT;PORIA COCOS SCLEROTIUM;PRUNUS ARMENIACA SEED;SCHISANDRA CHINENSIS FRUIT;TRICHOSANTHES SPP. SEED;TUSSILAGO FARFARA FLOWER BUD;ZINGIBER OFFICINALE FRESH RHIZOME	0	(0.0)	1	(0.2)
AMBROXOL	0	(0.0)	2	(0.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
COUGH AND COLD PREPARATIONS	**66**	**(13.7)**	**58**	**(11.9)**
AMBROXOL HYDROCHLORIDE	1	(0.2)	2	(0.4)
BENZONATATE	2	(0.4)	2	(0.4)
BORAGO OFFICINALIS OIL	1	(0.2)	0	(0.0)
BROMHEXINE HYDROCHLORIDE	0	(0.0)	3	(0.6)
CAMPHOR	1	(0.2)	0	(0.0)
CAMPHOR;EUCALYPTUS GLOBULUS OIL;MENTHOL	1	(0.2)	0	(0.0)
CARBOCISTEINE	1	(0.2)	0	(0.0)
CETRARIA ISLANDICA	1	(0.2)	0	(0.0)
CHLORPHENAMINE MALEATE;PARACETAMOL;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CHLORPHENIRAMINE POLISTIREX;HYDROCODONE POLISTIREX	0	(0.0)	1	(0.2)
CLOBUTINOL HYDROCHLORIDE	0	(0.0)	1	(0.2)
CODEINE	2	(0.4)	4	(0.8)
CODEINE PHOSPHATE	2	(0.4)	2	(0.4)
CODEINE PHOSPHATE HEMIHYDRATE;GUAIFENESIN	0	(0.0)	1	(0.2)
CODEINE PHOSPHATE;GUAIFENESIN	1	(0.2)	0	(0.0)
CODEINE PHOSPHATE;GUAIFENESIN;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CODEINE;GUAIFENESIN	0	(0.0)	1	(0.2)
COUGH AND COLD PREPARATIONS	3	(0.6)	1	(0.2)
DEXTROMETHORPHAN	1	(0.2)	1	(0.2)
DEXTROMETHORPHAN HYDROBROMIDE	3	(0.6)	3	(0.6)
DEXTROMETHORPHAN HYDROBROMIDE;GUAIFENESIN	1	(0.2)	1	(0.2)
DIHYDROCODEINE BITARTRATE	1	(0.2)	1	(0.2)
ELECTROLYTES NOS	7	(1.4)	2	(0.4)
GENTIANA LUTEA ROOT;PRIMULA SPP. FLOWER;RUMEX SPP. HERB;SAMBUCUS NIGRA FLOWER;VERBENA OFFICINALIS HERB	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
COUGH AND COLD PREPARATIONS	**66**	**(13.7)**	**58**	**(11.9)**
GLYCEROL	1	(0.2)	0	(0.0)
GLYCYRRHIZA GLABRA;MENTHOL;PHYLLANTHUS EMBLICA;ZINGIBER OFFICINALE	0	(0.0)	1	(0.2)
GUAIFENESIN	6	(1.2)	6	(1.2)
GUAIFENESIN;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
HEDERA HELIX LEAF	0	(0.0)	1	(0.2)
HEDERA HELIX;THYMUS VULGARIS	0	(0.0)	1	(0.2)
HELICIDINE	0	(0.0)	2	(0.4)
HOMATROPINE METHYLBROMIDE;HYDROCODONE BITARTRATE	1	(0.2)	2	(0.4)
HYDROCODONE	1	(0.2)	0	(0.0)
IODINE	0	(0.0)	1	(0.2)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
MENTHOL	1	(0.2)	0	(0.0)
MYRTOL	1	(0.2)	0	(0.0)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
PRIMULA VERIS;THYMUS VULGARIS	1	(0.2)	1	(0.2)
ROSA CANINA	0	(0.0)	1	(0.2)
SODIUM BICARBONATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
ZINC	1	(0.2)	5	(1.0)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	**156**	**(32.3)**	**87**	**(17.9)**
ACLIDINIUM BROMIDE	1	(0.2)	0	(0.0)
ACLIDINIUM BROMIDE;FORMOTEROL FUMARATE	0	(0.0)	1	(0.2)
BAMBUTEROL HYDROCHLORIDE	0	(0.0)	1	(0.2)
BECLOMETASONE DIPROPIONATE	5	(1.0)	4	(0.8)
BECLOMETASONE DIPROPIONATE;FORMOTEROL FUMARATE	1	(0.2)	1	(0.2)
BECLOMETASONE DIPROPIONATE;SALBUTAMOL	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	**156**	**(32.3)**	**87**	**(17.9)**
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BUDESONIDE	9	(1.9)	6	(1.2)
BUDESONIDE;FORMOTEROL FUMARATE	7	(1.4)	7	(1.4)
CICLESONIDE	1	(0.2)	1	(0.2)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
EPHEDRINE	1	(0.2)	1	(0.2)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
FENOTEROL HYDROBROMIDE;IPRATROPIUM BROMIDE	1	(0.2)	1	(0.2)
FLUNISOLIDE	1	(0.2)	0	(0.0)
FLUTICASONE	3	(0.6)	0	(0.0)
FLUTICASONE FUROATE	4	(0.8)	3	(0.6)
FLUTICASONE FUROATE;VILANTEROL TRIFENATATE	3	(0.6)	0	(0.0)
FLUTICASONE PROPIONATE	10	(2.1)	12	(2.5)
FLUTICASONE PROPIONATE;SALMETEROL XINAFOATE	6	(1.2)	3	(0.6)
FORMOTEROL FUMARATE	2	(0.4)	3	(0.6)
GLYCOPYRRONIUM BROMIDE	1	(0.2)	2	(0.4)
GLYCOPYRRONIUM BROMIDE;INDACATEROL MALEATE	0	(0.0)	1	(0.2)
IPRATROPIUM BROMIDE	2	(0.4)	6	(1.2)
IPRATROPIUM BROMIDE;SALBUTAMOL	1	(0.2)	3	(0.6)
LEVOSALBUTAMOL TARTRATE	0	(0.0)	1	(0.2)
METHYLEPHEDRINE HYDROCHLORIDE-DL	1	(0.2)	0	(0.0)
MOMETASONE FUROATE	30	(6.2)	10	(2.1)
MONTELUKAST	3	(0.6)	0	(0.0)
MONTELUKAST SODIUM	3	(0.6)	4	(0.8)
REVEFENACIN	0	(0.0)	1	(0.2)
SALBUTAMOL	17	(3.5)	13	(2.7)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	**156**	**(32.3)**	**87**	**(17.9)**
SALBUTAMOL SULFATE	9	(1.9)	4	(0.8)
SALMETEROL XINAFOATE	0	(0.0)	1	(0.2)
SELECTIVE BETA-2-ADRENORECEPTOR AGONISTS	0	(0.0)	1	(0.2)
TERBUTALINE SULFATE	0	(0.0)	1	(0.2)
TIOTROPIUM BROMIDE	3	(0.6)	4	(0.8)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
UMECLIDINIUM BROMIDE;VILANTEROL TRIFENATATE	0	(0.0)	1	(0.2)
NASAL PREPARATIONS	**186**	**(38.5)**	**117**	**(24.1)**
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
AZELASTINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
BECLOMETASONE DIPROPIONATE	5	(1.0)	4	(0.8)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BUDESONIDE	9	(1.9)	6	(1.2)
CAMPHOR;MENTHOL;METHYL SALICYLATE	1	(0.2)	0	(0.0)
CARDIOSPERMUM HALICACABUM;GALPHIMIA GLAUCA;LUFFA OPERCULATA	1	(0.2)	0	(0.0)
CETIRIZINE HYDROCHLORIDE;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CHLOROBUTANOL;CINEOLE;CITRUS SPP.;GERANIUM SPP.;LAVANDULA ANGUSTIFOLIA;PINUS SYLVESTRIS;RETINOL;THYMUS SPP.;VITAMIN E NOS	0	(0.0)	1	(0.2)
CICLESONIDE	1	(0.2)	1	(0.2)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DEXPANTHENOL	4	(0.8)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
NASAL PREPARATIONS	**186**	**(38.5)**	**117**	**(24.1)**
DEXPANTHENOL;RETINOL	1	(0.2)	0	(0.0)
EPHEDRINE	1	(0.2)	1	(0.2)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
FEXOFENADINE HYDROCHLORIDE;PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
FLUNISOLIDE	1	(0.2)	0	(0.0)
FLUTICASONE	3	(0.6)	0	(0.0)
FLUTICASONE FUROATE	4	(0.8)	3	(0.6)
FLUTICASONE PROPIONATE	10	(2.1)	12	(2.5)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYPROMELLOSE	1	(0.2)	0	(0.0)
IPRATROPIUM BROMIDE	2	(0.4)	6	(1.2)
KETOTIFEN FUMARATE	0	(0.0)	1	(0.2)
LORATADINE;PSEUDOEPHEDRINE SULFATE	0	(0.0)	1	(0.2)
MENTHOL	1	(0.2)	0	(0.0)
MOMETASONE FUROATE	30	(6.2)	10	(2.1)
MUPIROCIN	5	(1.0)	5	(1.0)
MUPIROCIN CALCIUM	0	(0.0)	1	(0.2)
OLOPATADINE HYDROCHLORIDE	1	(0.2)	2	(0.4)
OXYMETAZOLINE HYDROCHLORIDE	3	(0.6)	0	(0.0)
PHENYLEPHRINE	1	(0.2)	3	(0.6)
PHENYLEPHRINE HYDROCHLORIDE	2	(0.4)	2	(0.4)
POTASSIUM CHLORIDE;SODIUM CHLORIDE	2	(0.4)	0	(0.0)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PSEUDOEPHEDRINE	3	(0.6)	2	(0.4)
PSEUDOEPHEDRINE HYDROCHLORIDE	1	(0.2)	3	(0.6)
RETINOL	0	(0.0)	1	(0.2)
SACCHAROMYCES CEREVISIAE;SODIUM SULFIDE	1	(0.2)	1	(0.2)
SEA WATER	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
NASAL PREPARATIONS	**186**	**(38.5)**	**117**	**(24.1)**
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SODIUM BICARBONATE;SODIUM CHLORIDE	0	(0.0)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
TETRYZOLINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
TIXOCORTOL PIVALATE	1	(0.2)	1	(0.2)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
XYLITOL	0	(0.0)	1	(0.2)
ZINC	1	(0.2)	5	(1.0)
OTHER RESPIRATORY SYSTEM PRODUCTS	**3**	**(0.6)**	**4**	**(0.8)**
ACETAZOLAMIDE	1	(0.2)	0	(0.0)
AMBROXOL	0	(0.0)	2	(0.4)
AMBROXOL HYDROCHLORIDE	1	(0.2)	2	(0.4)
CARDIOSPERMUM HALICACABUM;GALPHIMIA GLAUCA;LUFFA OPERCULATA	1	(0.2)	0	(0.0)
THROAT PREPARATIONS	**127**	**(26.3)**	**98**	**(20.2)**
ALPHA-AMYLASE SWINE PANCREAS	0	(0.0)	1	(0.2)
AMBROXOL	0	(0.0)	2	(0.4)
AMBROXOL HYDROCHLORIDE	1	(0.2)	2	(0.4)
BACITRACIN	1	(0.2)	2	(0.4)
BACITRACIN;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
BENZOCAINE	0	(0.0)	1	(0.2)
BENZYDAMINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
BENZYDAMINE HYDROCHLORIDE;CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
BISMUTH	1	(0.2)	0	(0.0)
CARBOMER;HYALURONATE SODIUM;XANTHAN GUM	1	(0.2)	0	(0.0)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CETYLPYRIDINIUM CHLORIDE;DICHLOROBENZYL ALCOHOL;LIDOCAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CHLORHEXIDINE	2	(0.4)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
RESPIRATORY SYSTEM				
THROAT PREPARATIONS	**127**	**(26.3)**	**98**	**(20.2)**
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CHLORHEXIDINE GLUCONATE;LIDOCAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
FLURBIPROFEN	0	(0.0)	1	(0.2)
HEXETIDINE	2	(0.4)	0	(0.0)
HYALURONIC ACID	0	(0.0)	2	(0.4)
IBUPROFEN	86	(17.8)	61	(12.6)
IODINE	0	(0.0)	1	(0.2)
KETOPROFEN	8	(1.7)	4	(0.8)
KETOPROFEN LYSINE	1	(0.2)	0	(0.0)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
PHENOL	0	(0.0)	1	(0.2)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
SENSORY ORGANS				
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	**92**	**(19.0)**	**53**	**(10.9)**
BACITRACIN;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	1	(0.2)	2	(0.4)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)
CIPROFLOXACIN HYDROCHLORIDE;HYDROCORTISONE	2	(0.4)	0	(0.0)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	**92**	**(19.0)**	**53**	**(10.9)**
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	4	(0.8)	0	(0.0)
DEXAMETHASONE;TOBRAMYCIN	3	(0.6)	0	(0.0)
FLUDROCORTISONE ACETATE;LIDOCAINE HYDROCHLORIDE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	(0.0)	1	(0.2)
GENTAMICIN	2	(0.4)	1	(0.2)
GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
GENTAMICIN SULFATE;PREDNISOLONE	2	(0.4)	0	(0.0)
GRAMICIDIN;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
HYDROCORTISONE;OXYTETRACYCLINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
LEVOFLOXACIN	9	(1.9)	6	(1.2)
NORFLOXACIN	1	(0.2)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
ACETAZOLAMIDE	1	(0.2)	0	(0.0)
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
ACICLOVIR	3	(0.6)	4	(0.8)
AFLIBERCEPT	1	(0.2)	0	(0.0)
AMIKACIN	0	(0.0)	1	(0.2)
AMIKACIN SULFATE	0	(0.0)	1	(0.2)
AMPICILLIN	2	(0.4)	0	(0.0)
AMPICILLIN SODIUM	0	(0.0)	1	(0.2)
ANTIINFLAMMATORY AGENTS, NON-STEROIDS	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
ASCORBIC ACID	13	(2.7)	13	(2.7)
ASCORBIC ACID;BETACAROTENE;CUPRIC OXIDE;SODIUM SELENATE;TOCOPHERYL ACETATE;XANTOFYL;ZINC OXIDE	1	(0.2)	0	(0.0)
ASCORBIC ACID;BETACAROTENE;CUPRIC OXIDE;TOCOPHERYL ACETATE;ZINC OXIDE	1	(0.2)	0	(0.0)
ASCORBIC ACID;CUPRIC OXIDE;DL-ALPHA TOCOPHERYL ACETATE;XANTOFYL;ZEAXANTHIN;ZINC OXIDE	0	(0.0)	1	(0.2)
AZELASTINE HYDROCHLORIDE	4	(0.8)	2	(0.4)
AZITHROMYCIN	18	(3.7)	8	(1.6)
BACITRACIN	1	(0.2)	2	(0.4)
BACITRACIN ZINC;POLYMYXIN B SULFATE	0	(0.0)	1	(0.2)
BACITRACIN;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
BACITRACIN;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
BENZATHINE BENZYLPENICILLIN	1	(0.2)	0	(0.0)
BENZYLPENICILLIN	1	(0.2)	0	(0.0)
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE DIPROPIONATE;GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BETAMETHASONE VALERATE;GENTAMICIN SULFATE	1	(0.2)	2	(0.4)
BEVACIZUMAB	0	(0.0)	1	(0.2)
BILASTINE	6	(1.2)	0	(0.0)
BIMATOPROST	2	(0.4)	1	(0.2)
BIMATOPROST;TIMOLOL MALEATE	1	(0.2)	0	(0.0)
BLOOD, CALF, DEPROT., LMW PORTION	1	(0.2)	0	(0.0)
BORIC ACID;SODIUM BORATE	0	(0.0)	1	(0.2)
BRIMONIDINE TARTRATE	1	(0.2)	1	(0.2)
BRINZOLAMIDE	0	(0.0)	1	(0.2)
BRINZOLAMIDE;TIMOLOL MALEATE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
BROMFENAC SODIUM	1	(0.2)	0	(0.0)
BUPIVACAINE	0	(0.0)	4	(0.8)
BUPIVACAINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE;SODIUM CITRATE DIHYDRATE	1	(0.2)	0	(0.0)
CARBOMER	1	(0.2)	0	(0.0)
CARMELLOSE SODIUM	2	(0.4)	1	(0.2)
CARTEOLOL HYDROCHLORIDE	1	(0.2)	0	(0.0)
CEFUROXIME	1	(0.2)	6	(1.2)
CETHEXONIUM BROMIDE	0	(0.0)	1	(0.2)
CETIRIZINE HYDROCHLORIDE	30	(6.2)	25	(5.1)
CETYLPYRIDINIUM CHLORIDE	0	(0.0)	1	(0.2)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CHONDROITIN	1	(0.2)	0	(0.0)
CHONDROITIN SULFATE SODIUM	2	(0.4)	2	(0.4)
CHONDROITIN SULFATE;DL-ALPHA TOCOPHERYL ACETATE;GELATINE HYDROLYSATE;GLUCOSAMINE;MAGNESIUM; POTASSIUM;VITIS VINIFERA SEED	0	(0.0)	1	(0.2)
CICLOSPORIN	1	(0.2)	0	(0.0)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)
CIPROFLOXACIN HYDROCHLORIDE;HYDROCORTISONE	2	(0.4)	0	(0.0)
CLOBETASONE BUTYRATE	1	(0.2)	1	(0.2)
CLONIDINE	0	(0.0)	3	(0.6)
CLONIDINE HYDROCHLORIDE	0	(0.0)	2	(0.4)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)
CORTISONE	4	(0.8)	2	(0.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
CORTISONE ACETATE	3	(0.6)	0	(0.0)
CYANOCOBALAMIN	10	(2.1)	17	(3.5)
CYANOCOBALAMIN;HYALURONATE SODIUM;TAURINE	1	(0.2)	0	(0.0)
CYCLOPENTOLATE HYDROCHLORIDE	1	(0.2)	0	(0.0)
DESONIDE	1	(0.2)	0	(0.0)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE PHOSPHATE;POLYMYXIN B SULFATE;TRIMETHOPRIM	1	(0.2)	0	(0.0)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	4	(0.8)	0	(0.0)
DEXAMETHASONE;TOBRAMYCIN	3	(0.6)	0	(0.0)
DEXPANTHENOL	4	(0.8)	0	(0.0)
DEXPANTHENOL;RETINOL	1	(0.2)	0	(0.0)
DEXTRAN 70;HYPROMELLOSE	1	(0.2)	0	(0.0)
DICLOFENAC	9	(1.9)	7	(1.4)
DICLOFENAC DIETHYLAMINE	1	(0.2)	1	(0.2)
DICLOFENAC EPOLAMINE	1	(0.2)	0	(0.0)
DICLOFENAC SODIUM	16	(3.3)	16	(3.3)
DIFLUPREDNATE	1	(0.2)	0	(0.0)
DORZOLAMIDE HYDROCHLORIDE	0	(0.0)	1	(0.2)
DORZOLAMIDE HYDROCHLORIDE;TIMOLOL MALEATE	0	(0.0)	2	(0.4)
ECONAZOLE	2	(0.4)	2	(0.4)
EPHEDRINE	1	(0.2)	1	(0.2)
EPINEPHRINE	1	(0.2)	1	(0.2)
EPINEPHRINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
ERYTHROMYCIN	2	(0.4)	2	(0.4)
EUPHRASIA OFFICINALIS;HYALURONATE SODIUM	1	(0.2)	0	(0.0)
FLUCONAZOLE	9	(1.9)	6	(1.2)
FLUDROCORTISONE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
FLUDROCORTISONE ACETATE	1	(0.2)	0	(0.0)
FLUOCINOLONE ACETONIDE	1	(0.2)	2	(0.4)
FLUOROMETHOLONE	1	(0.2)	1	(0.2)
FLURBIPROFEN	0	(0.0)	1	(0.2)
FLURBIPROFEN SODIUM	1	(0.2)	0	(0.0)
FUSIDATE SODIUM	1	(0.2)	2	(0.4)
FUSIDIC ACID	11	(2.3)	7	(1.4)
GENTAMICIN	2	(0.4)	1	(0.2)
GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
GENTAMICIN SULFATE;PREDNISOLONE	2	(0.4)	0	(0.0)
GLYCEROL	1	(0.2)	0	(0.0)
GRAMICIDIN;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
HEPARIN	2	(0.4)	4	(0.8)
HEPARIN SODIUM	0	(0.0)	2	(0.4)
HEPARINOID	1	(0.2)	0	(0.0)
HYALURONATE SODIUM	6	(1.2)	3	(0.6)
HYALURONATE SODIUM;TREHALOSE	1	(0.2)	0	(0.0)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
HYDROCORTISONE;OXYTETRACYCLINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
HYETELLOSE	1	(0.2)	0	(0.0)
HYOSCINE	2	(0.4)	0	(0.0)
HYPROMELLOSE	1	(0.2)	0	(0.0)
INDOMETACIN	0	(0.0)	1	(0.2)
IODINE	0	(0.0)	1	(0.2)
ISOSPAGLUMIC ACID SODIUM	0	(0.0)	1	(0.2)
KETOROLAC TROMETHAMINE	8	(1.7)	7	(1.4)
KETOTIFEN FUMARATE	0	(0.0)	1	(0.2)
LATANOPROST	1	(0.2)	4	(0.8)
LATANOPROST;TIMOLOL MALEATE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
LEVOFLOXACIN	9	(1.9)	6	(1.2)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
MACROGOL	3	(0.6)	4	(0.8)
MACROGOL 400;PROPYLENE GLYCOL	3	(0.6)	2	(0.4)
MELOXICAM	6	(1.2)	9	(1.9)
METHYLCELLULOSE	0	(0.0)	1	(0.2)
METHYLPREDNISOLONE	43	(8.9)	7	(1.4)
METHYLPREDNISOLONE ACETATE	2	(0.4)	1	(0.2)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
MOXIFLOXACIN	4	(0.8)	2	(0.4)
MOXIFLOXACIN HYDROCHLORIDE	3	(0.6)	0	(0.0)
NAPROXEN	7	(1.4)	12	(2.5)
NAPROXEN SODIUM	4	(0.8)	11	(2.3)
NEOSTIGMINE METILSULFATE	1	(0.2)	0	(0.0)
NORFLOXACIN	1	(0.2)	0	(0.0)
OFLOXACIN	4	(0.8)	1	(0.2)
OLOPATADINE HYDROCHLORIDE	1	(0.2)	2	(0.4)
OTHER OPHTHALMOLOGICALS	2	(0.4)	0	(0.0)
OXYMETAZOLINE HYDROCHLORIDE	3	(0.6)	0	(0.0)
PANCREATIN	4	(0.8)	2	(0.4)
PARAFFIN	1	(0.2)	1	(0.2)
PARAFFIN SOFT	1	(0.2)	1	(0.2)
PARAFFIN SOFT;PARAFFIN, LIQUID;WOOL FAT	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID;PETROLATUM;WOOL FAT	1	(0.2)	0	(0.0)
PARAFFIN, LIQUID;WHITE SOFT PARAFFIN	3	(0.6)	1	(0.2)
PHENYLEPHRINE	1	(0.2)	3	(0.6)
PHENYLEPHRINE HYDROCHLORIDE	2	(0.4)	2	(0.4)
PILOCARPINE	1	(0.2)	0	(0.0)
PIROXICAM	0	(0.0)	1	(0.2)
POLYVINYL ALCOHOL;POVIDONE	1	(0.2)	0	(0.0)
POTASSIUM	0	(0.0)	4	(0.8)
POTASSIUM CHLORIDE	16	(3.3)	9	(1.9)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OPHTHALMOLOGICALS	**318**	**(65.8)**	**230**	**(47.3)**
POTASSIUM CHLORIDE;SODIUM CHLORIDE	2	(0.4)	0	(0.0)
POVIDONE	0	(0.0)	1	(0.2)
POVIDONE-IODINE	0	(0.0)	3	(0.6)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PREDNISONE	99	(20.5)	29	(6.0)
PROXYMETACAINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
RETINOL	0	(0.0)	1	(0.2)
RIBOFLAVIN	1	(0.2)	0	(0.0)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SEA WATER	1	(0.2)	0	(0.0)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
SULFADIAZINE SILVER	1	(0.2)	0	(0.0)
TACROLIMUS	1	(0.2)	0	(0.0)
TACROLIMUS MONOHYDRATE	2	(0.4)	1	(0.2)
TETRYZOLINE HYDROCHLORIDE	2	(0.4)	0	(0.0)
TIMOLOL	0	(0.0)	1	(0.2)
TIMOLOL MALEATE	0	(0.0)	3	(0.6)
TIMOLOL MALEATE;TRAVOPROST	0	(0.0)	1	(0.2)
TOBRAMYCIN	2	(0.4)	1	(0.2)
TOCOPHEROL	1	(0.2)	5	(1.0)
TRAVOPROST	1	(0.2)	1	(0.2)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
TROPICAMIDE	1	(0.2)	0	(0.0)
UBIDECARENONE	6	(1.2)	3	(0.6)
VANCOMYCIN	2	(0.4)	4	(0.8)
VANCOMYCIN HYDROCHLORIDE	0	(0.0)	2	(0.4)
XANTOFYL	1	(0.2)	2	(0.4)
ZINC	1	(0.2)	5	(1.0)
OTOLOGICALS	**183**	**(37.9)**	**102**	**(21.0)**
BENZOCAINE	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OTOLOGICALS	**183**	**(37.9)**	**102**	**(21.0)**
BETAMETHASONE	13	(2.7)	3	(0.6)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
CHLORAMPHENICOL	6	(1.2)	2	(0.4)
CHLORHEXIDINE	2	(0.4)	1	(0.2)
CHLORHEXIDINE GLUCONATE	2	(0.4)	0	(0.0)
CIPROFLOXACIN	15	(3.1)	12	(2.5)
CIPROFLOXACIN HYDROCHLORIDE	4	(0.8)	1	(0.2)
CIPROFLOXACIN HYDROCHLORIDE;FLUOCINOLONE ACETONIDE	1	(0.2)	0	(0.0)
CIPROFLOXACIN HYDROCHLORIDE;HYDROCORTISONE	2	(0.4)	0	(0.0)
CLOTRIMAZOLE	6	(1.2)	6	(1.2)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE PHOSPHATE;POLYMYXIN B SULFATE;TRIMETHOPRIM	1	(0.2)	0	(0.0)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
DEXAMETHASONE SODIUM PHOSPHATE;NEOMYCIN SULFATE	1	(0.2)	0	(0.0)
DEXAMETHASONE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	4	(0.8)	0	(0.0)
DEXAMETHASONE;TOBRAMYCIN	3	(0.6)	0	(0.0)
DOCUSATE SODIUM	6	(1.2)	7	(1.4)
FLUDROCORTISONE ACETATE;LIDOCAINE HYDROCHLORIDE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	0	(0.0)	1	(0.2)
FLUOCINOLONE ACETONIDE	1	(0.2)	2	(0.4)
FLUOCINOLONE ACETONIDE;LIDOCAINE HYDROCHLORIDE;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	1	(0.2)	0	(0.0)
GENTAMICIN	2	(0.4)	1	(0.2)
GENTAMICIN SULFATE	1	(0.2)	0	(0.0)
GLYCEROL	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SENSORY ORGANS				
OTOLOGICALS	**183**	**(37.9)**	**102**	**(21.0)**
GRAMICIDIN;NEOMYCIN SULFATE;NYSTATIN;TRIAMCINOLONE ACETONIDE	1	(0.2)	1	(0.2)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE ACETATE;NEOMYCIN SULFATE	0	(0.0)	1	(0.2)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
HYDROCORTISONE;OXYTETRACYCLINE HYDROCHLORIDE	1	(0.2)	0	(0.0)
LEVOFLOXACIN	9	(1.9)	6	(1.2)
LIDOCAINE	9	(1.9)	11	(2.3)
LIDOCAINE HYDROCHLORIDE	6	(1.2)	1	(0.2)
LIDOCAINE HYDROCHLORIDE;PHENAZONE	0	(0.0)	1	(0.2)
MICONAZOLE	2	(0.4)	0	(0.0)
MICONAZOLE NITRATE	1	(0.2)	2	(0.4)
OFLOXACIN	4	(0.8)	1	(0.2)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
PHENOL	0	(0.0)	1	(0.2)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PRUNUS AMYGDALUS OIL	2	(0.4)	0	(0.0)
SALICYLIC ACID	4	(0.8)	0	(0.0)
SEA WATER	1	(0.2)	0	(0.0)
SODIUM BICARBONATE	3	(0.6)	1	(0.2)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS				
CALCIUM HOMEOSTASIS	**3**	**(0.6)**	**1**	**(0.2)**
CALCIFEDIOL	3	(0.6)	1	(0.2)
CORTICOSTEROIDS FOR SYSTEMIC USE	**236**	**(48.9)**	**96**	**(19.8)**
BETAMETHASONE	13	(2.7)	3	(0.6)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS				
CORTICOSTEROIDS FOR SYSTEMIC USE	**236**	**(48.9)**	**96**	**(19.8)**
BETAMETHASONE ACETATE;BETAMETHASONE SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
BETAMETHASONE BUTYRATE PROPIONATE	1	(0.2)	0	(0.0)
BETAMETHASONE DIPROPIONATE	18	(3.7)	7	(1.4)
BETAMETHASONE DIPROPIONATE;BETAMETHASONE SODIUM PHOSPHATE	1	(0.2)	0	(0.0)
BETAMETHASONE VALERATE	16	(3.3)	3	(0.6)
BETAMETHASONE;BUPIVACAINE	1	(0.2)	0	(0.0)
BETAMETHASONE;DEXCHLORPHENIRAMINE MALEATE	0	(0.0)	1	(0.2)
CORTICOSTEROIDS FOR SYSTEMIC USE	6	(1.2)	3	(0.6)
CORTISONE	4	(0.8)	2	(0.4)
CORTISONE ACETATE	3	(0.6)	0	(0.0)
DEFLAZACORT	1	(0.2)	1	(0.2)
DEXAMETHASONE	10	(2.1)	11	(2.3)
DEXAMETHASONE SODIUM PHOSPHATE	1	(0.2)	1	(0.2)
FLUDROCORTISONE	2	(0.4)	0	(0.0)
FLUDROCORTISONE ACETATE	1	(0.2)	0	(0.0)
HYDROCORTISONE	42	(8.7)	5	(1.0)
HYDROCORTISONE ACETATE	20	(4.1)	8	(1.6)
HYDROCORTISONE BUTYRATE	3	(0.6)	0	(0.0)
HYDROCORTISONE SODIUM SUCCINATE	1	(0.2)	0	(0.0)
KETOCONAZOLE	6	(1.2)	6	(1.2)
LIDOCAINE HYDROCHLORIDE;METHYLPREDNISOLONE ACETATE	1	(0.2)	0	(0.0)
METHYLPREDNISOLONE	43	(8.9)	7	(1.4)
METHYLPREDNISOLONE ACETATE	2	(0.4)	1	(0.2)
METHYLPREDNISOLONE SODIUM SUCCINATE	12	(2.5)	4	(0.8)
PREDNISOLONE	27	(5.6)	14	(2.9)
PREDNISOLONE ACETATE	2	(0.4)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS				
CORTICOSTEROIDS FOR SYSTEMIC USE	**236**	**(48.9)**	**96**	**(19.8)**
PREDNISOLONE METASULFOBENZOATE SODIUM	1	(0.2)	0	(0.0)
PREDNISONE	99	(20.5)	29	(6.0)
TRIAMCINOLONE	28	(5.8)	5	(1.0)
TRIAMCINOLONE ACETONIDE	15	(3.1)	7	(1.4)
PANCREATIC HORMONES	**2**	**(0.4)**	**0**	**(0.0)**
GLUCAGON	1	(0.2)	0	(0.0)
GLUCAGON HYDROCHLORIDE	1	(0.2)	0	(0.0)
PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES	**0**	**(0.0)**	**2**	**(0.4)**
LEUPRORELIN ACETATE	0	(0.0)	1	(0.2)
VASOPRESSIN	0	(0.0)	1	(0.2)
THYROID THERAPY	**134**	**(27.7)**	**47**	**(9.7)**
CARBIMAZOLE	3	(0.6)	0	(0.0)
IODINE	0	(0.0)	1	(0.2)
LEVOTHYROXINE SODIUM	123	(25.5)	35	(7.2)
LEVOTHYROXINE SODIUM;POTASSIUM IODIDE	0	(0.0)	1	(0.2)
LIOTHYRONINE SODIUM	1	(0.2)	0	(0.0)
PROPRANOLOL	7	(1.4)	4	(0.8)
PROPRANOLOL HYDROCHLORIDE	5	(1.0)	3	(0.6)
THIAMAZOLE	7	(1.4)	4	(0.8)
THYROID	1	(0.2)	1	(0.2)
VARIOUS				
ALL OTHER NON-THERAPEUTIC PRODUCTS	**43**	**(8.9)**	**34**	**(7.0)**
ASCORBIC ACID	13	(2.7)	13	(2.7)
COCOS NUCIFERA OIL	0	(0.0)	1	(0.2)
HYALURONIC ACID	0	(0.0)	2	(0.4)
HYETELLOSE	1	(0.2)	0	(0.0)
HYPROMELLOSE	1	(0.2)	0	(0.0)
MENTHOL	1	(0.2)	0	(0.0)
OTHER NON-THERAPEUTIC AUXILIARY PRODUCTS	1	(0.2)	0	(0.0)
PENICILLIN NOS	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
ALL OTHER NON-THERAPEUTIC PRODUCTS	**43**	**(8.9)**	**34**	**(7.0)**
PLASTERS	1	(0.2)	0	(0.0)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
WASHING AGENTS ETC.	2	(0.4)	0	(0.0)
ALL OTHER THERAPEUTIC PRODUCTS	**56**	**(11.6)**	**51**	**(10.5)**
ACETYLCYSTEINE	6	(1.2)	3	(0.6)
ASCORBIC ACID	13	(2.7)	13	(2.7)
CALCIUM ACETATE	1	(0.2)	0	(0.0)
CALCIUM CARBONATE	11	(2.3)	7	(1.4)
CALCIUM CARBONATE;MAGNESIUM CARBONATE	0	(0.0)	1	(0.2)
CALCIUM FOLINATE	1	(0.2)	0	(0.0)
CALCIUM;MAGNESIUM	1	(0.2)	1	(0.2)
CALCIUM;VITAMIN D NOS	2	(0.4)	0	(0.0)
CHONDROITIN	1	(0.2)	0	(0.0)
CHONDROITIN SULFATE SODIUM	2	(0.4)	2	(0.4)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE MONONITRATE	0	(0.0)	1	(0.2)
CYANOCOBALAMIN;PYRIDOXINE;THIAMINE	2	(0.4)	0	(0.0)
GLUTATHIONE SODIUM	1	(0.2)	0	(0.0)
GLYCOPYRRONIUM BROMIDE	1	(0.2)	2	(0.4)
HOMEOPATHIC PREPARATION	0	(0.0)	1	(0.2)
HYDROXOCOBALAMIN	1	(0.2)	0	(0.0)
HYDROXOCOBALAMIN ACETATE	1	(0.2)	1	(0.2)
IODINE	0	(0.0)	1	(0.2)
IRON	3	(0.6)	6	(1.2)
LACTOBACILLUS RHAMNOSUS	1	(0.2)	0	(0.0)
NALMEFENE HYDROCHLORIDE DIHYDRATE	0	(0.0)	1	(0.2)
NITROGEN	1	(0.2)	0	(0.0)
OTHER THERAPEUTIC PRODUCTS	3	(0.6)	5	(1.0)
OXYGEN	4	(0.8)	6	(1.2)
PROTAMINE SULFATE	0	(0.0)	2	(0.4)
PYCNOGENOL	1	(0.2)	0	(0.0)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
SODIUM POLYSTYRENE SULFONATE	3	(0.6)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
ALL OTHER THERAPEUTIC PRODUCTS	**56**	**(11.6)**	**51**	**(10.5)**
SUGAMMADEX	0	(0.0)	1	(0.2)
SUGAMMADEX SODIUM	3	(0.6)	0	(0.0)
XYLITOL	0	(0.0)	1	(0.2)
ALLERGENS	**1**	**(0.2)**	**1**	**(0.2)**
OLEA EUROPAEA	1	(0.2)	1	(0.2)
CONTRAST MEDIA	**1**	**(0.2)**	**1**	**(0.2)**
IOHEXOL	1	(0.2)	0	(0.0)
IOPAMIDOL	1	(0.2)	0	(0.0)
IOXITALAMATE MEGLUMINE	0	(0.0)	1	(0.2)
DIAGNOSTIC AGENTS	**14**	**(2.9)**	**5**	**(1.0)**
FOLIC ACID	8	(1.7)	2	(0.4)
GLUCOSE	1	(0.2)	0	(0.0)
MAGNESIUM SULFATE	6	(1.2)	3	(0.6)
GENERAL NUTRIENTS	**10**	**(2.1)**	**18**	**(3.7)**
AMINO ACIDS NOS;CARTHAMUS TINCTORIUS OIL;FRUCTOSE;GLYCINE MAX SEED OIL;MINERALS NOS;VITAMINS NOS	1	(0.2)	0	(0.0)
CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;PROTEIN;VITAMINS NOS	0	(0.0)	1	(0.2)
CARBOHYDRATES NOS;FATS NOS;MINERALS NOS;PROTEINS NOS;VITAMINS NOS	1	(0.2)	0	(0.0)
FATTY ACIDS NOS	1	(0.2)	1	(0.2)
FISH OIL	5	(1.0)	9	(1.9)
FISH OIL;TOCOPHEROL	0	(0.0)	1	(0.2)
GLUCOSE	1	(0.2)	0	(0.0)
LYSINE	0	(0.0)	2	(0.4)
LYSINE HYDROCHLORIDE	0	(0.0)	1	(0.2)
MINERALS NOS;VITAMINS NOS	1	(0.2)	1	(0.2)
NUTRIENTS NOS	1	(0.2)	1	(0.2)
XYLITOL	0	(0.0)	1	(0.2)
HOMEOPATHIC PREPARATION	**90**	**(18.6)**	**77**	**(15.8)**
ARNICA MONTANA	1	(0.2)	0	(0.0)
ASCORBIC ACID	13	(2.7)	13	(2.7)
CALCIUM CARBONATE	11	(2.3)	7	(1.4)
CHARCOAL, ACTIVATED	0	(0.0)	2	(0.4)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
HOMEOPATHIC PREPARATION	**90**	**(18.6)**	**77**	**(15.8)**
CORTISONE	4	(0.8)	2	(0.4)
CORTISONE ACETATE	3	(0.6)	0	(0.0)
CYANOCOBALAMIN	10	(2.1)	17	(3.5)
EPINEPHRINE	1	(0.2)	1	(0.2)
ESTRIOL	1	(0.2)	0	(0.0)
FERROUS PHOSPHATE	0	(0.0)	1	(0.2)
GINKGO BILOBA	1	(0.2)	3	(0.6)
HOMEOPATHIC PREPARATION	0	(0.0)	1	(0.2)
HOMEOPATHICS NOS	2	(0.4)	0	(0.0)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
IODINE	0	(0.0)	1	(0.2)
IRON	3	(0.6)	6	(1.2)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
PARAFFIN, LIQUID	1	(0.2)	0	(0.0)
POTASSIUM	0	(0.0)	4	(0.8)
POTASSIUM CHLORIDE	16	(3.3)	9	(1.9)
POTASSIUM PHOSPHATE DIBASIC	0	(0.0)	1	(0.2)
RIBOFLAVIN	1	(0.2)	0	(0.0)
ROSA CANINA	0	(0.0)	1	(0.2)
SELENIUM	4	(0.8)	0	(0.0)
SILYBUM MARIANUM	1	(0.2)	0	(0.0)
SODIUM CHLORIDE	25	(5.2)	23	(4.7)
SODIUM PHOSPHATE	0	(0.0)	1	(0.2)
THYROID	1	(0.2)	1	(0.2)
UBIDECARENONE	6	(1.2)	3	(0.6)
UREA	10	(2.1)	3	(0.6)
ZINC	1	(0.2)	5	(1.0)
INVESTIGATIONAL DRUG	**1**	**(0.2)**	**1**	**(0.2)**
OCTENIDINE;PREDNICARBATE	1	(0.2)	0	(0.0)
SR 9009	0	(0.0)	1	(0.2)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	**53**	**(11.0)**	**39**	**(8.0)**

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	**53**	**(11.0)**	**39**	**(8.0)**
ADENOPHORA SPP. ROOT;CITRUS MAXIMA PEEL;ERIOBOTRYA JAPONICA LEAF;FRITILLARIA CIRRHOSA BULB;GLYCYRRHIZA URALENSIS ROOT;HONEY;MENTHOL;PINELLIA TERNATA RHIZOME;PLATYCODON GRANDIFLORUS ROOT; POLYGALA SPP. ROOT;PORIA COCOS SCLEROTIUM;PRUNUS ARMENIACA SEED;SCHISANDRA CHINENSIS FRUIT;TRICHOSANTHES SPP. SEED;TUSSILAGO FARFARA FLOWER BUD;ZINGIBER OFFICINALE FRESH RHIZOME	0	(0.0)	1	(0.2)
AESCULUS HIPPOCASTANUM BARK;ANANAS COMOSUS;SCUTELLARIA BAICALENSIS ROOT	0	(0.0)	1	(0.2)
ALLIUM SATIVUM	0	(0.0)	1	(0.2)
ALLIUM SATIVUM OIL	1	(0.2)	0	(0.0)
ALOE VERA	2	(0.4)	0	(0.0)
ARNICA MONTANA	1	(0.2)	0	(0.0)
BORAGO OFFICINALIS OIL	1	(0.2)	0	(0.0)
BOSWELLIA SACRA	0	(0.0)	1	(0.2)
BOSWELLIA SPP.;COMMIPHORA MYRRHA;CURCUMA LONGA RHIZOME;PIPER NIGRUM;VITAMIN D NOS	1	(0.2)	0	(0.0)
CAMELLIA SINENSIS	1	(0.2)	0	(0.0)
CAMPHOR;EUCALYPTUS GLOBULUS OIL;MENTHOL	1	(0.2)	0	(0.0)
CANNABIS SATIVA	2	(0.4)	4	(0.8)
CANNABIS SATIVA OIL	6	(1.2)	3	(0.6)
CARDIOSPERMUM HALICACABUM;GALPHIMIA GLAUCA;LUFFA OPERCULATA	1	(0.2)	0	(0.0)
CETRARIA ISLANDICA	1	(0.2)	0	(0.0)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	**53**	**(11.0)**	**39**	**(8.0)**
COCOS NUCIFERA OIL	0	(0.0)	1	(0.2)
CRATAEGUS SPP. DRY EXTRACT;VALERIANA OFFICINALIS DRY EXTRACT	1	(0.2)	0	(0.0)
CUCURBITA PEPO OIL	0	(0.0)	1	(0.2)
CURCUMA LONGA	8	(1.7)	5	(1.0)
CYAMOPSIS TETRAGONOLOBA GUM	0	(0.0)	1	(0.2)
ECHINACEA PURPUREA	0	(0.0)	1	(0.2)
EPILOBIUM PARVIFLORUM;SELENOMETHIONINE;SERENOA REPENS FRUIT;SOLANUM LYCOPERSICUM;ZINC GLUCONATE	1	(0.2)	0	(0.0)
GENTIANA LUTEA ROOT;PRIMULA SPP. FLOWER;RUMEX SPP. HERB;SAMBUCUS NIGRA FLOWER;VERBENA OFFICINALIS HERB	1	(0.2)	0	(0.0)
GINKGO BILOBA	1	(0.2)	3	(0.6)
GINKGO BILOBA EXTRACT	1	(0.2)	0	(0.0)
HEDERA HELIX LEAF	0	(0.0)	1	(0.2)
HEDERA HELIX;THYMUS VULGARIS	0	(0.0)	1	(0.2)
HERBAL EXTRACT NOS;VALERIANA OFFICINALIS EXTRACT	0	(0.0)	1	(0.2)
HERBAL NOS	1	(0.2)	2	(0.4)
HYPERICUM PERFORATUM	0	(0.0)	1	(0.2)
IMPATIENS BALSAMINA	1	(0.2)	0	(0.0)
KRILL OIL	1	(0.2)	1	(0.2)
LINUM USITATISSIMUM SEED	0	(0.0)	3	(0.6)
MENTHA X PIPERITA OIL	1	(0.2)	0	(0.0)
MONASCUS PURPUREUS	0	(0.0)	2	(0.4)
OLEA EUROPAEA	1	(0.2)	1	(0.2)
ORIGANUM VULGARE OIL	0	(0.0)	1	(0.2)
PANAX QUINQUEFOLIUS ROOT	1	(0.2)	0	(0.0)
PLANTAGO OVATA	4	(0.8)	2	(0.4)
PLANTAGO OVATA HUSK	1	(0.2)	0	(0.0)
PLANTAGO OVATA SEED	0	(0.0)	1	(0.2)

Participants With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
VARIOUS				
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	**53**	**(11.0)**	**39**	**(8.0)**
PLANTAGO OVATA SEED HUSK	1	(0.2)	0	(0.0)
PRIMULA VERIS;THYMUS VULGARIS	1	(0.2)	1	(0.2)
PRUNUS AFRICANA	1	(0.2)	0	(0.0)
PRUNUS AFRICANA EXTRACT	1	(0.2)	0	(0.0)
PRUNUS AMYGDALUS OIL	2	(0.4)	0	(0.0)
PRUNUS DOMESTICA	1	(0.2)	0	(0.0)
PUNICA GRANATUM	0	(0.0)	1	(0.2)
ROSA CANINA	0	(0.0)	1	(0.2)
SENNA ALEXANDRINA	4	(0.8)	3	(0.6)
SERENOA REPENS	2	(0.4)	2	(0.4)
SERENOA REPENS EXTRACT	1	(0.2)	1	(0.2)
SILYBUM MARIANUM	1	(0.2)	0	(0.0)
SIMMONDSIA CHINENSIS OIL	0	(0.0)	1	(0.2)
SPIRULINA SPP.	1	(0.2)	0	(0.0)
STERCULIA URENS GUM	1	(0.2)	0	(0.0)
THEOBROMA CACAO OIL	1	(0.2)	0	(0.0)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	3	(0.6)	1	(0.2)
VACCINIUM MACROCARPON	0	(0.0)	1	(0.2)
VALERIANA OFFICINALIS	0	(0.0)	1	(0.2)
ZINGIBER OFFICINALE	2	(0.4)	1	(0.2)

Every participant is counted a single time for each applicable specific concomitant medication. A participant with multiple concomitant medications within a medication category is counted a single time for that category. Each specific concomitant medication is listed under all relevant medication classes based on the medication's generic name, regardless of route of administration or reason for use.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adcm]

14.1.6 Extent of Exposure

Table 14.1-18
Summary of Drug Exposure
(APaT Population)

	Pembrolizumab (N=483)	Placebo (N=486)	Total (N=969)
Number of Days on Therapy			
Mean	281.6	309.5	295.6
Median	337.0	337.0	337.0
SD	114.86	88.43	103.35
Range	1.0 to 498.0	1.0 to 475.0	1.0 to 498.0
Number of Administrations			
Mean	13.8	15.1	14.4
Median	17.0	17.0	17.0
SD	5.20	3.97	4.68
Range	1.0 to 17.0	1.0 to 17.0	1.0 to 17.0
Number of Days on Therapy is calculated as last dose date - first dose date +1. Database Cutoff Date: 04JAN2023.			

Source: [P716V04MK3475: adam-adsl; adexsum]

Table 14.1-19
Exposure by Duration
(APaT Population)

	Pembrolizumab (N=483)		Placebo (N=486)		Total (N=969)	
	n	(%)	n	(%)	n	(%)
Duration of Exposure						
> 0 m	483	(100.0)	486	(100.0)	969	(100.0)
≥ 1 m	455	(94.2)	472	(97.1)	927	(95.7)
≥ 3 m	430	(89.0)	461	(94.9)	891	(92.0)
≥ 6 m	376	(77.8)	428	(88.1)	804	(83.0)
≥ 9 m	341	(70.6)	400	(82.3)	741	(76.5)
≥ 10 m	333	(68.9)	385	(79.2)	718	(74.1)
≥ 12 m	52	(10.8)	51	(10.5)	103	(10.6)

Each participant is counted once on each applicable duration category row.
Duration of exposure is the time from the first dose date to the last dose date.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adexsum]

14.2 Efficacy Data

14.2.1 Efficacy Results

Table 14.2-1
Summary of Follow-up Duration
(ITT Population)

	Pembrolizumab (N=487)	Placebo (N=489)	Total (N=976)
Follow-up duration (months)[a]			
Median (Range)	38.6 (10.3 - 51.1)	38.5 (4.6 - 51.2)	38.5 (4.6 - 51.2)
Mean (SD)	38.2 (6.7)	37.8 (7.7)	38.0 (7.2)

[a]Follow-up duration is defined as the time from randomization date to the date of death or the database cutoff date if the patient was still alive.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adintdt]

Table 14.2-2
Disease Status
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
Type of First Event in RFS Analysis						
No event	370	(75.98)	315	(64.42)	685	(70.18)
Event	117	(24.02)	174	(35.58)	291	(29.82)
Local	31	(6.37)	33	(6.75)	64	(6.56)
Regional	20	(4.11)	31	(6.34)	51	(5.23)
LocoRegional	7	(1.44)	5	(1.02)	12	(1.23)
Distant[a]	52	(10.68)	97	(19.84)	149	(15.27)
Death	7	(1.44)	8	(1.64)	15	(1.54)
DMFS Event						
No event	413	(84.80)	370	(75.66)	783	(80.23)
Event	74	(15.20)	119	(24.34)	193	(19.77)

[a] Includes Distant event diagnosed within 30 days from Local/Regional/Locoregional event

Local: Tumor recurrence is in the immediate vicinity of primary tumor (i.e. skin, in transit lesions, micro-satellite metastases).

Regional: Regional Lymph node basin involvement.

Loco-regional: Tumor recurrence is in the immediate vicinity of primary tumor and regional lymph node basin metastasis is noted. Tumor has not spread beyond regional lymph nodes.

Distant: Metastasis is beyond the regional lymph node basin.

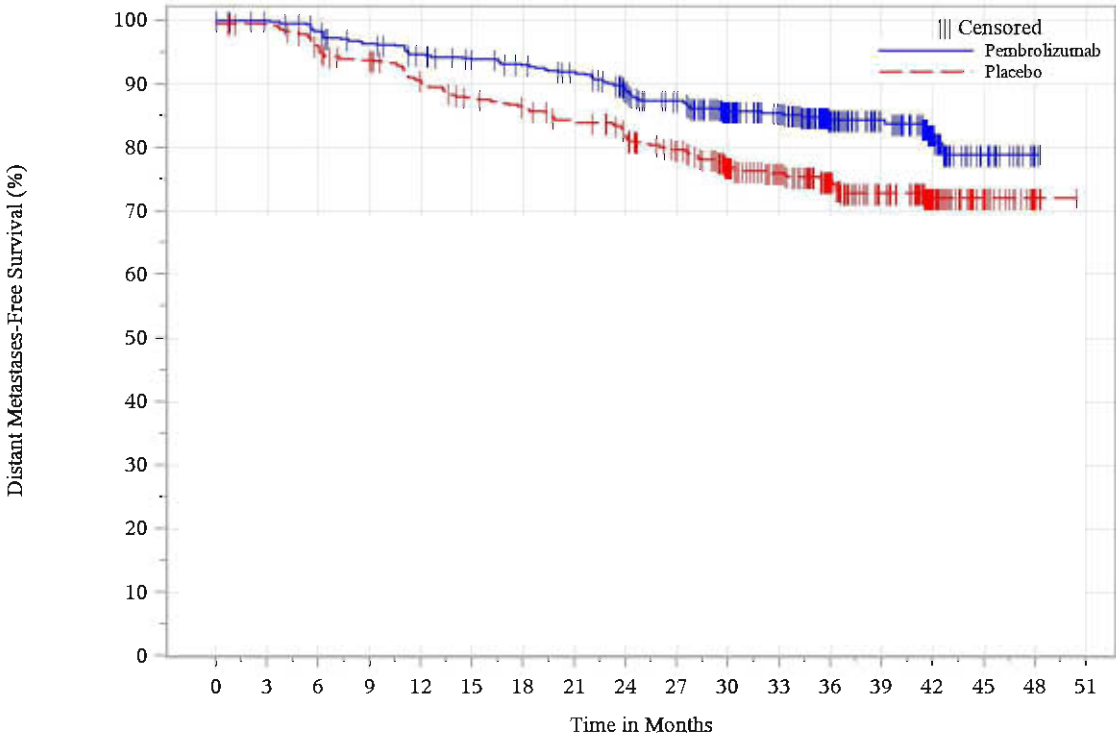
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adintdt]

14.2.1.1 Distant Metastasis-free Survival

14.2.1.1.1 Distant Metastasis-free Survival in All Participants

Figure 14.2-1
Kaplan-Meier Estimates of Distant Metastases-Free Survival
(ITT Population)



At Risk

Pembrolizumab	487	480	469	456	444	434	427	417	396	376	322	276	185	130	71	22	5	0
Placebo	489	482	463	449	427	412	402	389	372	350	287	243	176	131	62	32	7	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-3
Analysis of Distant Metastases-Free Survival
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	487	74 (15.2)	15505.8	0.5	NR (NR, NR)	84.4 (80.6, 87.5)
Placebo	489	119 (24.3)	14891.4	0.8	NR (NR, NR)	74.7 (70.4, 78.5)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.59 (0.44, 0.79)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T Stage (T3b vs. T4a vs. T4b).
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-4
Distant Metastases-Free Survival Rate Over Time
(ITT Population)

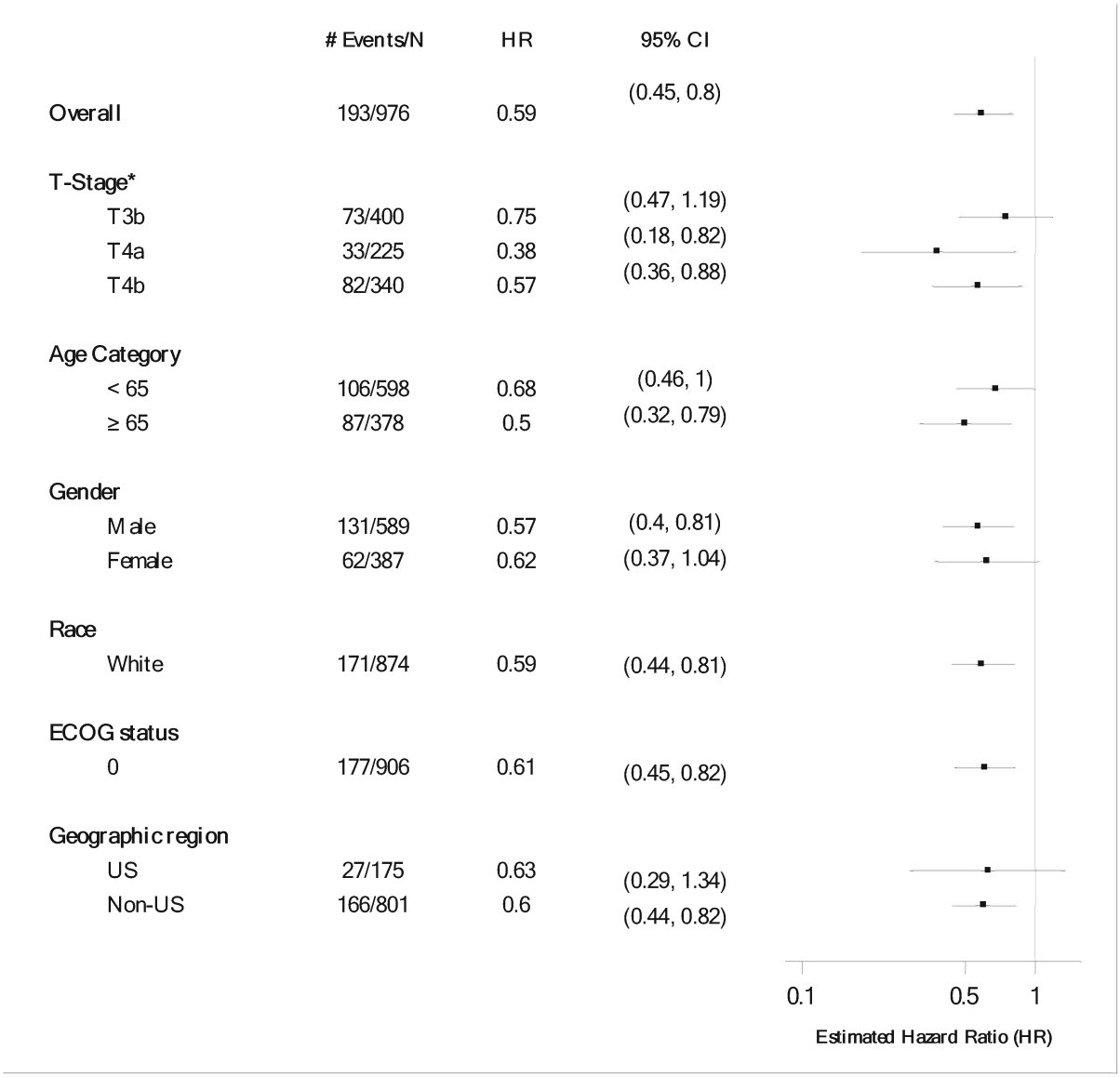
	Pembrolizumab (N=487) % (95% CI)[a]	Placebo (N=489) % (95% CI)[a]
Distant Metastases-Free Survival rate at time point		
6 months	98.3 (96.7, 99.2)	95.9 (93.7, 97.3)
12 months	94.7 (92.3, 96.4)	90.4 (87.4, 92.7)
18 months	93.0 (90.3, 95.0)	86.4 (83.0, 89.2)
24 months	89.3 (86.1, 91.7)	82.0 (78.3, 85.2)
30 months	85.8 (82.2, 88.7)	76.9 (72.8, 80.5)
36 months	84.4 (80.6, 87.5)	74.7 (70.4, 78.5)
42 months	82.2 (77.5, 85.9)	72.2 (67.4, 76.5)
48 months	79.0 (72.2, 84.2)	72.2 (67.4, 76.5)

[a] From product-limit (Kaplan-Meier) method for censored data.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

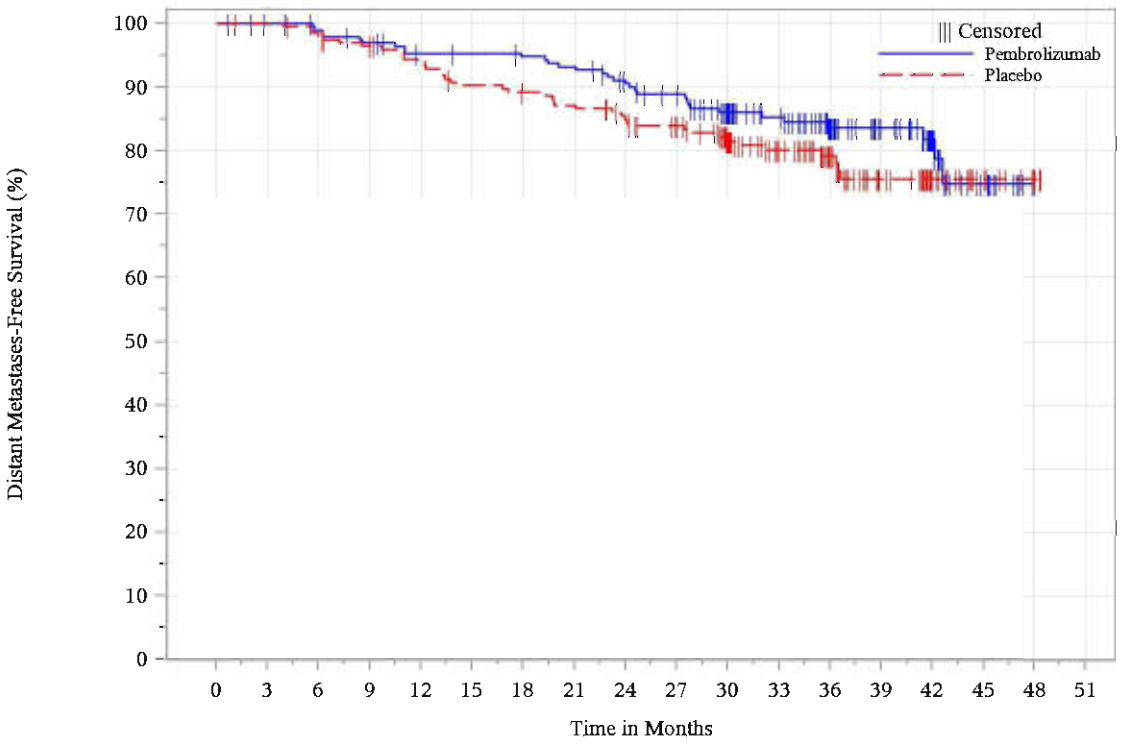
14.2.1.1.2 Distant Metastasis-free Survival by Subgroup

Figure 14.2-2
Forest Plot of Distant Metastases-Free Survival Hazard Ratio by Subgroup Factors
(ITT Population)



A subgroup with number of participants < 10% ITT population is not displayed on the plot.
*Based on actual baseline tumor stage collected on eCRF.
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-3
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T3b within Overall Cancer Stage IIB
(ITT Population)

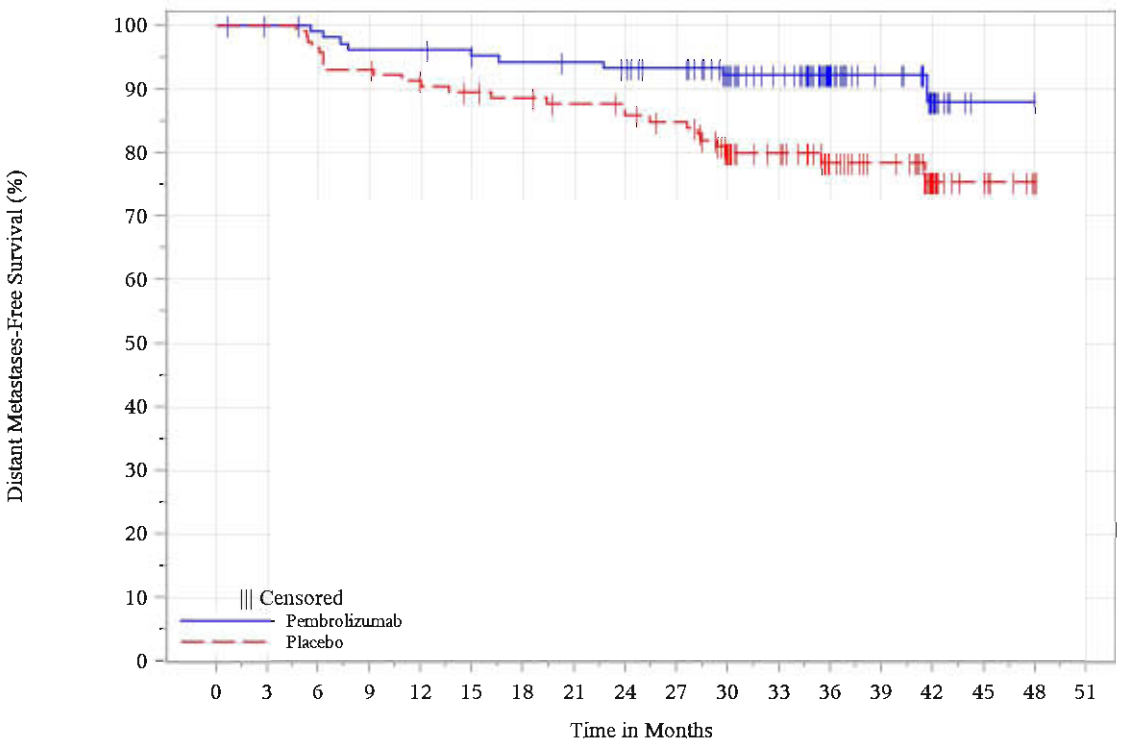


At Risk

Pembrolizumab	200	197	193	188	182	181	179	176	168	161	136	114	79	55	34	12	1	0
Placebo	200	199	194	189	183	174	171	167	160	151	124	100	72	47	22	11	3	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-4
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T4a within Overall Cancer Stage IIB
(ITT Population)

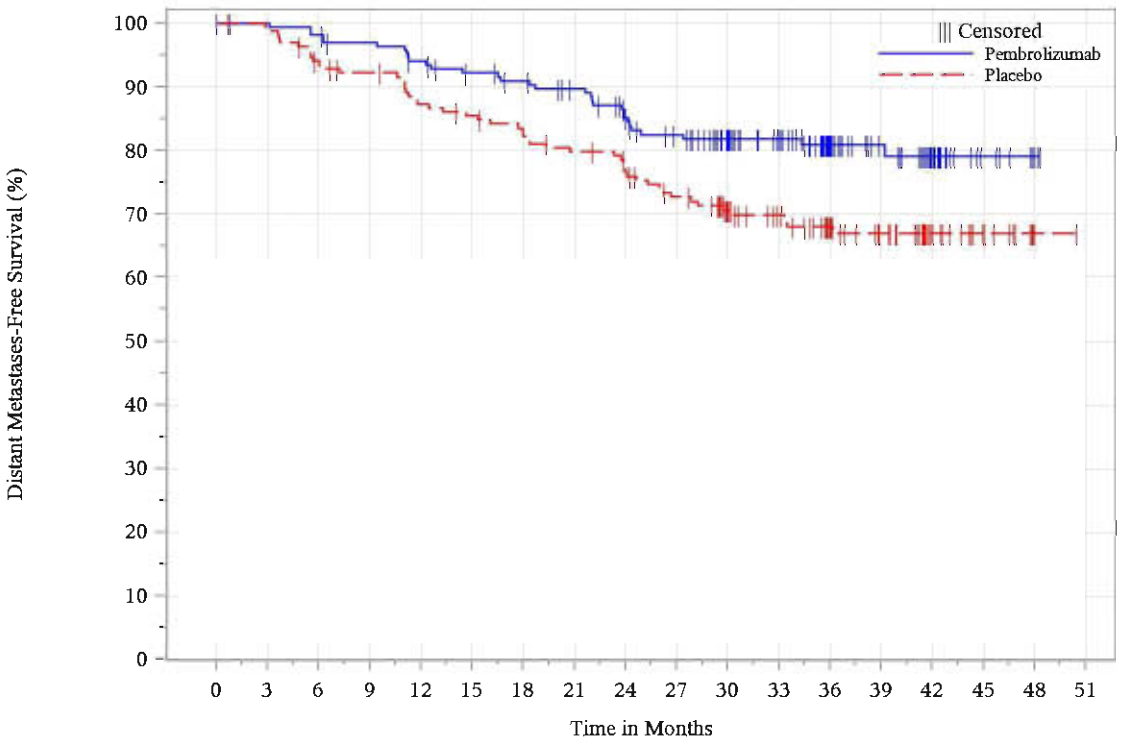


At Risk

Pembrolizumab	109	107	105	102	102	99	98	97	95	91	77	65	41	28	13	1	1	0
Placebo	116	116	112	108	102	100	98	95	92	89	72	61	41	32	16	8	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-5
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T4b within Overall Cancer Stage IIC
(ITT Population)



At Risk

Pembrolizumab	171	169	166	162	156	150	146	140	129	120	105	93	61	44	24	9	3	0
Placebo	169	166	156	151	142	138	133	127	120	110	91	82	63	52	24	13	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-5
Analysis of Distant Metastases-Free Survival
for Participants with Actual Baseline Tumor Stage T3b within Overall Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	200	32 (16.0)	6479.0	0.5	NR (NR, NR)	83.7 (77.3, 88.5)
Placebo	200	41 (20.5)	6235.1	0.7	NR (NR, NR)	79.2 (72.4, 84.5)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.75 (0.47, 1.19)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-6
Analysis of Distant Metastases-Free Survival
for Participants with Actual Baseline Tumor Stage T4a within Overall Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	109	9 (8.3)	3544.6	0.3	NR (NR, NR)	92.2 (85.0, 96.0)
Placebo	116	24 (20.7)	3620.7	0.7	NR (NR, NR)	78.5 (69.3, 85.3)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.38 (0.18, 0.82)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-7
Analysis of Distant Metastases-Free Survival
for Participants with Actual Baseline Tumor Stage T4b within Overall Cancer Stage IIC
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	171	31 (18.1)	5307.5	0.6	NR (NR, NR)	80.9 (73.7, 86.3)
Placebo	169	51 (30.2)	5023.8	1.0	NR (NR, NR)	68.1 (60.1, 74.9)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.57 (0.36, 0.88)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-8
Analysis of Distant Metastases-Free Survival
for Participants with Baseline Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	309	41 (13.3)	10023.6	0.4	NR (NR, NR)	86.7 (82.0, 90.2)
Placebo	316	65 (20.6)	9855.7	0.7	NR (NR, NR)	78.9 (73.7, 83.3)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.62 (0.42, 0.92)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

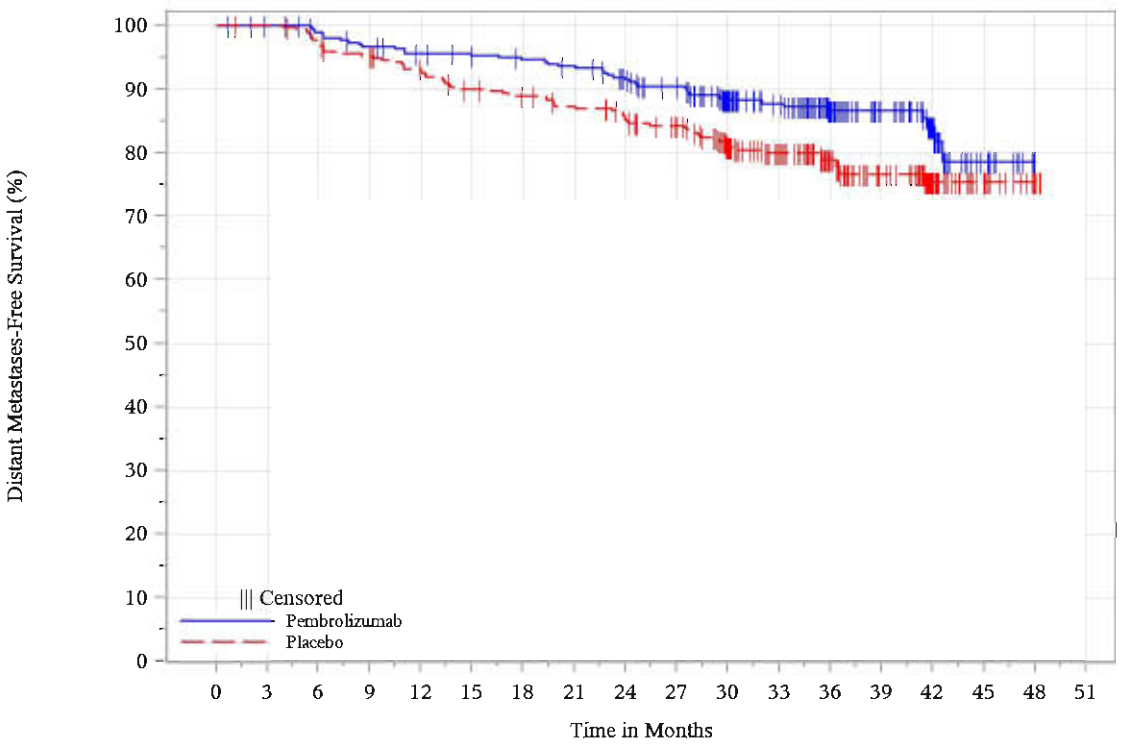
Table 14.2-9
Analysis of Distant Metastases-Free Survival
for Participants with Baseline Cancer Stage IIC
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	171	31 (18.1)	5307.5	0.6	NR (NR, NR)	80.9 (73.7, 86.3)
Placebo	169	51 (30.2)	5023.8	1.0	NR (NR, NR)	68.1 (60.1, 74.9)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.57 (0.36, 0.88)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-6
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Baseline Cancer Stage IIB
(ITT Population)

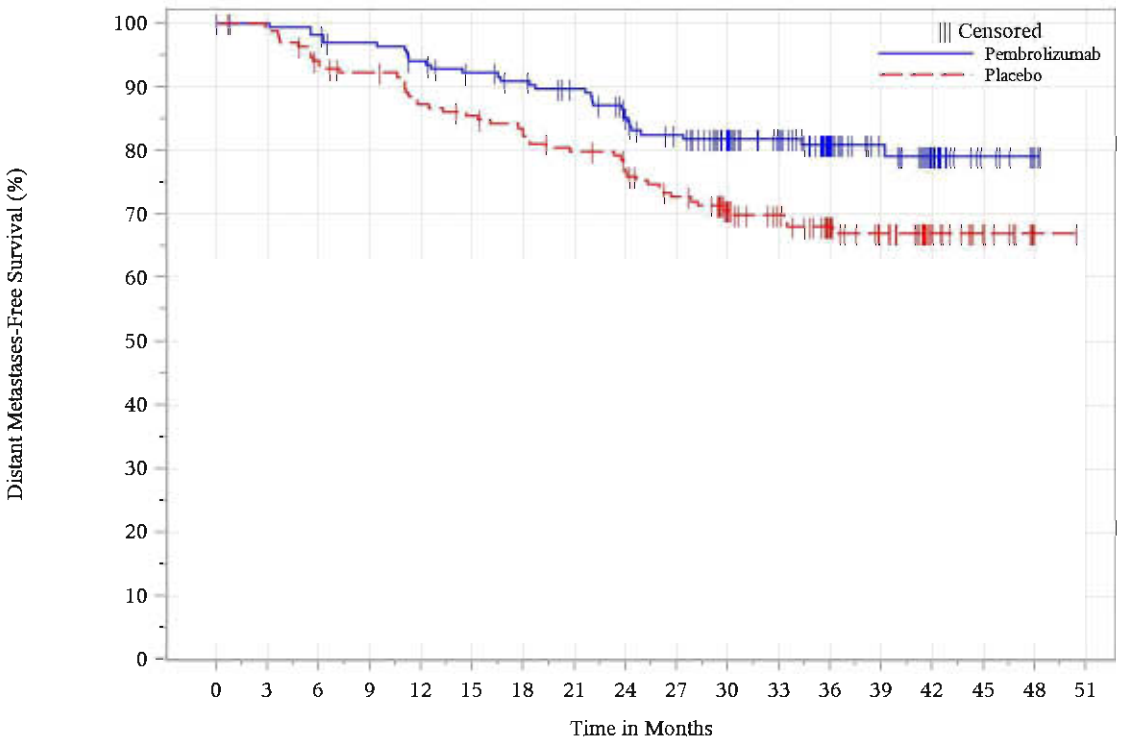


At Risk

Pembrolizumab	309	304	298	290	284	280	277	273	263	252	213	179	120	83	47	13	2	0
Placebo	316	315	306	297	285	274	269	262	252	240	196	161	113	79	38	19	5	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-7
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Baseline Cancer Stage IIC
(ITT Population)

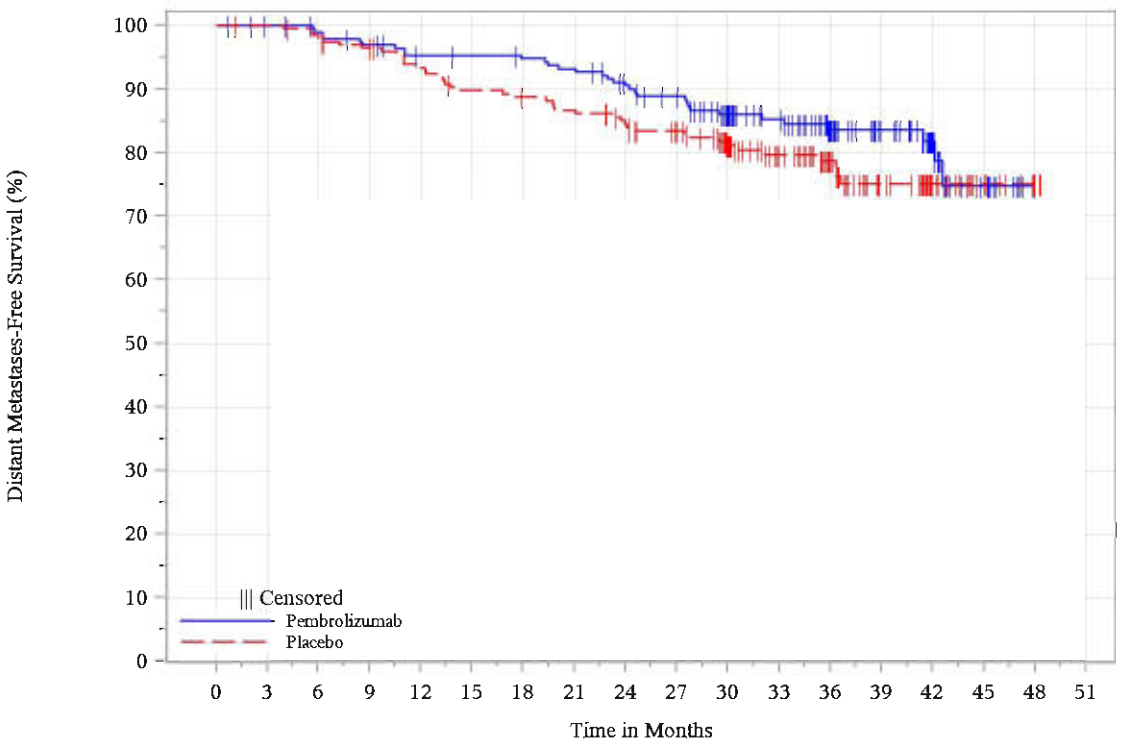


At Risk

Pembrolizumab	171	169	166	162	156	150	146	140	129	120	105	93	61	44	24	9	3	0
Placebo	169	166	156	151	142	138	133	127	120	110	91	82	63	52	24	13	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-8
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T3b
(ITT Population)

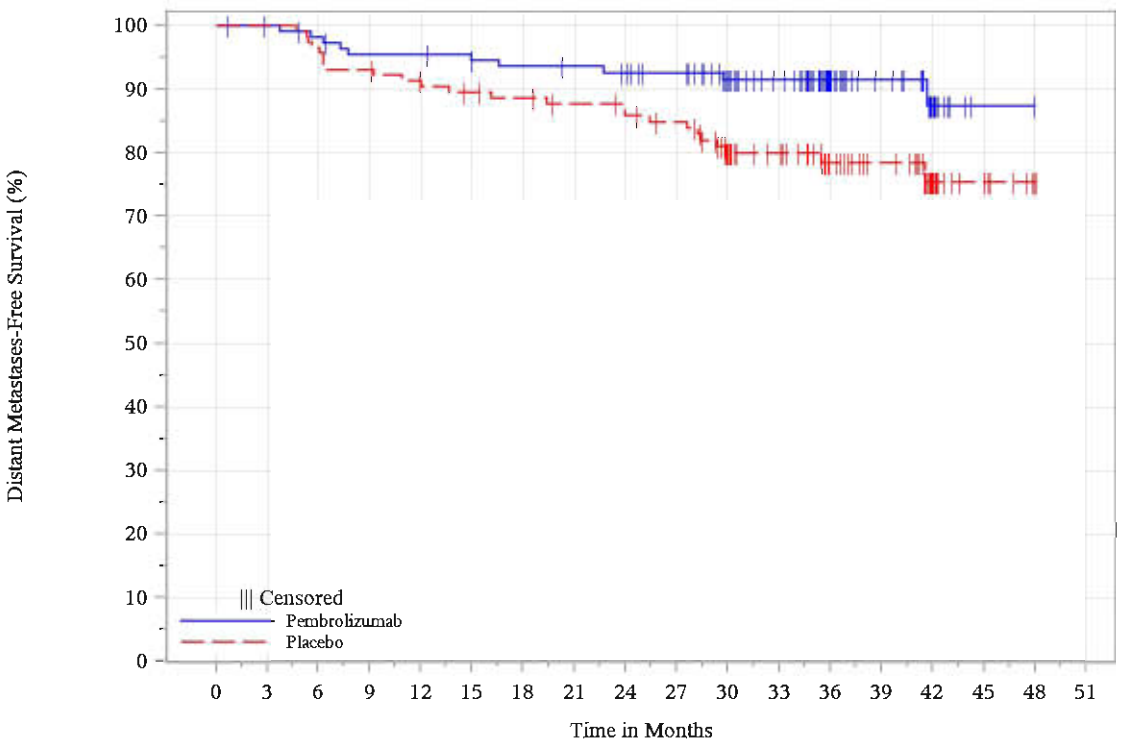


At Risk

Pembrolizumab	200	197	193	188	182	181	179	176	168	161	136	114	79	55	34	12	1	0
Placebo	201	200	195	190	183	174	171	167	160	151	124	100	72	47	22	11	3	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-9
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T4a
(ITT Population)

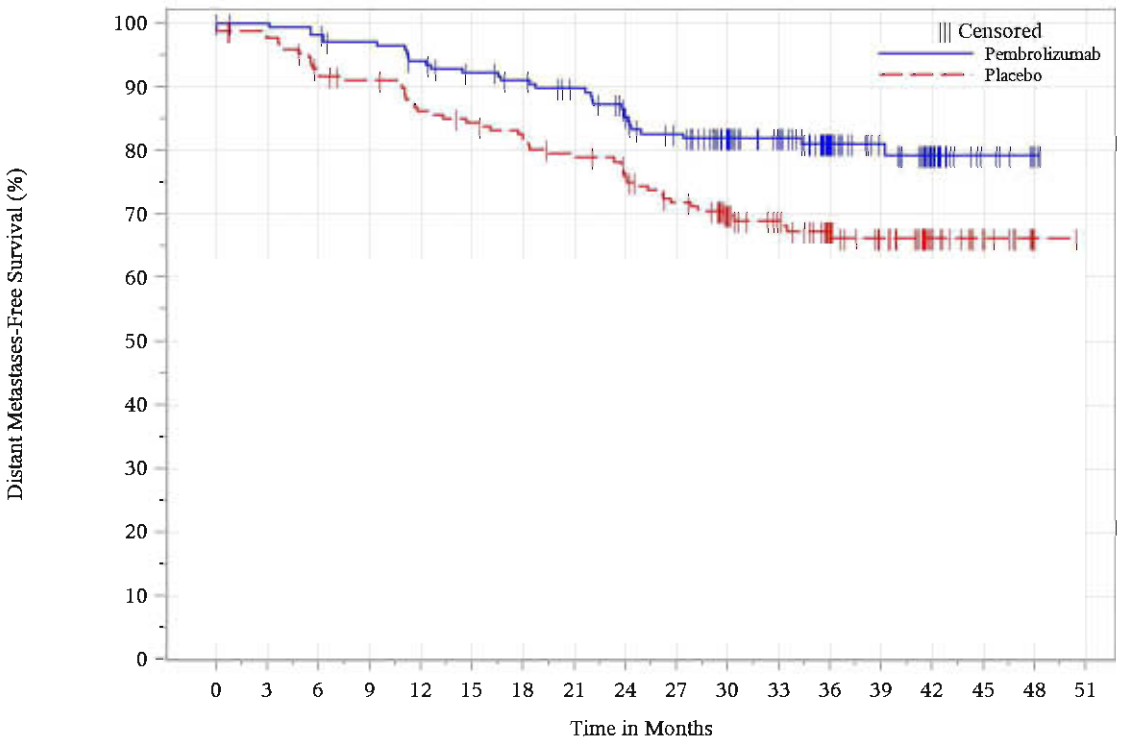


At Risk

Pembrolizumab	113	111	108	104	104	101	100	99	97	93	79	67	43	29	13	1	1	0
Placebo	116	116	112	108	102	100	98	95	92	89	72	61	41	32	16	8	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-10
Kaplan-Meier Estimates of Distant Metastases-Free Survival for Participants with Actual Baseline Tumor Stage T4b
(ITT Population)



At Risk

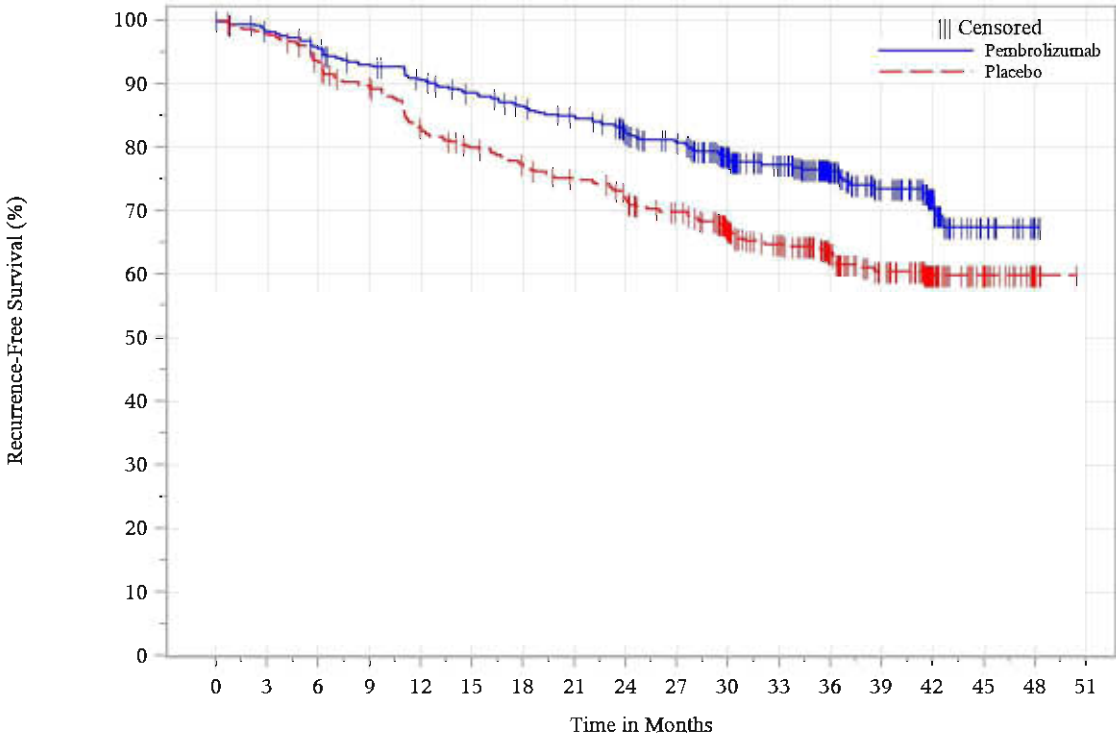
Pembrolizumab	172	170	167	163	157	151	147	141	130	121	106	94	62	45	24	9	3	0
Placebo	172	166	156	151	142	138	133	127	120	110	91	82	63	52	24	13	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

14.2.1.2 Recurrence-free Survival

14.2.1.2.1 Recurrence-free Survival in All Participants

Figure 14.2-11
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule)
(ITT Population)



At Risk

Pembrolizumab	487	472	457	441	426	413	400	390	371	353	300	254	173	117	62	18	4	0
Placebo	489	477	452	430	395	378	363	350	331	311	252	210	149	113	51	30	7	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-10
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	487	117 (24.0)	14728.3	0.8	NR (NR, NR)	76.2 (71.9, 79.9)
Placebo	489	174 (35.6)	13729.1	1.3	NR (NR, NR)	63.4 (58.7, 67.7)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.62 (0.49, 0.79)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T Stage (T3b vs. T4a vs. T4b).
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-11
Recurrence-Free Survival Rate Over Time
(ITT Population)

	Pembrolizumab (N=487) % (95% CI)[a]	Placebo (N=489) % (95% CI)[a]
Recurrence-Free Survival rate at time point		
6 months	95.6 (93.4, 97.1)	93.4 (90.8, 95.3)
12 months	90.6 (87.6, 92.9)	83.0 (79.3, 86.1)
18 months	86.5 (83.1, 89.3)	77.3 (73.2, 80.8)
24 months	82.6 (78.8, 85.7)	72.1 (67.8, 75.9)
30 months	78.6 (74.6, 82.1)	66.8 (62.4, 70.9)
36 months	76.2 (71.9, 79.9)	63.4 (58.7, 67.7)
42 months	72.0 (66.8, 76.5)	59.9 (54.8, 64.7)
48 months	67.4 (60.0, 73.7)	59.9 (54.8, 64.7)

[a] From product-limit (Kaplan-Meier) method for censored data.

Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

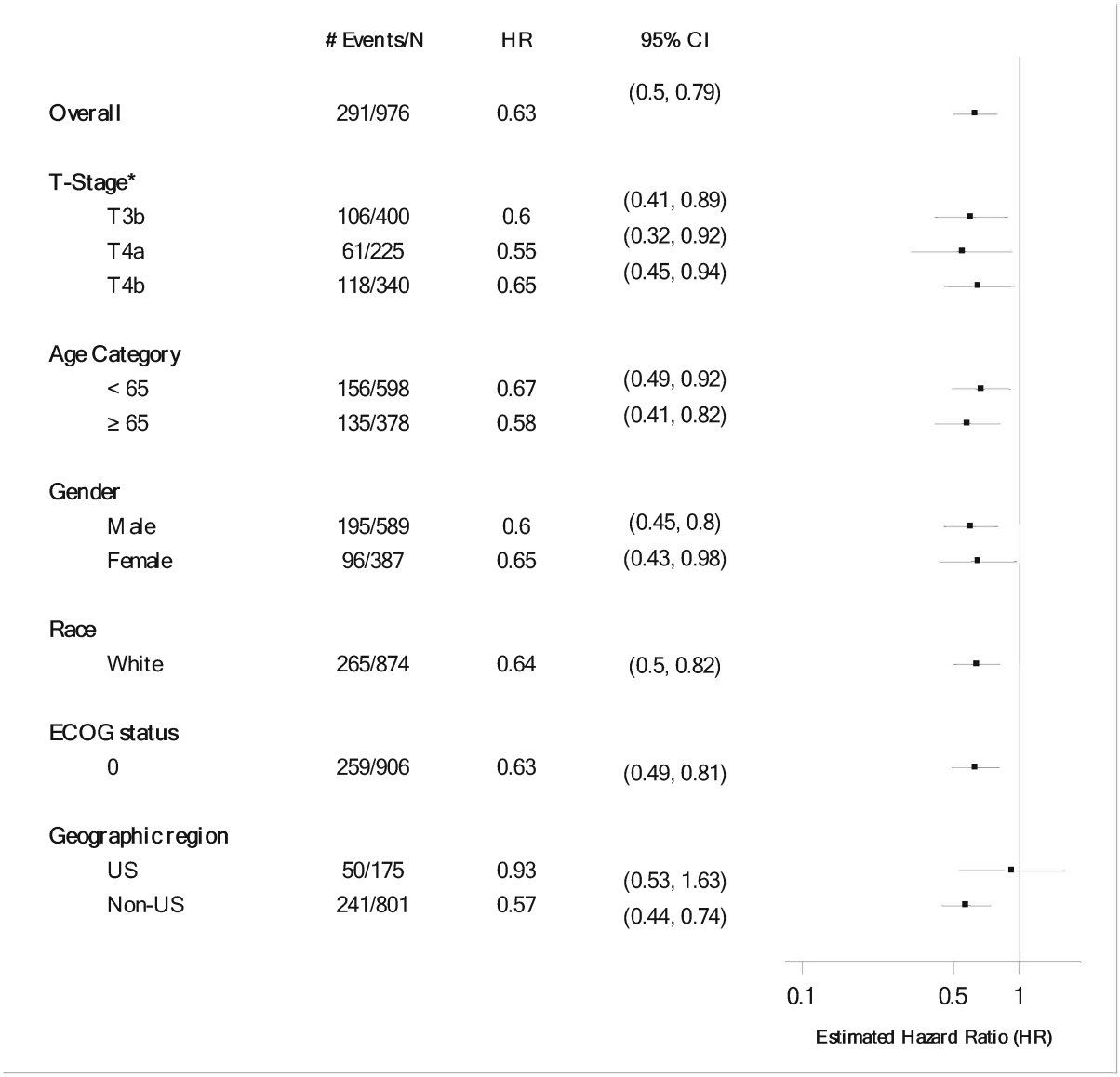
Table 14.2-12
Participants with Recurrence Crossover/re-treatment with Pembrolizumab in Part 2 (ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants with RFS event	117		174		291	
Participants Crossover/re-treat in Part 2	8	(6.8)	63	(36.2)	71	(24.4)
Database Cutoff Date: 04JAN2023						

Source: [P716V04MK3475: adam-adsl; adintdt]

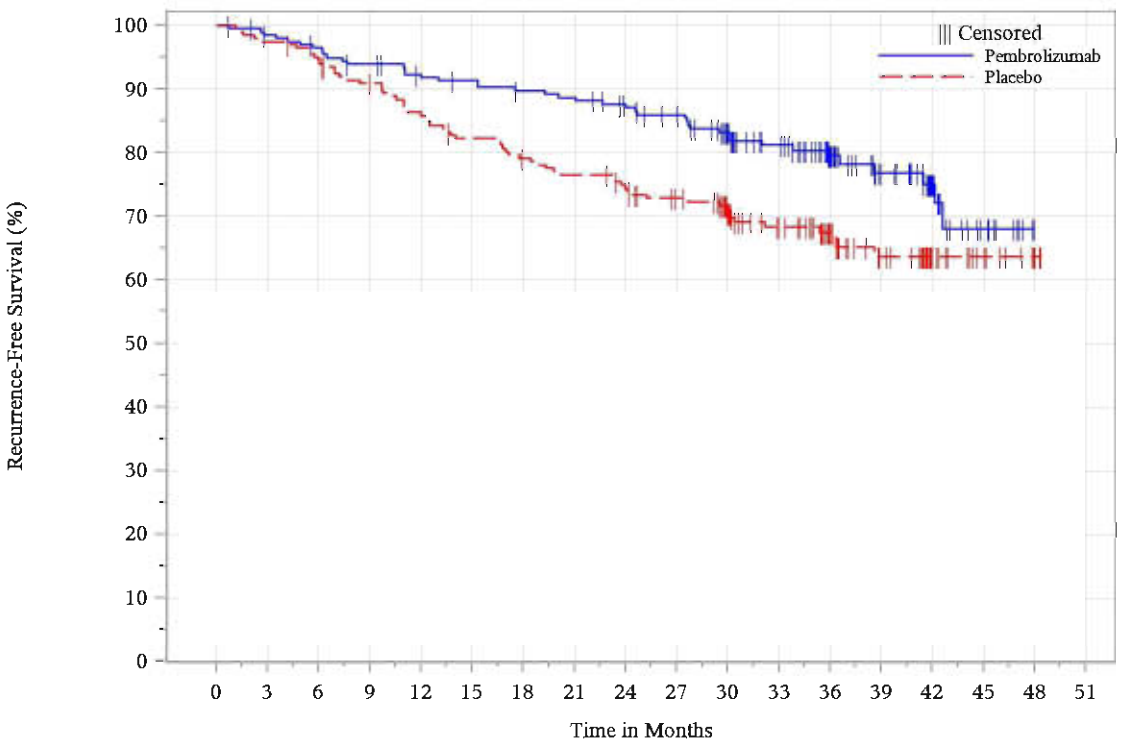
14.2.1.2.2 Recurrence-free Survival by Subgroup

Figure 14.2-12
Forest Plot of Recurrence-Free Survival Hazard Ratio by Subgroup Factors
(ITT Population)



A subgroup with number of participants < 10% ITT population is not displayed on the plot.
*Based on actual baseline tumor stage collected on eCRF.
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-13
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T3b within Overall Cancer Stage IIB (ITT Population)

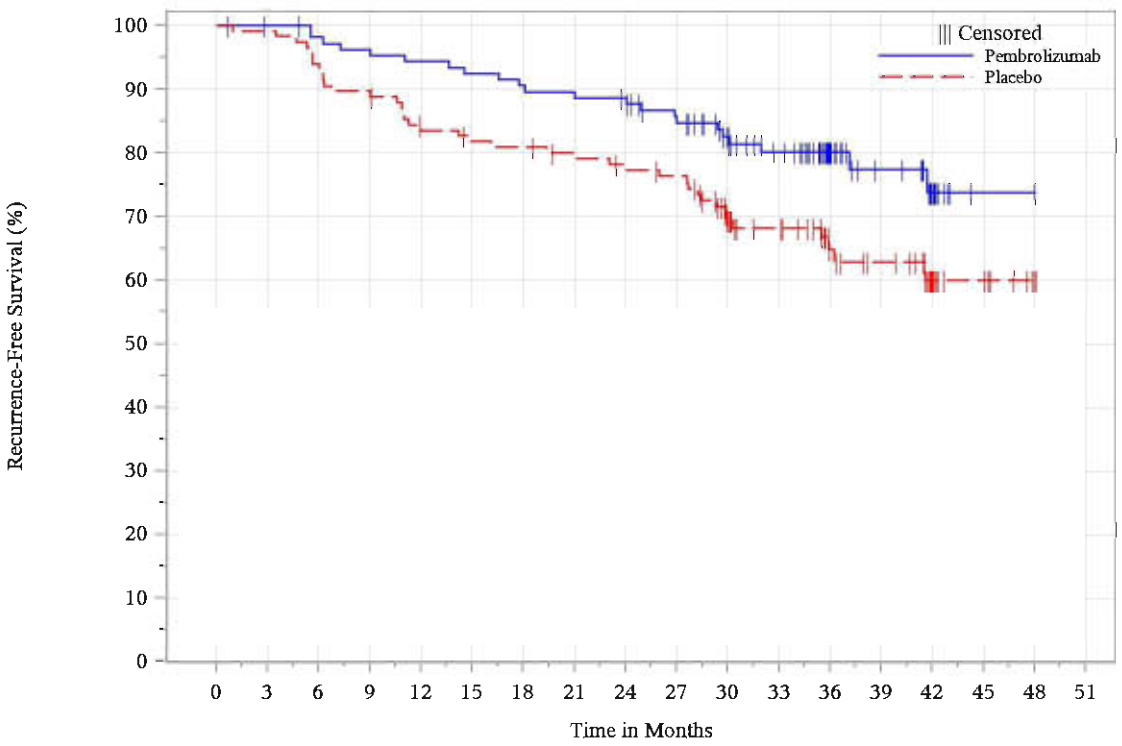


At Risk

Pembrolizumab	200	194	189	183	176	174	170	168	162	156	133	110	77	51	31	11	1	0
Placebo	200	195	188	179	169	160	153	148	142	132	109	88	63	43	18	10	3	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-14
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T4a within Overall Cancer Stage IIB (ITT Population)

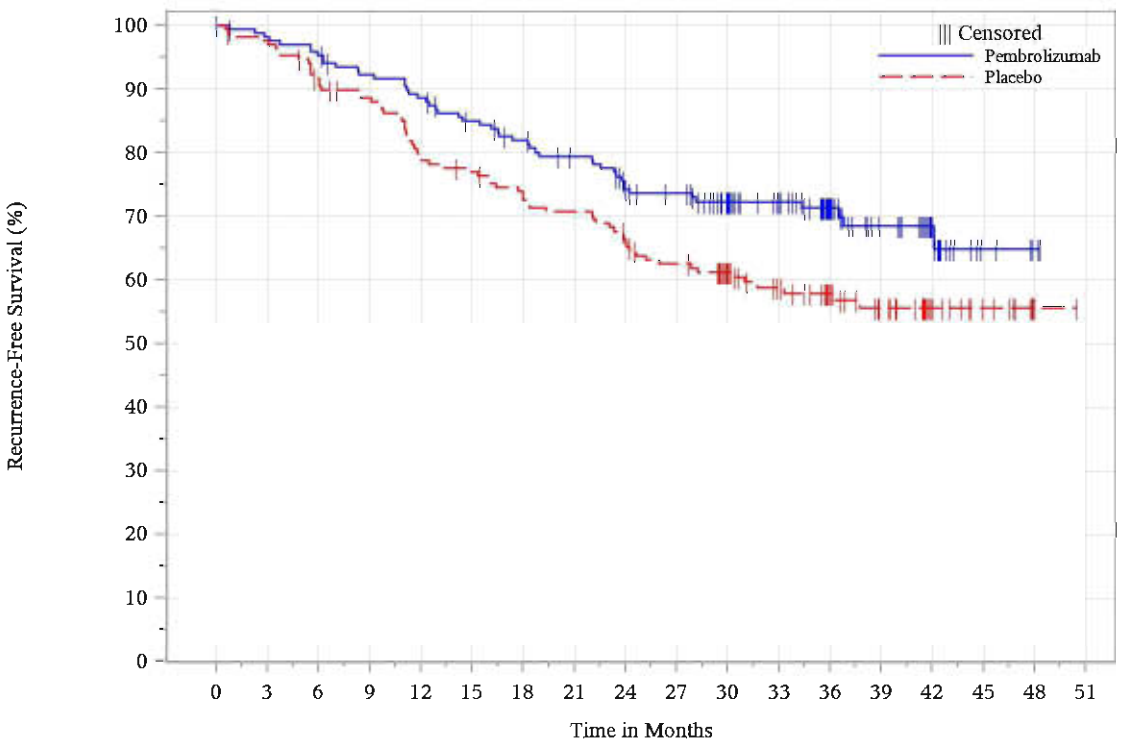


At Risk

Pembrolizumab	109	107	104	102	100	98	96	95	93	86	71	59	38	26	12	1	1	0
Placebo	116	115	109	104	95	92	91	88	84	82	63	52	33	27	13	8	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-15
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T4b within Overall Cancer Stage IIC (ITT Population)

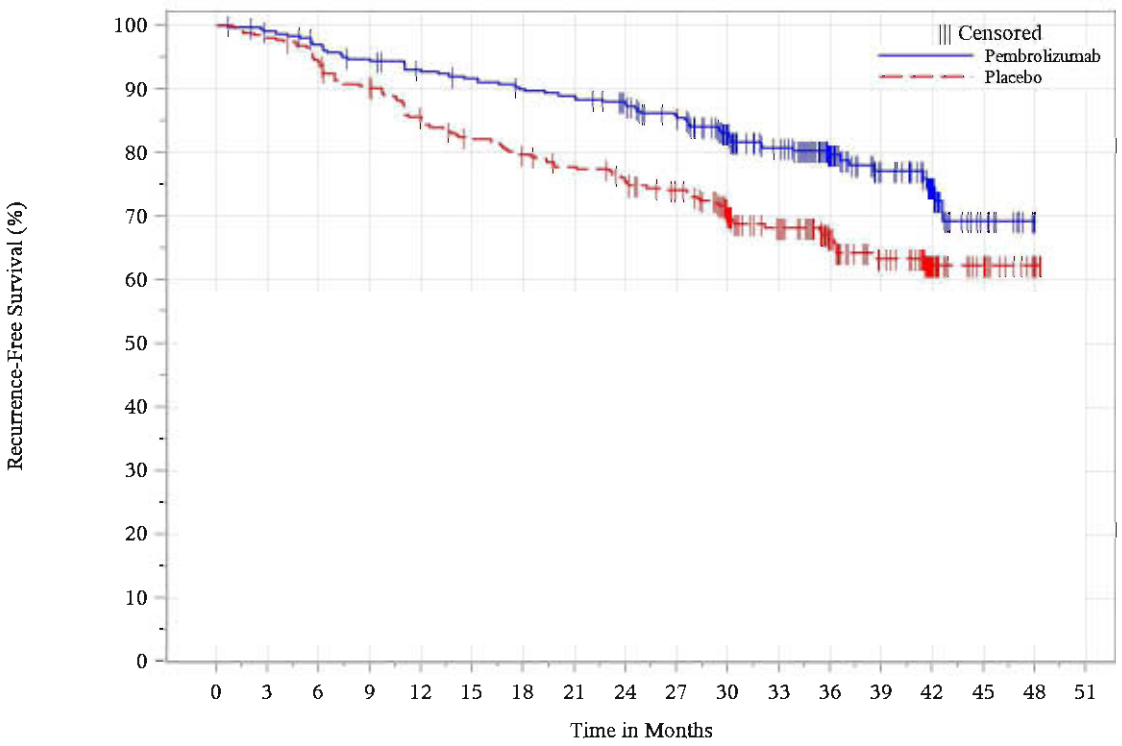


At Risk

Pembrolizumab	171	166	161	154	148	139	132	125	114	109	94	83	56	38	19	6	2	0
Placebo	169	164	152	145	130	125	118	114	105	97	80	70	53	43	20	12	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-16
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Baseline Cancer Stage IIB
(ITT Population)

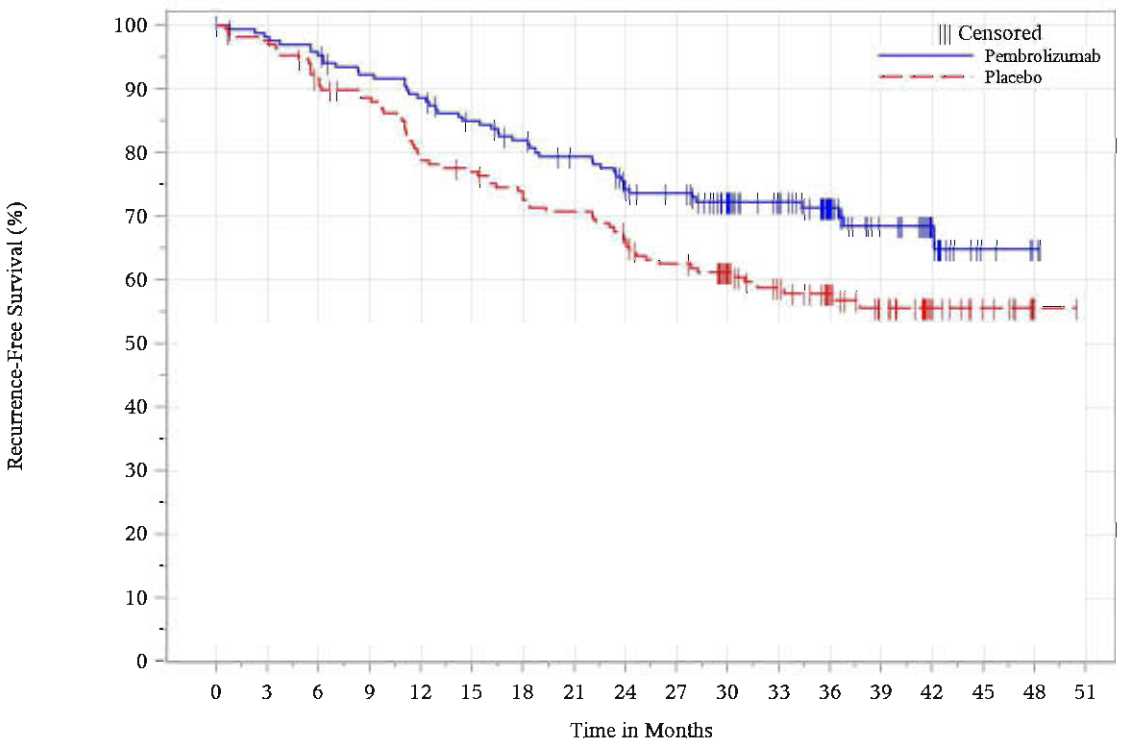


At Risk

Pembrolizumab	309	301	293	285	276	272	266	263	255	242	204	169	115	77	43	12	2	0
Placebo	316	310	297	283	264	252	244	236	226	214	172	140	96	70	31	18	5	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-17
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Baseline Cancer Stage IIC
(ITT Population)



At Risk

Pembrolizumab	171	166	161	154	148	139	132	125	114	109	94	83	56	38	19	6	2	0
Placebo	169	164	152	145	130	125	118	114	105	97	80	70	53	43	20	12	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-13
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
for Participants with Actual Baseline Tumor Stage T3b within Overall Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	200	42 (21.0)	6268.3	0.7	NR (NR, NR)	79.5 (72.7, 84.8)
Placebo	200	64 (32.0)	5735.1	1.1	NR (NR, NR)	67.5 (60.1, 73.8)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.60 (0.41, 0.89)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-14
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
for Participants with Actual Baseline Tumor Stage T4a within Overall Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	109	22 (20.2)	3438.6	0.6	NR (NR, NR)	80.1 (70.8, 86.7)
Placebo	116	39 (33.6)	3367.8	1.2	NR (41.6, NR)	64.9 (54.5, 73.5)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.55 (0.32, 0.92)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-15
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
for Participants with Actual Baseline Tumor Stage T4b within Overall Cancer Stage IIC
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	171	49 (28.7)	4922.4	1.0	NR (NR, NR)	71.4 (63.7, 77.8)
Placebo	169	69 (40.8)	4586.6	1.5	NR (33.3, NR)	58.0 (49.9, 65.3)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.65 (0.45, 0.94)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-16
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
for Participants with Baseline Cancer Stage IIB
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	309	64 (20.7)	9706.9	0.7	NR (NR, NR)	79.7 (74.4, 84.0)
Placebo	316	103 (32.6)	9102.9	1.1	NR (NR, NR)	66.5 (60.7, 71.8)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.58 (0.43, 0.79)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

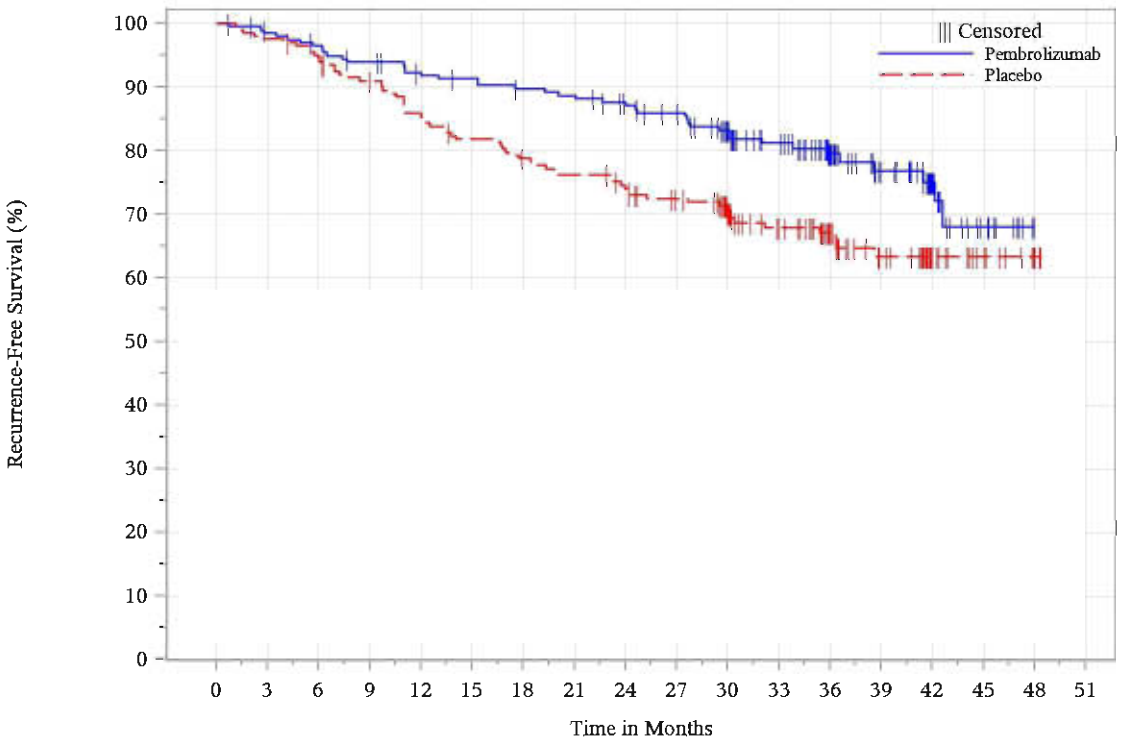
Table 14.2-17
Analysis of Recurrence-Free Survival (Primary Censoring Rule)
for Participants with Baseline Cancer Stage IIC
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median RFS [a] (months) (95% CI)	RFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	171	49 (28.7)	4922.4	1.0	NR (NR, NR)	71.4 (63.7, 77.8)
Placebo	169	69 (40.8)	4586.6	1.5	NR (33.3, NR)	58.0 (49.9, 65.3)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.65 (0.45, 0.94)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model unstratified with treatment as a covariate.
NR = Not reached.
Recurrence-free survival is defined as time from randomization to the date of first recurrence of melanoma at any site (local, in-transit or regional lymph nodes or distant recurrence) or death due to any cause, whichever occurs first.
Baseline cancer stage is based on the actual cancer stage recorded on the eCRF
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-18
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T3b
(ITT Population)

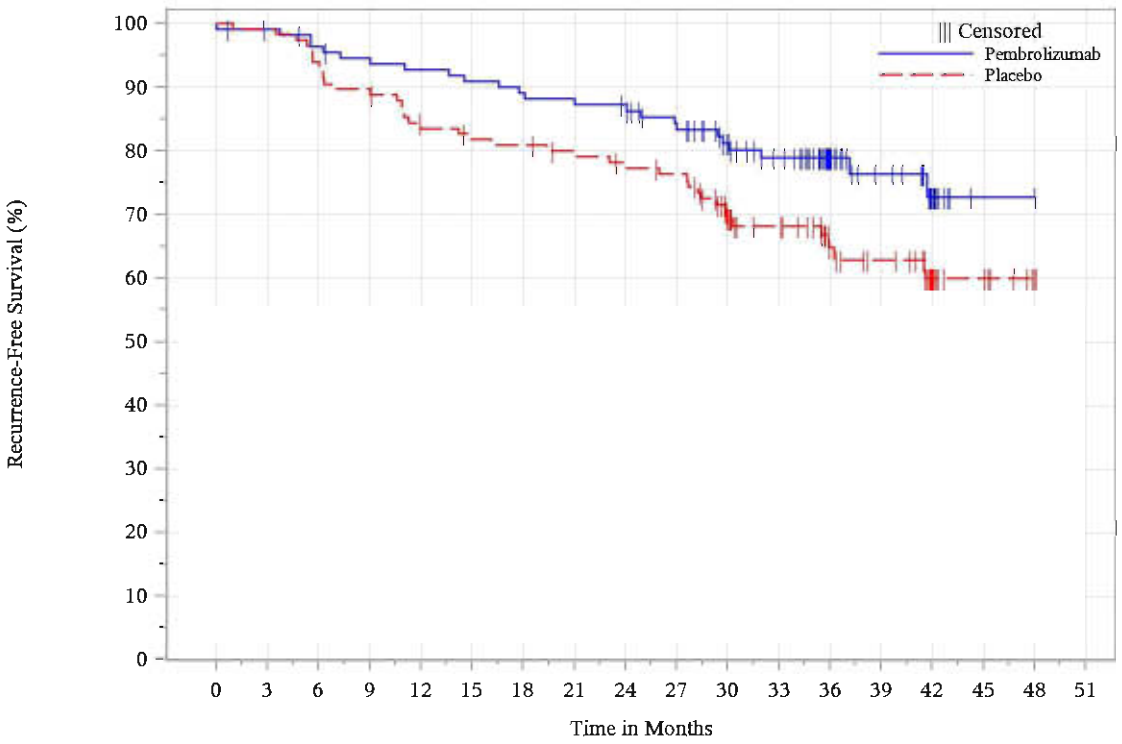


At Risk

Pembrolizumab	200	194	189	183	176	174	170	168	162	156	133	110	77	51	31	11	1	0
Placebo	201	196	189	180	169	160	153	148	142	132	109	88	63	43	18	10	3	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-19
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T4a
(ITT Population)

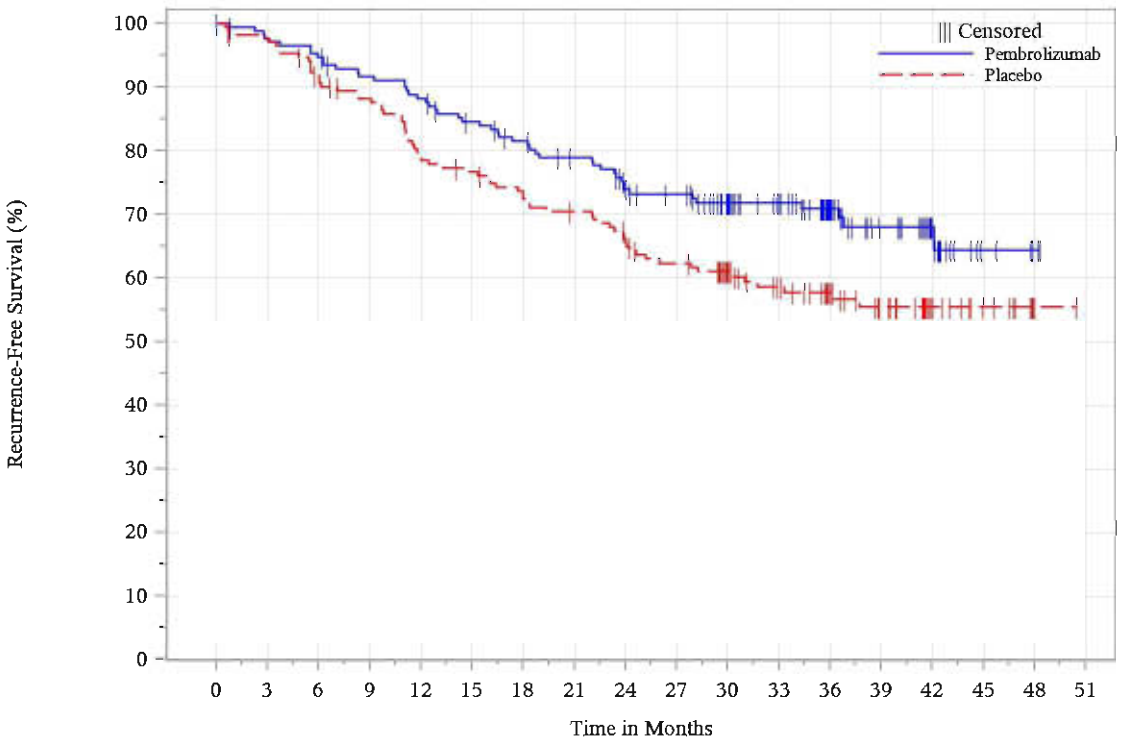


At Risk

Pembrolizumab	113	110	106	103	101	99	97	96	94	87	72	60	39	27	12	1	1	0
Placebo	116	115	109	104	95	92	91	88	84	82	63	52	33	27	13	8	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Figure 14.2-20
Kaplan-Meier Estimates of Recurrence-Free Survival (Primary Censoring Rule) for Participants with Actual Baseline Tumor Stage T4b
(ITT Population)



At Risk

Pembrolizumab	172	166	161	154	148	139	132	125	114	109	94	83	56	38	19	6	2	0
Placebo	172	166	154	146	131	126	119	114	105	97	80	70	53	43	20	12	2	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

14.2.1.3 Subsequent Therapies

Table 14.2-18
Participants With Subsequent Therapies
(Incidence > 0% in One or More Treatment Groups)
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	487		489		976	
with one or more Subsequent Therapies	79	(16.2)	91	(18.6)	170	(17.4)
with no Subsequent Therapies	408	(83.8)	398	(81.4)	806	(82.6)
Adjuvant Therapy	**11**	**(2.3)**	**21**	**(4.3)**	**32**	**(3.3)**
BINIMETINIB	0	(0.0)	1	(0.2)	1	(0.1)
CANCER VACCINES	0	(0.0)	2	(0.4)	2	(0.2)
CARBOPLATIN	1	(0.2)	0	(0.0)	1	(0.1)
CYCLOPHOSPHAMIDE	1	(0.2)	0	(0.0)	1	(0.1)
DABRAFENIB	3	(0.6)	1	(0.2)	4	(0.4)
DOXORUBICIN	1	(0.2)	0	(0.0)	1	(0.1)
ENCORAFENIB	0	(0.0)	1	(0.2)	1	(0.1)
IMMUNOTHERAPY	1	(0.2)	0	(0.0)	1	(0.1)
IPILIMUMAB	1	(0.2)	0	(0.0)	1	(0.1)
LETROZOLE	1	(0.2)	0	(0.0)	1	(0.1)
NIRAPARIB	1	(0.2)	0	(0.0)	1	(0.1)
NIVOLUMAB	2	(0.4)	12	(2.5)	14	(1.4)
OTHER THERAPEUTIC PRODUCTS	0	(0.0)	1	(0.2)	1	(0.1)
PACLITAXEL	1	(0.2)	0	(0.0)	1	(0.1)
PEMBROLIZUMAB	2	(0.4)	8	(1.6)	10	(1.0)
PREDNISONE	1	(0.2)	0	(0.0)	1	(0.1)
RITUXIMAB	1	(0.2)	0	(0.0)	1	(0.1)
TRAMETINIB	3	(0.6)	1	(0.2)	4	(0.4)
VINCRISTINE	1	(0.2)	0	(0.0)	1	(0.1)
First Line of Therapy	**68**	**(14.0)**	**73**	**(14.9)**	**141**	**(14.4)**
AGI 101H	1	(0.2)	0	(0.0)	1	(0.1)
ANASTROZOLE	0	(0.0)	1	(0.2)	1	(0.1)
BEMPEGALDESLEUKIN	0	(0.0)	1	(0.2)	1	(0.1)
BEVACIZUMAB	1	(0.2)	0	(0.0)	1	(0.1)
BINIMETINIB	9	(1.8)	5	(1.0)	14	(1.4)
BMS 986249	1	(0.2)	1	(0.2)	2	(0.2)
CAPECITABINE	1	(0.2)	0	(0.0)	1	(0.1)
CARBOPLATIN	2	(0.4)	1	(0.2)	3	(0.3)
COBIMETINIB	1	(0.2)	2	(0.4)	3	(0.3)
CYCLOPHOSPHAMIDE	0	(0.0)	1	(0.2)	1	(0.1)
DABRAFENIB	9	(1.8)	6	(1.2)	15	(1.5)

Participants With Subsequent Therapies
(Incidence > 0% in One or More Treatment Groups)
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
First Line of Therapy	**68**	**(14.0)**	**73**	**(14.9)**	**141**	**(14.4)**
DABRAFENIB MESILATE	1	(0.2)	0	(0.0)	1	(0.1)
DACARBAZINE	1	(0.2)	0	(0.0)	1	(0.1)
DOXORUBICIN	0	(0.0)	1	(0.2)	1	(0.1)
ENCORAFENIB	9	(1.8)	5	(1.0)	14	(1.4)
ETOPOSIDE	0	(0.0)	1	(0.2)	1	(0.1)
IMATINIB MESILATE	1	(0.2)	0	(0.0)	1	(0.1)
INVESTIGATIONAL DRUG	0	(0.0)	2	(0.4)	2	(0.2)
IPILIMUMAB	20	(4.1)	28	(5.7)	48	(4.9)
LENVATINIB	0	(0.0)	2	(0.4)	2	(0.2)
LETROZOLE	0	(0.0)	1	(0.2)	1	(0.1)
NIVOLUMAB	24	(4.9)	35	(7.2)	59	(6.0)
OTHER ANTINEOPLASTIC AGENTS	1	(0.2)	0	(0.0)	1	(0.1)
OXALIPLATIN	1	(0.2)	0	(0.0)	1	(0.1)
PACLITAXEL	2	(0.4)	0	(0.0)	2	(0.2)
PEMBROLIZUMAB	11	(2.3)	21	(4.3)	32	(3.3)
PEMBROLIZUMAB;QUAVONLIMAB	0	(0.0)	1	(0.2)	1	(0.1)
QUAVONLIMAB	3	(0.6)	2	(0.4)	5	(0.5)
RELATLIMAB	0	(0.0)	2	(0.4)	2	(0.2)
RIBOCICLIB	0	(0.0)	1	(0.2)	1	(0.1)
SUNITINIB MALATE	1	(0.2)	0	(0.0)	1	(0.1)
TALIMOGENE LAHERPAREPVEC	2	(0.4)	0	(0.0)	2	(0.2)
TOCILIZUMAB	0	(0.0)	1	(0.2)	1	(0.1)
TRAMETINIB	9	(1.8)	6	(1.2)	15	(1.5)
TRAMETINIB DIMETHYL SULFOXIDE	1	(0.2)	0	(0.0)	1	(0.1)
VEMURAFENIB	1	(0.2)	2	(0.4)	3	(0.3)
VIBOSTOLIMAB	1	(0.2)	0	(0.0)	1	(0.1)
Neo-Adjuvant Therapy	**0**	**(0.0)**	**3**	**(0.6)**	**3**	**(0.3)**
IPILIMUMAB	0	(0.0)	1	(0.2)	1	(0.1)
NIVOLUMAB	0	(0.0)	2	(0.4)	2	(0.2)
PEMBROLIZUMAB	0	(0.0)	1	(0.2)	1	(0.1)
Second Line of Therapy	**23**	**(4.7)**	**17**	**(3.5)**	**40**	**(4.1)**
ALDESLEUKIN	1	(0.2)	0	(0.0)	1	(0.1)
ATEZOLIZUMAB	1	(0.2)	0	(0.0)	1	(0.1)

Participants With Subsequent Therapies
(Incidence > 0% in One or More Treatment Groups)
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Second Line of Therapy	**23**	**(4.7)**	**17**	**(3.5)**	**40**	**(4.1)**
AXITINIB	1	(0.2)	0	(0.0)	1	(0.1)
BINIMETINIB	2	(0.4)	2	(0.4)	4	(0.4)
CARBOPLATIN	1	(0.2)	1	(0.2)	2	(0.2)
COBIMETINIB	1	(0.2)	0	(0.0)	1	(0.1)
DABRAFENIB	2	(0.4)	1	(0.2)	3	(0.3)
ENCORAFENIB	2	(0.4)	2	(0.4)	4	(0.4)
IPILIMUMAB	10	(2.1)	6	(1.2)	16	(1.6)
LETROZOLE	0	(0.0)	1	(0.2)	1	(0.1)
NIVOLUMAB	11	(2.3)	10	(2.0)	21	(2.2)
PACLITAXEL	1	(0.2)	2	(0.4)	3	(0.3)
PEMBROLIZUMAB	2	(0.4)	1	(0.2)	3	(0.3)
REGORAFENIB	1	(0.2)	0	(0.0)	1	(0.1)
RELATLIMAB	0	(0.0)	1	(0.2)	1	(0.1)
SRK 181	1	(0.2)	0	(0.0)	1	(0.1)
TEMOZOLOMIDE	1	(0.2)	0	(0.0)	1	(0.1)
TRAMETINIB	2	(0.4)	1	(0.2)	3	(0.3)
VEMURAFENIB	1	(0.2)	0	(0.0)	1	(0.1)
ZETELETINIB	0	(0.0)	1	(0.2)	1	(0.1)
Third or Higher Lines of Therapy	**9**	**(1.8)**	**8**	**(1.6)**	**17**	**(1.7)**
ALDESLEUKIN	1	(0.2)	0	(0.0)	1	(0.1)
BINIMETINIB	1	(0.2)	0	(0.0)	1	(0.1)
BINTRAFUSP ALFA	0	(0.0)	1	(0.2)	1	(0.1)
CARBOPLATIN	2	(0.4)	0	(0.0)	2	(0.2)
CISPLATIN	1	(0.2)	0	(0.0)	1	(0.1)
CYCLOPHOSPHAMIDE	1	(0.2)	0	(0.0)	1	(0.1)
DABRAFENIB	1	(0.2)	0	(0.0)	1	(0.1)
DABRAFENIB MESILATE	0	(0.0)	1	(0.2)	1	(0.1)
DACARBAZINE	4	(0.8)	1	(0.2)	5	(0.5)
DF 6002	0	(0.0)	1	(0.2)	1	(0.1)
ENCORAFENIB	1	(0.2)	0	(0.0)	1	(0.1)
FELADILIMAB	0	(0.0)	2	(0.4)	2	(0.2)
IPILIMUMAB	2	(0.4)	1	(0.2)	3	(0.3)
KITE 718	0	(0.0)	1	(0.2)	1	(0.1)
LENVATINIB	1	(0.2)	0	(0.0)	1	(0.1)
NAPORAFENIB	0	(0.0)	1	(0.2)	1	(0.1)

Participants With Subsequent Therapies
(Incidence > 0% in One or More Treatment Groups)
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Third or Higher Lines of Therapy	**9**	**(1.8)**	**8**	**(1.6)**	**17**	**(1.7)**
NIVOLUMAB	3	(0.6)	4	(0.8)	7	(0.7)
PACLITAXEL	2	(0.4)	0	(0.0)	2	(0.2)
PEMBROLIZUMAB	1	(0.2)	1	(0.2)	2	(0.2)
RIBOCICLIB	0	(0.0)	1	(0.2)	1	(0.1)
SIMLUKAFUSP ALFA	0	(0.0)	1	(0.2)	1	(0.1)
SUNITINIB MALATE	0	(0.0)	1	(0.2)	1	(0.1)
TALIMOGENE LAHERPAREPVEC	1	(0.2)	0	(0.0)	1	(0.1)
TEMOZOLOMIDE	0	(0.0)	1	(0.2)	1	(0.1)
TRAMETINIB	1	(0.2)	0	(0.0)	1	(0.1)
TRAMETINIB DIMETHYL SULFOXIDE	0	(0.0)	1	(0.2)	1	(0.1)
TUMOR-INFILTRATING LYMPHOCYTES	1	(0.2)	0	(0.0)	1	(0.1)
VINBLASTINE SULFATE	1	(0.2)	0	(0.0)	1	(0.1)
VINCRISTINE	1	(0.2)	0	(0.0)	1	(0.1)

Every participant is counted a single time for each applicable row and column.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adcm]

14.2.1.3.1 Subsequent Therapies After First Distant Metastasis

Table 14.2-19
Subsequent Surgical Procedure Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Participants with Surgical Procedure Post First Distant Metastasis[a]	**21 (28.4)**	**32 (26.9)**	**53 (27.5)**
Lung Metastasis Resection	10 (13.5)	22 (18.5)	32 (16.6)
Craniotomy	3 (4.1)	2 (1.7)	5 (2.6)
Skin Metastasis Resection	2 (2.7)	1 (0.8)	3 (1.6)
Skin Excisional Biopsy	1 (1.4)	0 (0.0)	1 (0.5)
Lymphadenectomy	1 (1.4)	2 (1.7)	3 (1.6)
Adrenal Metastasis Resection	1 (1.4)	0 (0.0)	1 (0.5)
Intestinal Metastasis Resection	1 (1.4)	1 (0.8)	2 (1.0)
Pleural Biopsy	1 (1.4)	0 (0.0)	1 (0.5)
Spinal Metastasis Resection	1 (1.4)	0 (0.0)	1 (0.5)
Tonsillectomy	1 (1.4)	0 (0.0)	1 (0.5)
Parotidectomy	0 (0.0)	1 (0.8)	1 (0.5)
Cholecystectomy	0 (0.0)	1 (0.8)	1 (0.5)
Lymph Node Biopsy	0 (0.0)	1 (0.8)	1 (0.5)
Thyroid Gland Biopsy	0 (0.0)	1 (0.8)	1 (0.5)
Retroperitoneal Metastasis Resection	0 (0.0)	1 (0.8)	1 (0.5)

[a] Participants with multiple surgeries are counted in multiple categories.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 14.2-20
Subsequent Radiation Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Subsequent Radiation Post First Distant Metastasis	**21 (28.4)**	**16 (13.4)**	**37 (19.2)**
Control of Brain Metastases	11 (14.9)	4 (3.4)	15 (7.8)
Control of Recurrent Disease	3 (4.1)	4 (3.4)	7 (3.6)
Palliative Treatment or Symptom Control	1 (1.4)	2 (1.7)	3 (1.6)
Palliative Treatment or Symptom Control of Metastatic Disease	6 (8.1)	6 (5.0)	12 (6.2)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 14.2-21
Subsequent Therapy Post First Distant Metastasis
(ITT Population - Participants with DMFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with DMFS events	74	119	193
Subsequent Therapy Post First Distant Metastasis	**56 (75.7)**	**79 (66.4)**	**135 (69.9)**
Anti PD-1 Therapy	10 (13.5)	23 (19.3)	33 (17.1)
Anti CTLA-4 Therapy	4 (5.4)	4 (3.4)	8 (4.1)
Immunotherapy	2 (2.7)	1 (0.8)	3 (1.6)
Protein Kinase Inhibitor	1 (1.4)	0 (0.0)	1 (0.5)
BRAF/MEK Targeted Therapy	16 (21.6)	14 (11.8)	30 (15.5)
Anti PD-1/Anti CTLA-4 Combination Therapy	19 (25.7)	33 (27.7)	52 (26.9)
Anti PD-1/Immunotherapy Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Anti CTLA-4 /Immunotherapy Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Anti CTLA-4/TKI Combination Therapy	0 (0.0)	1 (0.8)	1 (0.5)
Anti PD-1/Other Targeted Combination Therapy	1 (1.4)	0 (0.0)	1 (0.5)
Chemotherapy	2 (2.7)	0 (0.0)	2 (1.0)
Anti PD-1/TKI Combination Therapy	0 (0.0)	2 (1.7)	2 (1.0)
Other Targeted Therapy	1 (1.4)	0 (0.0)	1 (0.5)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

14.2.1.3.2 Subsequent Therapies After First Recurrence

Table 14.2-22
Subsequent Surgical Procedure in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Participants with Surgical Procedure in Part 1 Post First Recurrence[a]	**65 (55.6)**	**87 (50.0)**	**152 (52.2)**
Lymphadenectomy	21 (17.9)	33 (19.0)	54 (18.6)
Skin Excisional Biopsy	13 (11.1)	15 (8.6)	28 (9.6)
Skin Metastasis Resection	12 (10.3)	15 (8.6)	27 (9.3)
Lung Metastasis Resection	10 (8.5)	21 (12.1)	31 (10.7)
Amputation	3 (2.6)	0 (0.0)	3 (1.0)
Craniotomy	2 (1.7)	1 (0.6)	3 (1.0)
Parotidectomy	1 (0.9)	1 (0.6)	2 (0.7)
Adrenal Metastasis Resection	1 (0.9)	0 (0.0)	1 (0.3)
Intestinal Metastasis Resection	1 (0.9)	1 (0.6)	2 (0.7)
Lymph Node Biopsy	1 (0.9)	3 (1.7)	4 (1.4)
Pleural Biopsy	1 (0.9)	0 (0.0)	1 (0.3)
Spinal Metastasis Resection	1 (0.9)	0 (0.0)	1 (0.3)
Tonsillectomy	1 (0.9)	0 (0.0)	1 (0.3)
Thyroid Gland Biopsy	0 (0.0)	1 (0.6)	1 (0.3)
Retroperitoneal Metastasis Resection	0 (0.0)	1 (0.6)	1 (0.3)

[a] Participants with multiple surgeries are counted in multiple categories.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 14.2-23
Subsequent Radiation in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Subsequent Radiation in Part 1 Post First Recurrence	**24 (20.5)**	**17 (9.8)**	**41 (14.1)**
Control of Brain Metastases	9 (7.7)	3 (1.7)	12 (4.1)
Control of Recurrent Disease	8 (6.8)	9 (5.2)	17 (5.8)
Palliative Treatment or Symptom Control	1 (0.9)	2 (1.1)	3 (1.0)
Palliative Treatment or Symptom Control of Metastatic Disease	6 (5.1)	3 (1.7)	9 (3.1)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

Table 14.2-24
Subsequent Therapy in Part 1 Post First Recurrence
(ITT Population - Participants with RFS events)

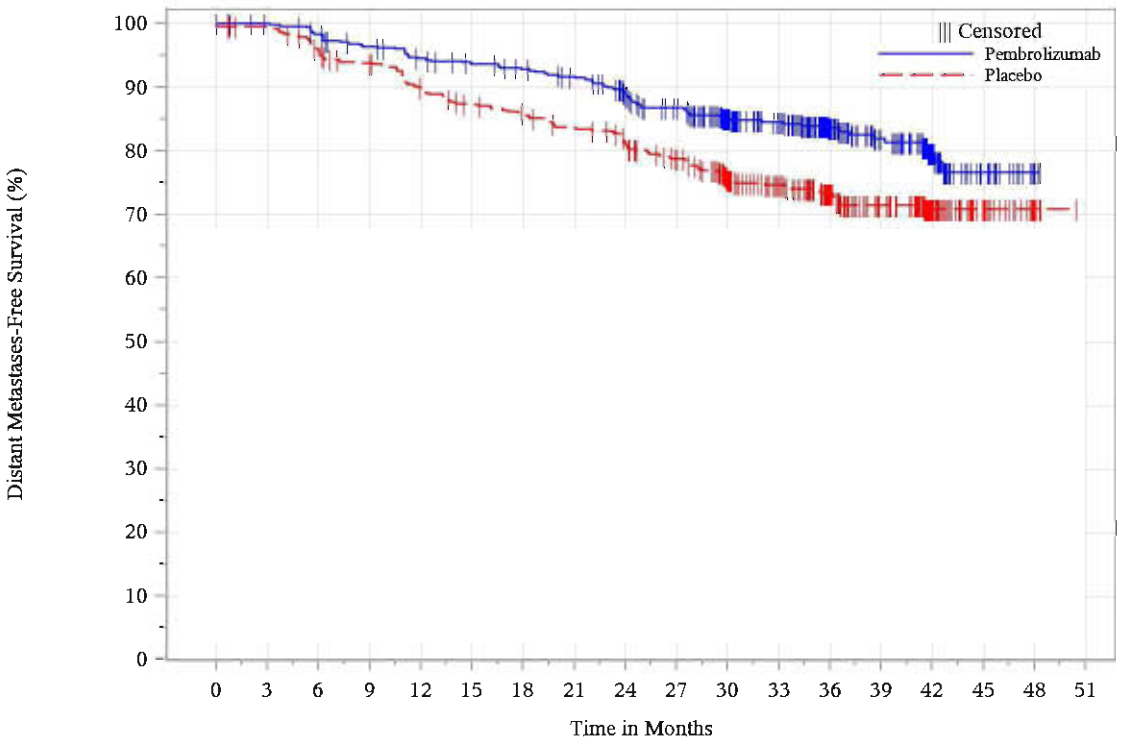
	Pembrolizumab n (%)	Placebo n (%)	Total n (%)
Participants with RFS events	117	174	291
Subsequent Therapy in Part 1 Post First Recurrence	**73 (62.4)**	**87 (50.0)**	**160 (55.0)**
Anti PD-1 Therapy	15 (12.8)	34 (19.5)	49 (16.8)
Anti CTLA-4 Therapy	4 (3.4)	1 (0.6)	5 (1.7)
Immunotherapy	3 (2.6)	0 (0.0)	3 (1.0)
Protein Kinase Inhibitor	2 (1.7)	0 (0.0)	2 (0.7)
BRAF/MEK Targeted Therapy	23 (19.7)	14 (8.0)	37 (12.7)
Anti PD-1/Anti CTLA-4 Combination Therapy	21 (17.9)	28 (16.1)	49 (16.8)
Anti PD-1/Immunotherapy Combination Therapy	2 (1.7)	4 (2.3)	6 (2.1)
Anti PD-1/Anti CTLA-4 /Immunotherapy Combination Therapy	0 (0.0)	1 (0.6)	1 (0.3)
Anti PD-1/Anti CTLA-4/TKI Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Anti PD-1/Anti Lag-3 Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Chemotherapy	2 (1.7)	0 (0.0)	2 (0.7)
Anti PD-1/TKI Combination Therapy	0 (0.0)	2 (1.1)	2 (0.7)
Other Targeted Therapy	1 (0.9)	0 (0.0)	1 (0.3)
Database Cutoff Date: 04JAN2023			

Source: [P716V04MK3475: adam-adsl; adtte; adsubtrt]

14.2.1.4 Sensitvity Analyses

14.2.1.4.1 DMFS Sensitivity Analyses

Figure 14.2-21
Kaplan-Meier Estimates of Distant Metastases-Free Survival (Sensitivity Analysis Including Death)
(ITT Population)



At Risk

Pembrolizumab	487	480	470	457	445	437	430	421	400	378	324	277	187	130	71	22	5	0
Placebo	489	482	463	449	427	412	402	390	373	351	287	243	176	131	62	32	7	0

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-25
Analysis of Distant Metastases-Free Survival (Sensitivity Analysis Including Death)
(ITT Population)

Treatment	N	Number of Events (%)	Person-month	Event Rate/ 100 Person-months	Median DMFS [a] (months) (95% CI)	DMFS Rate at 36 months in % [a] (95% CI)
Pembrolizumab	487	81 (16.6)	15576.1	0.5	NR (NR, NR)	83.6 (79.8, 86.8)
Placebo	489	126 (25.8)	14905.1	0.8	NR (NR, NR)	73.4 (69.0, 77.3)
Pairwise Comparisons					Hazard Ratio[b] (95% CI)[b]	
Pembrolizumab vs. Placebo					0.61 (0.46, 0.81)	

[a] From product-limit (Kaplan-Meier) method for censored data.
[b] Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by melanoma T Stage (T3b vs. T4a vs. T4b).
NR = Not reached.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

Table 14.2-26
Distant Metastases-Free Survival (Sensitivity Analysis Including Death) Rate Over Time (ITT Population)

	Pembrolizumab (N=487) % (95% CI)[a]	Placebo (N=489) % (95% CI)[a]
Distant Metastases-Free Survival (Sensitivity Analysis Including Death) rate at time point		
6 months	98.3 (96.7, 99.2)	95.9 (93.7, 97.3)
12 months	94.5 (92.1, 96.2)	89.8 (86.7, 92.2)
18 months	92.8 (90.1, 94.8)	85.8 (82.3, 88.6)
24 months	89.1 (85.9, 91.6)	81.3 (77.5, 84.5)
30 months	85.2 (81.6, 88.2)	75.6 (71.4, 79.2)
36 months	83.6 (79.8, 86.8)	73.4 (69.0, 77.3)
42 months	79.8 (74.8, 83.9)	70.9 (66.1, 75.2)
48 months	76.7 (69.9, 82.1)	70.9 (66.1, 75.2)

[a] From product-limit (Kaplan-Meier) method for censored data.
Distant metastasis-free survival is defined as the time from randomization to the first diagnosis of a distant metastasis.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adtte]

14.2.1.5 Patient-reported Outcomes

14.2.1.5.1 EORTC QLQ-C30

Table 14.2-27
Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**482**	**(99.8)**	**483**	**(99.4)**
	Completed	449	(93.0)	459	(94.4)
	Compliance (% in those expected to complete questionnaires)	449	(93.2)	459	(95.0)
	Not completed	33	(6.8)	24	(4.9)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	16	(3.3)	8	(1.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	15	(3.1)	10	(2.1)
	With visit, no record	2	(0.4)	6	(1.2)
	Missing by Design	**1**	**(0.2)**	**3**	**(0.6)**
	Discontinued from the study	0	(0.0)	0	(0.0)
	Pro collection not scheduled	0	(0.0)	0	(0.0)
	Translation not available in subjects language	1	(0.2)	3	(0.6)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
BASELINE	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 12	**Expected to Complete Questionnaires**	**482**	**(99.8)**	**486**	**(100.0)**
	Completed	409	(84.7)	440	(90.5)
	Compliance (% in those expected to complete questionnaires)	409	(84.9)	440	(90.5)
	Not completed	73	(15.1)	46	(9.5)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	19	(3.9)	11	(2.3)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	3	(0.6)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	2	(0.4)
	Other	30	(6.2)	22	(4.5)
	With visit, no record	14	(2.9)	10	(2.1)
	Missing by Design	**1**	**(0.2)**	**0**	**(0.0)**
	Discontinued from the study	0	(0.0)	0	(0.0)
	Pro collection not scheduled	0	(0.0)	0	(0.0)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 12	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 24	**Expected to Complete Questionnaires**	**460**	**(95.2)**	**469**	**(96.5)**
	Completed	384	(79.5)	393	(80.9)
	Compliance (% in those expected to complete questionnaires)	384	(83.5)	393	(83.8)
	Not completed	76	(15.7)	76	(15.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	25	(5.2)	23	(4.7)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	8	(1.6)
	Other	27	(5.6)	24	(4.9)
	With visit, no record	16	(3.3)	20	(4.1)
	Missing by Design	**23**	**(4.8)**	**17**	**(3.5)**
	Discontinued from the study	1	(0.2)	4	(0.8)
	Pro collection not scheduled	13	(2.7)	2	(0.4)
	Translation not available in subjects language	1	(0.2)	1	(0.2)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 24	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	3	(0.6)	4	(0.8)
	Visit not scheduled	5	(1.0)	6	(1.2)
WEEK 36	**Expected to Complete Questionnaires**	**438**	**(90.7)**	**443**	**(91.2)**
	Completed	352	(72.9)	366	(75.3)
	Compliance (% in those expected to complete questionnaires)	352	(80.4)	366	(82.6)
	Not completed	86	(17.8)	77	(15.8)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	29	(6.0)	31	(6.4)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	8	(1.7)	5	(1.0)
	Other	23	(4.8)	23	(4.7)
	With visit, no record	25	(5.2)	17	(3.5)
	Missing by Design	**45**	**(9.3)**	**43**	**(8.8)**
	Discontinued from the study	5	(1.0)	8	(1.6)
	Pro collection not scheduled	8	(1.7)	7	(1.4)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 36	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	14	(2.9)	13	(2.7)
	Visit not scheduled	17	(3.5)	14	(2.9)
WEEK 48	**Expected to Complete Questionnaires**	**414**	**(85.7)**	**417**	**(85.8)**
	Completed	354	(73.3)	380	(78.2)
	Compliance (% in those expected to complete questionnaires)	354	(85.5)	380	(91.1)
	Not completed	60	(12.4)	37	(7.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	11	(2.3)	7	(1.4)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	4	(0.8)
	Other	24	(5.0)	16	(3.3)
	With visit, no record	17	(3.5)	10	(2.1)
	Missing by Design	**69**	**(14.3)**	**69**	**(14.2)**
	Discontinued from the study	7	(1.4)	11	(2.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

		Pembrolizumab N=483		Placebo N=486	
Treatment Visit	Category	n	(%)	n	(%)
WEEK 48	Pro collection not scheduled	21	(4.3)	17	(3.5)
	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	3	(0.6)
	Visit not reached	27	(5.6)	21	(4.3)
	Visit not scheduled	13	(2.7)	16	(3.3)
WEEK 60	**Expected to Complete Questionnaires**	**376**	**(77.8)**	**364**	**(74.9)**
	Completed	311	(64.4)	304	(62.6)
	Compliance (% in those expected to complete questionnaires)	311	(82.7)	304	(83.5)
	Not completed	65	(13.5)	60	(12.3)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	19	(3.9)	21	(4.3)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	2	(0.4)	3	(0.6)
	Other	37	(7.7)	33	(6.8)
	With visit, no record	5	(1.0)	3	(0.6)
	Missing by Design	**107**	**(22.2)**	**122**	**(25.1)**

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 60	Discontinued from the study	10	(2.1)	17	(3.5)
	Pro collection not scheduled	6	(1.2)	21	(4.3)
	Translation not available in subjects language	2	(0.4)	1	(0.2)
	Subject died	1	(0.2)	0	(0.0)
	Visit not reached	43	(8.9)	42	(8.6)
	Visit not scheduled	45	(9.3)	41	(8.4)
WEEK 72	**Expected to Complete Questionnaires**	**347**	**(71.8)**	**339**	**(69.8)**
	Completed	295	(61.1)	293	(60.3)
	Compliance (% in those expected to complete questionnaires)	295	(85.0)	293	(86.4)
	Not completed	52	(10.8)	46	(9.5)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.2)
	Not completed due to site staff error	11	(2.3)	20	(4.1)
	Subject in hospital or hospice	0	(0.0)	1	(0.2)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	7	(1.4)	5	(1.0)
	Other	31	(6.4)	18	(3.7)
	With visit, no record	2	(0.4)	1	(0.2)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 72	**Missing by Design**	**136**	**(28.2)**	**147**	**(30.2)**
	Discontinued from the study	14	(2.9)	21	(4.3)
	Pro collection not scheduled	15	(3.1)	14	(2.9)
	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	79	(16.4)	80	(16.5)
	Visit not scheduled	27	(5.6)	31	(6.4)
WEEK 84	**Expected to Complete Questionnaires**	**333**	**(68.9)**	**325**	**(66.9)**
	Completed	288	(59.6)	277	(57.0)
	Compliance (% in those expected to complete questionnaires)	288	(86.5)	277	(85.2)
	Not completed	45	(9.3)	48	(9.9)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	16	(3.3)	14	(2.9)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	1	(0.2)
	Subject lost to follow-up/unable to contact	1	(0.2)	1	(0.2)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	8	(1.7)	2	(0.4)
	Other	19	(3.9)	29	(6.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 84	With visit, no record	0	(0.0)	1	(0.2)
	Missing by Design	**150**	**(31.1)**	**161**	**(33.1)**
	Discontinued from the study	21	(4.3)	28	(5.8)
	Pro collection not scheduled	10	(2.1)	9	(1.9)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	82	(17.0)	97	(20.0)
	Visit not scheduled	36	(7.5)	27	(5.6)
WEEK 96	**Expected to Complete Questionnaires**	**359**	**(74.3)**	**341**	**(70.2)**
	Completed	313	(64.8)	302	(62.1)
	Compliance (% in those expected to complete questionnaires)	313	(87.2)	302	(88.6)
	Not completed	46	(9.5)	39	(8.0)
	Subject did not complete due to disease under study	1	(0.2)	0	(0.0)
	Not completed due to site staff error	14	(2.9)	13	(2.7)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	3	(0.6)	5	(1.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 96	Other	26	(5.4)	20	(4.1)
	With visit, no record	1	(0.2)	0	(0.0)
	Missing by Design	**124**	**(25.7)**	**145**	**(29.8)**
	Discontinued from the study	28	(5.8)	37	(7.6)
	Pro collection not scheduled	12	(2.5)	10	(2.1)
	Translation not available in subjects language	1	(0.2)	2	(0.4)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	62	(12.8)	81	(16.7)
	Visit not scheduled	21	(4.3)	15	(3.1)
MONTH 30	**Expected to Complete Questionnaires**	**304**	**(62.9)**	**287**	**(59.1)**
	Completed	256	(53.0)	258	(53.1)
	Compliance (% in those expected to complete questionnaires)	256	(84.2)	258	(89.9)
	Not completed	48	(9.9)	29	(6.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	23	(4.8)	8	(1.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	1	(0.2)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
MONTH 30	Subject refused for other reasons	5	(1.0)	2	(0.4)
	Other	19	(3.9)	18	(3.7)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**179**	**(37.1)**	**199**	**(40.9)**
	Discontinued from the study	43	(8.9)	45	(9.3)
	Pro collection not scheduled	19	(3.9)	25	(5.1)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	111	(23.0)	124	(25.5)
	Visit not scheduled	5	(1.0)	5	(1.0)
MONTH 36	**Expected to Complete Questionnaires**	**184**	**(38.1)**	**168**	**(34.6)**
	Completed	149	(30.8)	147	(30.2)
	Compliance (% in those expected to complete questionnaires)	149	(81.0)	147	(87.5)
	Not completed	35	(7.2)	21	(4.3)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	14	(2.9)	7	(1.4)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	1	(0.2)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
MONTH 36	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	3	(0.6)	0	(0.0)
	Other	17	(3.5)	14	(2.9)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**299**	**(61.9)**	**318**	**(65.4)**
	Discontinued from the study	54	(11.2)	55	(11.3)
	Pro collection not scheduled	1	(0.2)	7	(1.4)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	243	(50.3)	254	(52.3)
	Visit not scheduled	1	(0.2)	2	(0.4)

Expected to complete questionnaire includes all subjects who do not have missing data due to a missing by design reason.

Compliance is the proportion of subjects who completed the PRO questionnaire among those who are **expected to complete the questionnaire** at this time point, excluding those missing by design. All the other categories are defined as the proportion of subjects in the analysis population (N).

Missing by design includes: discontinuation, PRO collection not scheduled, translations not available, and no visit scheduled.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-28
Analysis of Change from Baseline in EORTC QLQ-C30 Global Health Status/QoL to Week 48
(PRO FAS Population)

Treatment	Baseline		Week 48		Change from Baseline to Week 48	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	449	81.94 (16.15)	354	77.73 (18.50)	480	-4.64 (-6.32, -2.96)
Placebo	459	80.97 (15.99)	380	80.83 (15.91)	485	-0.96 (-2.60, 0.68)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-3.68 (-5.88, -1.47)	0.0011

[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 48, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-29
Analysis of Change from Baseline in EORTC QLQ-C30 Global Health Status/QoL to Week 72
(PRO FAS Population)

Treatment	Baseline		Week 72		Change from Baseline to Week 72	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	449	81.94 (16.15)	295	78.73 (16.73)	480	-3.92 (-5.67, -2.18)
Placebo	459	80.97 (15.99)	292	79.74 (16.10)	485	-1.85 (-3.60, -0.10)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-2.07 (-4.40, 0.26)	0.0815

[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 72, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-30
Analysis of Change from Baseline in EORTC QLQ-C30 Physical Functioning to Week 48
(PRO FAS Population)

Treatment	Baseline		Week 48		Change from Baseline to Week 48	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	449	92.00 (12.47)	354	89.42 (15.33)	480	-3.36 (-4.70, -2.03)
Placebo	459	91.72 (13.78)	380	90.68 (15.25)	485	-1.87 (-3.17, -0.56)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-1.49 (-3.32, 0.33)	0.1087

[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 48, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-31
Analysis of Change from Baseline in EORTC QLQ-C30 Physical Functioning to Week 72
(PRO FAS Population)

Treatment	Baseline		Week 72		Change from Baseline to Week 72	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	449	92.00 (12.47)	295	90.12 (13.48)	480	-2.64 (-3.99, -1.29)
Placebo	459	91.72 (13.78)	292	90.91 (15.03)	485	-1.86 (-3.21, -0.50)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-0.79 (-2.65, 1.07)	0.4074

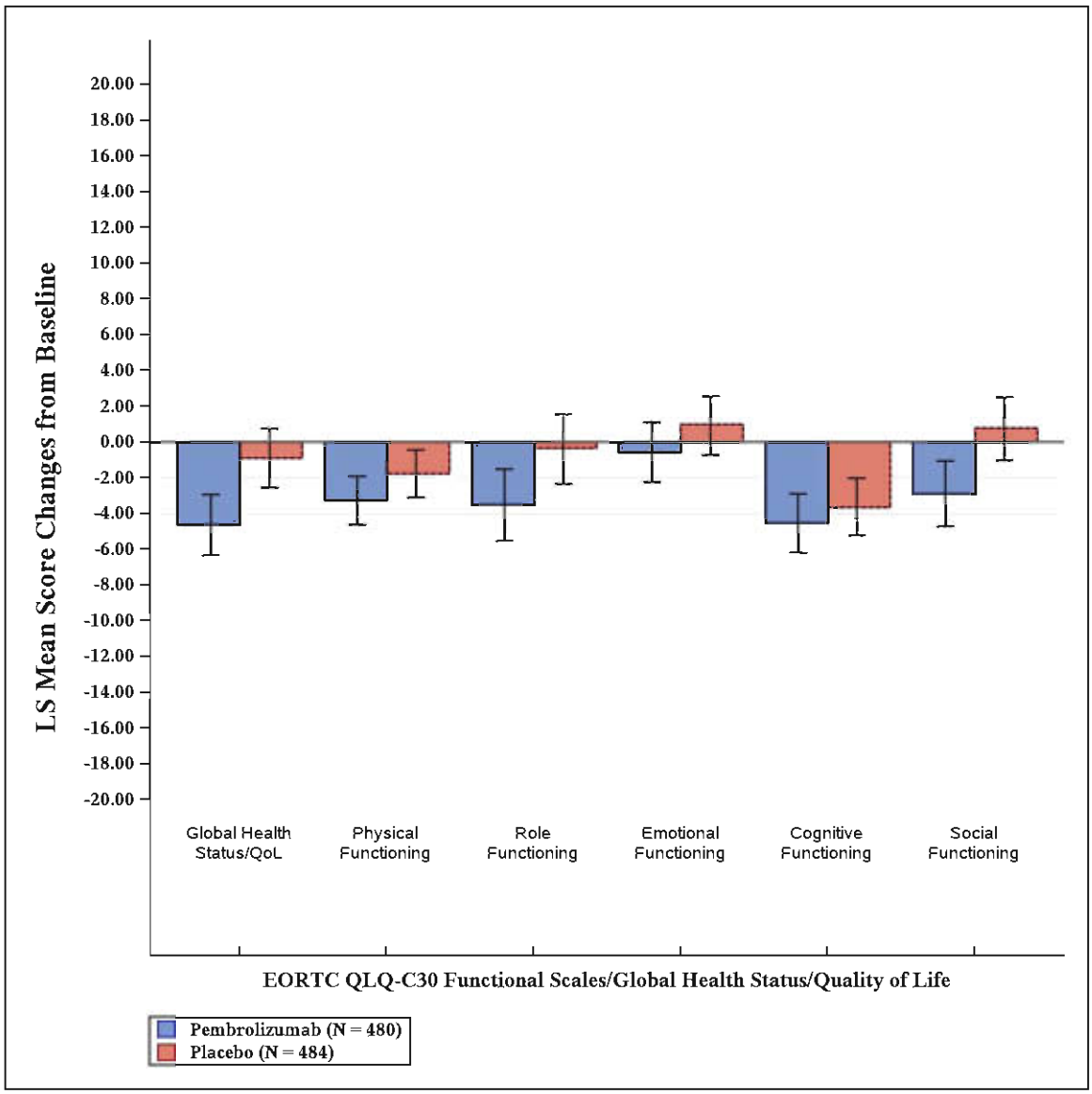
[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 72, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

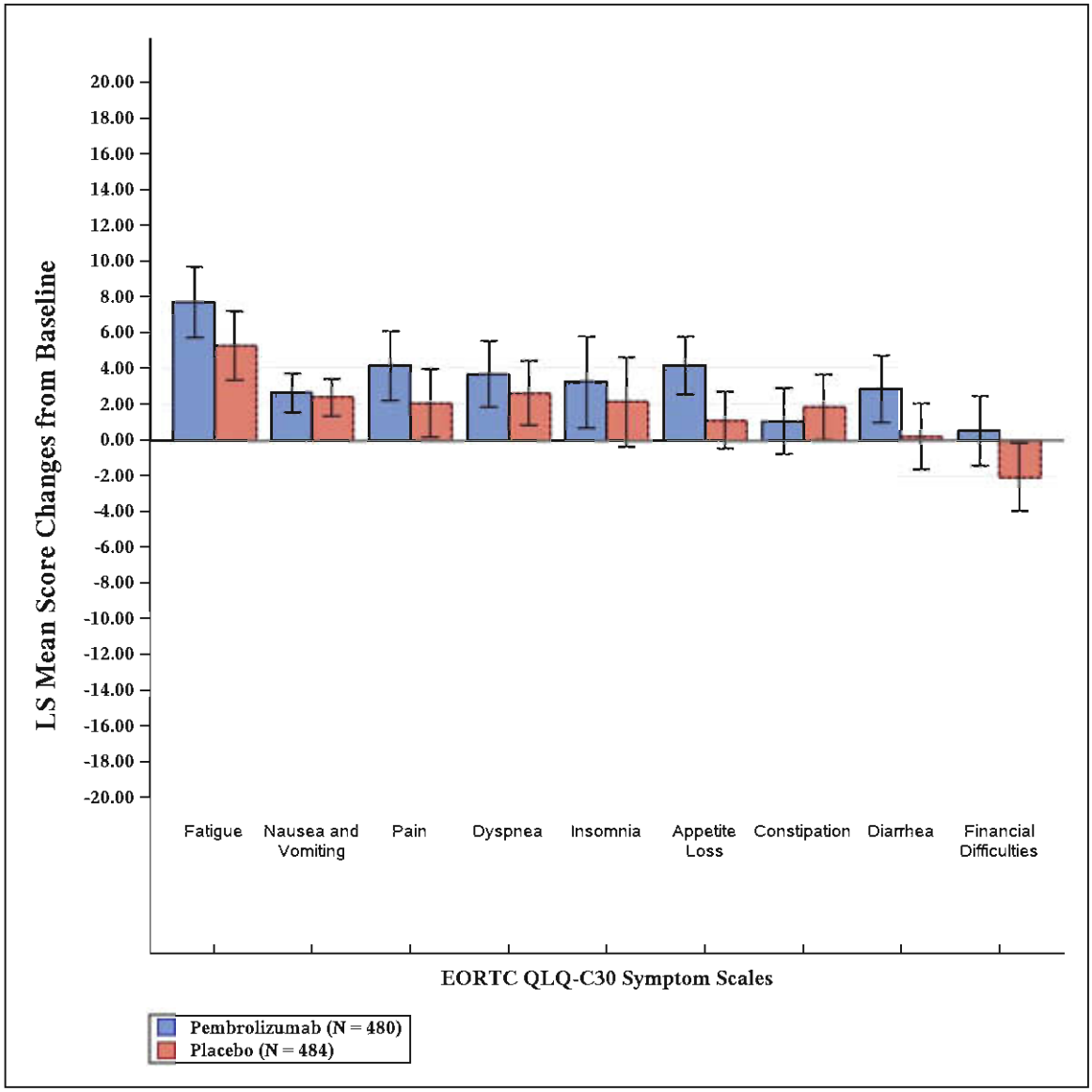
Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-22
LS Mean Change from Baseline to Week 48 and 95% CI in EORTC QLQ-C30 Functional Scales/Global Health Status/Quality of Life
(PRO FAS Population)



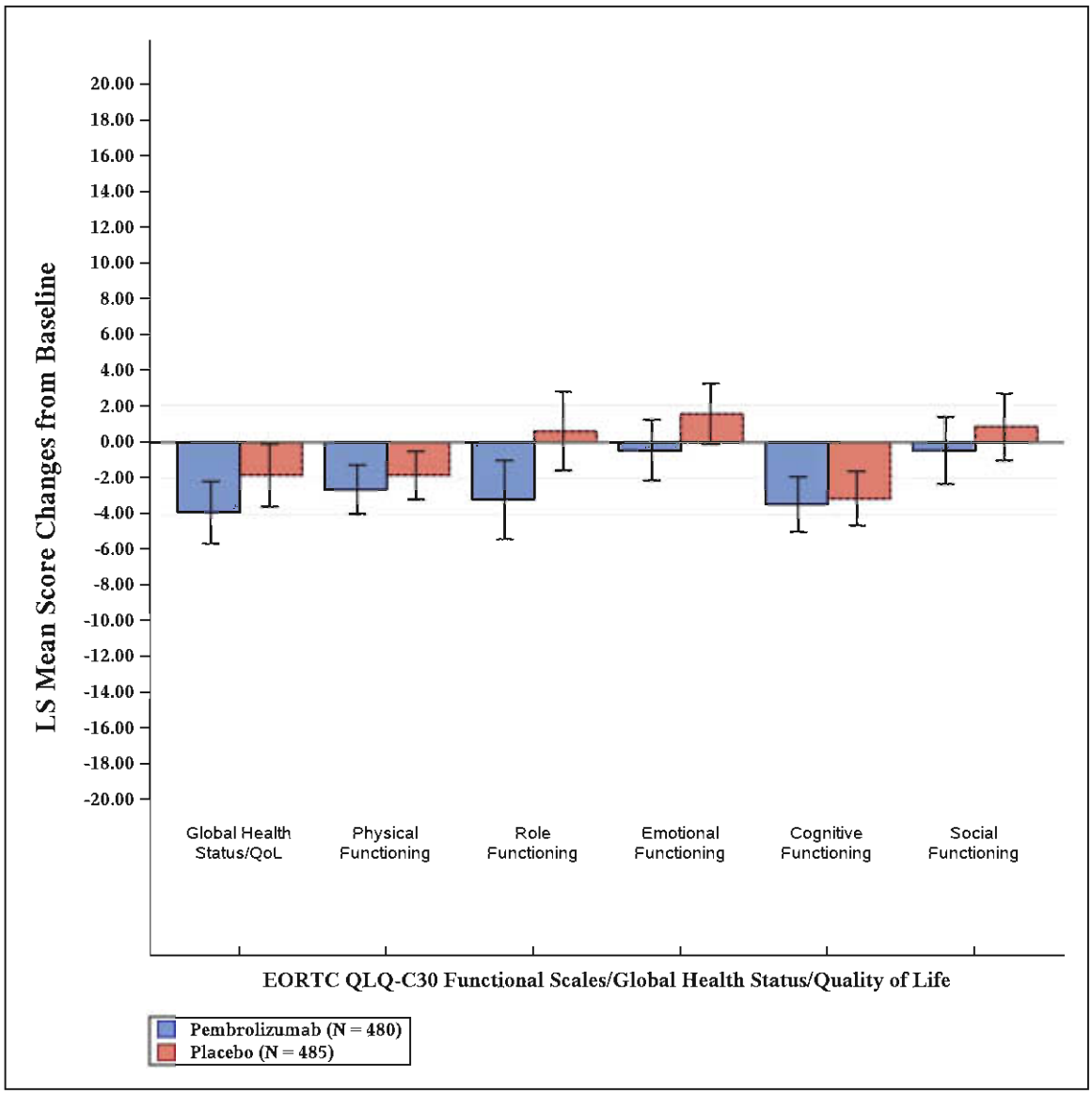
*For global health status/quality of life score and all functional scales, a higher score denotes better HRQOL or function. N is the number of subjects in the analysis population in each treatment group.
Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-23
LS Mean Change from Baseline to Week 48 and 95% CI in EORTC QLQ-C30 Symptom Scales
(PRO FAS Population)



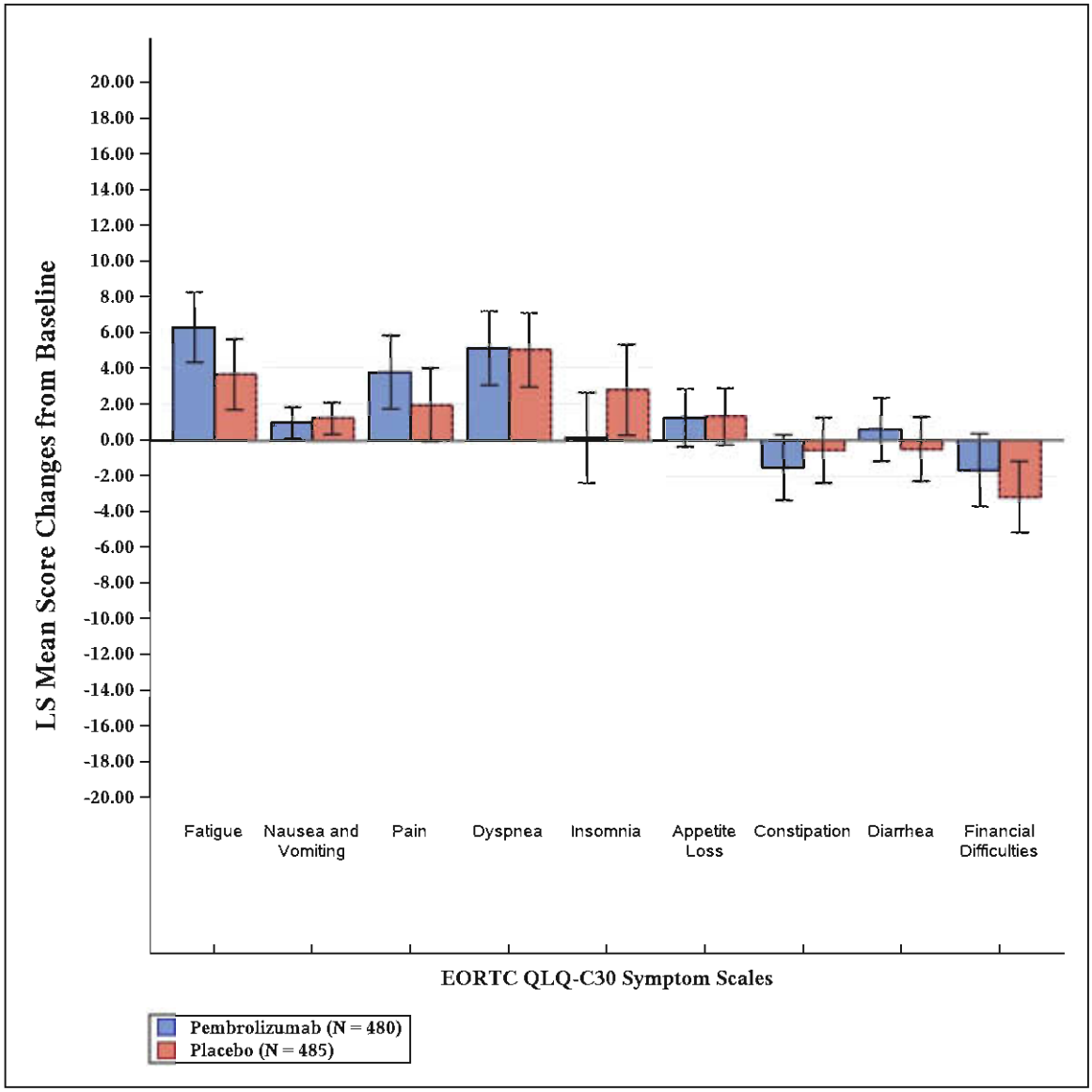
*For symptoms scales, a higher score denotes worse symptoms. N is the number of subjects in the analysis population.
Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-24
LS Mean Change from Baseline to Week 72 and 95% CI in EORTC QLQ-C30 Functional Scales/Global Health Status/Quality of Life
(PRO FAS Population)



*For global health status/quality of life score and all functional scales, a higher score denotes better HRQOL or function. N is the number of subjects in the analysis population in each treatment group.
Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-25
LS Mean Change from Baseline to Week 72 and 95% CI in EORTC QLQ-C30 Symptom Scales
(PRO FAS Population)

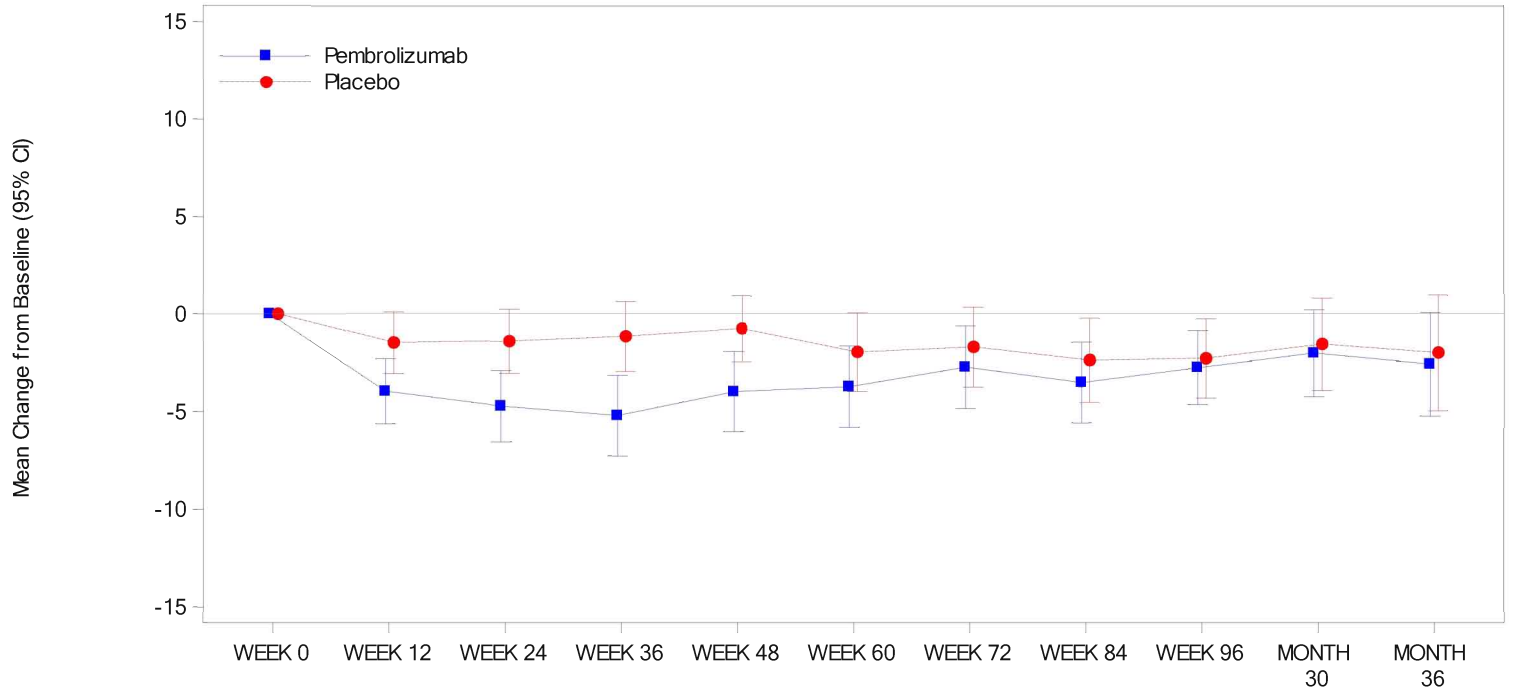


*For symptoms scales, a higher score denotes worse symptoms. N is the number of subjects in the analysis population.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-26
Empirical Mean Change from Baseline and 95% CI for the EORTC QLQ-C30 Global Health Status/QoL Over Time by Treatment Group

(PRO FAS Population)

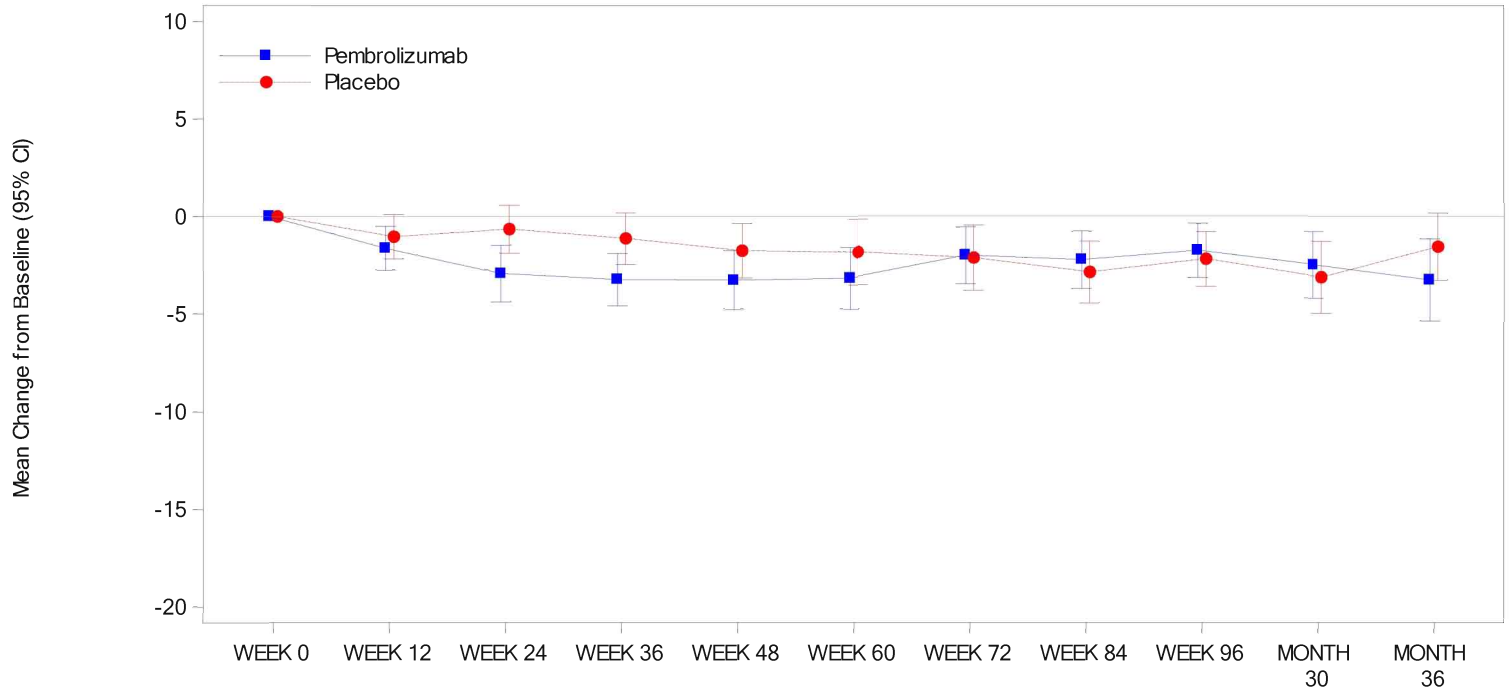


Number of Participants

Pembrolizumab	449	387	359	329	329	295	278	268	291	243	142
Placebo	459	418	372	351	360	289	274	260	285	241	138

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-27
Empirical Mean Change from Baseline and 95% CI for the EORTC QLQ-C30 Physical Functioning Over Time by Treatment Group (PRO FAS Population)



Number of Participants											
Pembrolizumab	449	387	359	329	329	295	278	268	291	243	142
Placebo	459	418	372	351	360	289	274	260	285	241	138

Database Cutoff Date: 04JAN2023
Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-32
Summary and Analysis of Overall Improvement/Stability Rate for EORTC QLQ-C30 Global Health Status/QoL
(PRO FAS Population)

	Pembrolizumab (N=483)			Placebo (N=486)			Total (N=969)		
Summary	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Improved	**85**	**17.6**	**(14.3, 21.3)**	**108**	**22.2**	**(18.6, 26.2)**	**193**	**19.9**	**(17.4, 22.6)**
Stable	259	53.6	(49.1, 58.1)	270	55.6	(51.0, 60.0)	529	54.6	(51.4, 57.8)
Improved + Stable	**344**	**71.2**	**(67.0, 75.2)**	**378**	**77.8**	**(73.8, 81.4)**	**722**	**74.5**	**(71.6, 77.2)**
Deteriorated	78	16.1	(13.0, 19.7)	59	12.1	(9.4, 15.4)	137	14.1	(12.0, 16.5)
Others	10	2.1	(1.0, 3.8)	13	2.7	(1.4, 4.5)	23	2.4	(1.5, 3.5)
No Assessment	51	10.6	(8.0, 13.6)	36	7.4	(5.2, 10.1)	87	9.0	(7.3, 11.0)

	Difference in % Improved	
Analysis	Estimate (95% CI)[b]	p-Value[b]
Pembrolizumab vs. Placebo	-4.6 (-9.7, 0.4)	0.9640[c]

	Difference in % Improved + Stable	
Analysis	Estimate (95% CI)[b]	p-Value[b]
Pembrolizumab vs. Placebo	-6.6 (-12.0, -1.1)	0.9905[c]

[a] Based on binomial exact confidence interval method.

[b] Based on Miettinen & Nurminen method with population-based weighting stratified by strata.

[c] One-sided p-value for testing. H0: difference in % = 0 versus H1: difference in % > 0.

Improved defined as a 10 point or more increase in score (in the positive direction) from baseline at any time during the study and confirmed by a 10 point or more improvement at a visit scheduled at least 6 weeks later.

Stability is defined as, when the criteria for improvement are not met, a less than 10 points worsening in score from baseline at any time during the study and confirmed by a less than 10 points worsening at a visit scheduled at least 6 weeks later.

Overall improvement/stability defined as the composite of improvement and stability.

Deterioration is defined as, when the criteria for improvement/stability are not met, a greater than 10 points worsening in score from baseline at any time during the study.

Others is defined as subjects who do not achieve improvement/stability with confirmation and do not have deterioration.

No assessment is defined as subjects do not have any record or do not have any post-baseline assessment for Global Health Status/QoL.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-33
Summary and Analysis of Overall Improvement/Stability Rate for EORTC QLQ-C30 Physical Functioning
(PRO FAS Population)

	Pembrolizumab (N=483)			Placebo (N=486)			Total (N=969)		
Summary	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Improved	**59**	**12.2**	**(9.4, 15.5)**	**47**	**9.7**	**(7.2, 12.7)**	**106**	**10.9**	**(9.0, 13.1)**
Stable	316	65.4	(61.0, 69.7)	358	73.7	(69.5, 77.5)	674	69.6	(66.6, 72.4)
Improved + Stable	**375**	**77.6**	**(73.7, 81.3)**	**405**	**83.3**	**(79.7, 86.5)**	**780**	**80.5**	**(77.9, 82.9)**
Deteriorated	45	9.3	(6.9, 12.3)	26	5.3	(3.5, 7.7)	71	7.3	(5.8, 9.2)
Others	12	2.5	(1.3, 4.3)	19	3.9	(2.4, 6.0)	31	3.2	(2.2, 4.5)
No Assessment	51	10.6	(8.0, 13.6)	36	7.4	(5.2, 10.1)	87	9.0	(7.3, 11.0)

	Difference in % Improved	
Analysis	Estimate (95% CI)[b]	p-Value[b]
Pembrolizumab vs. Placebo	2.5 (-1.4, 6.5)	0.1023[c]

	Difference in % Improved + Stable	
Analysis	Estimate (95% CI)[b]	p-Value[b]
Pembrolizumab vs. Placebo	-5.7 (-10.7, -0.7)	0.9874[c]

[a] Based on binomial exact confidence interval method.

[b] Based on Miettinen & Nurminen method with population-based weighting stratified by strata.

[c] One-sided p-value for testing. H0: difference in % = 0 versus H1: difference in % > 0.

Improved defined as a 10 point or more increase in score (in the positive direction) from baseline at any time during the study and confirmed by a 10 point or more improvement at a visit scheduled at least 6 weeks later.

Stability is defined as, when the criteria for improvement are not met, a less than 10 points worsening in score from baseline at any time during the study and confirmed by a less than 10 points worsening at a visit scheduled at least 6 weeks later.

Overall improvement/stability defined as the composite of improvement and stability.

Deterioration is defined as, when the criteria for improvement/stability are not met, a greater than 10 points worsening in score from baseline at any time during the study.

Others is defined as subjects who do not achieve improvement/stability with confirmation and do not have deterioration.

No assessment is defined as subjects do not have any record or do not have any post-baseline assessment for physical functioning.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

14.2.1.5.2 EQ-5D-5L

Table 14.2-34
Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**482**	**(99.8)**	**483**	**(99.4)**
	Completed	456	(94.4)	466	(95.9)
	Compliance (% in those expected to complete questionnaires)	456	(94.6)	466	(96.5)
	Not completed	26	(5.4)	17	(3.5)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	14	(2.9)	7	(1.4)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	11	(2.3)	5	(1.0)
	With visit, no record	1	(0.2)	5	(1.0)
	Missing by Design	**1**	**(0.2)**	**3**	**(0.6)**
	Discontinued from the study	0	(0.0)	0	(0.0)
	Pro collection not scheduled	0	(0.0)	0	(0.0)
	Translation not available in subjects language	1	(0.2)	3	(0.6)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
BASELINE	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 12	**Expected to Complete Questionnaires**	**482**	**(99.8)**	**486**	**(100.0)**
	Completed	420	(87.0)	442	(90.9)
	Compliance (% in those expected to complete questionnaires)	420	(87.1)	442	(90.9)
	Not completed	62	(12.8)	44	(9.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	18	(3.7)	10	(2.1)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	3	(0.6)	0	(0.0)
	Subject refused for other reasons	4	(0.8)	2	(0.4)
	Other	23	(4.8)	22	(4.5)
	With visit, no record	13	(2.7)	9	(1.9)
	Missing by Design	**1**	**(0.2)**	**0**	**(0.0)**
	Discontinued from the study	0	(0.0)	0	(0.0)
	Pro collection not scheduled	0	(0.0)	0	(0.0)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 12	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 24	**Expected to Complete Questionnaires**	**460**	**(95.2)**	**471**	**(96.9)**
	Completed	395	(81.8)	407	(83.7)
	Compliance (% in those expected to complete questionnaires)	395	(85.9)	407	(86.4)
	Not completed	65	(13.5)	64	(13.2)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	24	(5.0)	18	(3.7)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	7	(1.4)
	Other	18	(3.7)	19	(3.9)
	With visit, no record	15	(3.1)	19	(3.9)
	Missing by Design	**23**	**(4.8)**	**15**	**(3.1)**
	Discontinued from the study	1	(0.2)	4	(0.8)
	Pro collection not scheduled	13	(2.7)	2	(0.4)
	Translation not available in subjects language	1	(0.2)	1	(0.2)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 24	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	3	(0.6)	2	(0.4)
	Visit not scheduled	5	(1.0)	6	(1.2)
WEEK 36	**Expected to Complete Questionnaires**	**438**	**(90.7)**	**450**	**(92.6)**
	Completed	356	(73.7)	385	(79.2)
	Compliance (% in those expected to complete questionnaires)	356	(81.3)	385	(85.6)
	Not completed	82	(17.0)	65	(13.4)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	27	(5.6)	25	(5.1)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	8	(1.7)	4	(0.8)
	Other	22	(4.6)	19	(3.9)
	With visit, no record	24	(5.0)	16	(3.3)
	Missing by Design	**45**	**(9.3)**	**36**	**(7.4)**
	Discontinued from the study	5	(1.0)	8	(1.6)
	Pro collection not scheduled	8	(1.7)	7	(1.4)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 36	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	14	(2.9)	9	(1.9)
	Visit not scheduled	17	(3.5)	11	(2.3)
WEEK 48	**Expected to Complete Questionnaires**	**414**	**(85.7)**	**428**	**(88.1)**
	Completed	357	(73.9)	392	(80.7)
	Compliance (% in those expected to complete questionnaires)	357	(86.2)	392	(91.6)
	Not completed	57	(11.8)	36	(7.4)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	11	(2.3)	7	(1.4)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	3	(0.6)
	Other	22	(4.6)	17	(3.5)
	With visit, no record	16	(3.3)	9	(1.9)
	Missing by Design	**69**	**(14.3)**	**58**	**(11.9)**
	Discontinued from the study	7	(1.4)	11	(2.3)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 48	Pro collection not scheduled	21	(4.3)	16	(3.3)
	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	3	(0.6)
	Visit not reached	27	(5.6)	14	(2.9)
	Visit not scheduled	13	(2.7)	13	(2.7)
WEEK 60	**Expected to Complete Questionnaires**	**376**	**(77.8)**	**381**	**(78.4)**
	Completed	315	(65.2)	322	(66.3)
	Compliance (% in those expected to complete questionnaires)	315	(83.8)	322	(84.5)
	Not completed	61	(12.6)	59	(12.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	18	(3.7)	20	(4.1)
	Subject in hospital or hospice	1	(0.2)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	2	(0.4)	3	(0.6)
	Other	35	(7.2)	34	(7.0)
	With visit, no record	4	(0.8)	2	(0.4)
	Missing by Design	**107**	**(22.2)**	**105**	**(21.6)**

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 60	Discontinued from the study	10	(2.1)	17	(3.5)
	Pro collection not scheduled	6	(1.2)	20	(4.1)
	Translation not available in subjects language	2	(0.4)	1	(0.2)
	Subject died	1	(0.2)	0	(0.0)
	Visit not reached	43	(8.9)	31	(6.4)
	Visit not scheduled	45	(9.3)	36	(7.4)
WEEK 72	**Expected to Complete Questionnaires**	**347**	**(71.8)**	**358**	**(73.7)**
	Completed	299	(61.9)	309	(63.6)
	Compliance (% in those expected to complete questionnaires)	299	(86.2)	309	(86.3)
	Not completed	48	(9.9)	49	(10.1)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.2)
	Not completed due to site staff error	10	(2.1)	22	(4.5)
	Subject in hospital or hospice	0	(0.0)	1	(0.2)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	6	(1.2)	6	(1.2)
	Other	30	(6.2)	18	(3.7)
	With visit, no record	1	(0.2)	1	(0.2)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 72	**Missing by Design**	**136**	**(28.2)**	**128**	**(26.3)**
	Discontinued from the study	14	(2.9)	20	(4.1)
	Pro collection not scheduled	15	(3.1)	13	(2.7)
	Translation not available in subjects language	1	(0.2)	1	(0.2)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	79	(16.4)	66	(13.6)
	Visit not scheduled	27	(5.6)	28	(5.8)
WEEK 84	**Expected to Complete Questionnaires**	**335**	**(69.4)**	**342**	**(70.4)**
	Completed	291	(60.2)	294	(60.5)
	Compliance (% in those expected to complete questionnaires)	291	(86.9)	294	(86.0)
	Not completed	44	(9.1)	48	(9.9)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	16	(3.3)	14	(2.9)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	1	(0.2)
	Subject lost to follow-up/unable to contact	1	(0.2)	1	(0.2)
	Subject did not complete due to side effects of treatment	1	(0.2)	0	(0.0)
	Subject refused for other reasons	8	(1.7)	2	(0.4)
	Other	18	(3.7)	29	(6.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 84	With visit, no record	0	(0.0)	1	(0.2)
	Missing by Design	**148**	**(30.6)**	**144**	**(29.6)**
	Discontinued from the study	21	(4.3)	28	(5.8)
	Pro collection not scheduled	10	(2.1)	9	(1.9)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	80	(16.6)	83	(17.1)
	Visit not scheduled	36	(7.5)	24	(4.9)
WEEK 96	**Expected to Complete Questionnaires**	**362**	**(74.9)**	**362**	**(74.5)**
	Completed	317	(65.6)	321	(66.0)
	Compliance (% in those expected to complete questionnaires)	317	(87.6)	321	(88.7)
	Not completed	45	(9.3)	41	(8.4)
	Subject did not complete due to disease under study	1	(0.2)	0	(0.0)
	Not completed due to site staff error	14	(2.9)	14	(2.9)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.2)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	3	(0.6)	5	(1.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
WEEK 96	Other	25	(5.2)	21	(4.3)
	With visit, no record	1	(0.2)	0	(0.0)
	Missing by Design	**121**	**(25.1)**	**124**	**(25.5)**
	Discontinued from the study	28	(5.8)	37	(7.6)
	Pro collection not scheduled	12	(2.5)	10	(2.1)
	Translation not available in subjects language	1	(0.2)	2	(0.4)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	60	(12.4)	63	(13.0)
	Visit not scheduled	20	(4.1)	12	(2.5)
MONTH 30	**Expected to Complete Questionnaires**	**308**	**(63.8)**	**310**	**(63.8)**
	Completed	261	(54.0)	280	(57.6)
	Compliance (% in those expected to complete questionnaires)	261	(84.7)	280	(90.3)
	Not completed	47	(9.7)	30	(6.2)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	24	(5.0)	8	(1.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.2)	1	(0.2)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
MONTH 30	Subject refused for other reasons	5	(1.0)	2	(0.4)
	Other	17	(3.5)	19	(3.9)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**175**	**(36.2)**	**176**	**(36.2)**
	Discontinued from the study	43	(8.9)	45	(9.3)
	Pro collection not scheduled	19	(3.9)	24	(4.9)
	Translation not available in subjects language	1	(0.2)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	107	(22.2)	104	(21.4)
	Visit not scheduled	5	(1.0)	3	(0.6)
MONTH 36	**Expected to Complete Questionnaires**	**187**	**(38.7)**	**182**	**(37.4)**
	Completed	153	(31.7)	159	(32.7)
	Compliance (% in those expected to complete questionnaires)	153	(81.8)	159	(87.4)
	Not completed	34	(7.0)	23	(4.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	14	(2.9)	8	(1.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	1	(0.2)	0	(0.0)

Completion and Compliance Percentages for EQ-5D-5L by Visit and by Treatment
(PRO FAS Population)

Treatment Visit	Category	Pembrolizumab N=483		Placebo N=486	
		n	(%)	n	(%)
MONTH 36	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	3	(0.6)	0	(0.0)
	Other	16	(3.3)	15	(3.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**296**	**(61.3)**	**304**	**(62.6)**
	Discontinued from the study	54	(11.2)	54	(11.1)
	Pro collection not scheduled	1	(0.2)	7	(1.4)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	240	(49.7)	241	(49.6)
	Visit not scheduled	1	(0.2)	2	(0.4)

Expected to complete questionnaire includes all subjects who do not have missing data due to a missing by design reason.

Compliance is the proportion of subjects who completed the PRO questionnaire among those who are **expected to complete the questionnaire** at this time point, excluding those missing by design. All the other categories are defined as the proportion of subjects in the analysis population (N).

Missing by design includes: discontinuation, PRO collection not scheduled, translations not available, and no visit scheduled.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-35
Analysis of Change from Baseline in EQ-5D-5L VAS to Week 48
(PRO FAS Population)

Treatment	Baseline		Week 48		Change from Baseline to Week 48	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	456	84.28 (12.88)	357	82.69 (14.86)	483	-2.37 (-3.69, -1.06)
Placebo	466	84.86 (12.76)	382	84.96 (13.31)	486	-0.31 (-1.59, 0.97)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-2.07 (-3.82, -0.31)	0.0209

[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 48, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Table 14.2-36
Analysis of Change from Baseline in EQ-5D-5L VAS to Week 72
(PRO FAS Population)

Treatment	Baseline		Week 72		Change from Baseline to Week 72	
	N	Mean (SD)	N	Mean (SD)	N	LS Mean (95% CI)[a]
Pembrolizumab	456	84.28 (12.88)	299	83.30 (13.45)	483	-2.38 (-3.66, -1.09)
Placebo	466	84.86 (12.76)	293	85.39 (12.59)	486	0.17 (-1.13, 1.46)

Pairwise Comparison	Difference in LS Means[a] (95% CI)	p-Value[a]
Pembrolizumab vs. Placebo	-2.54 (-4.28, -0.81)	0.0042

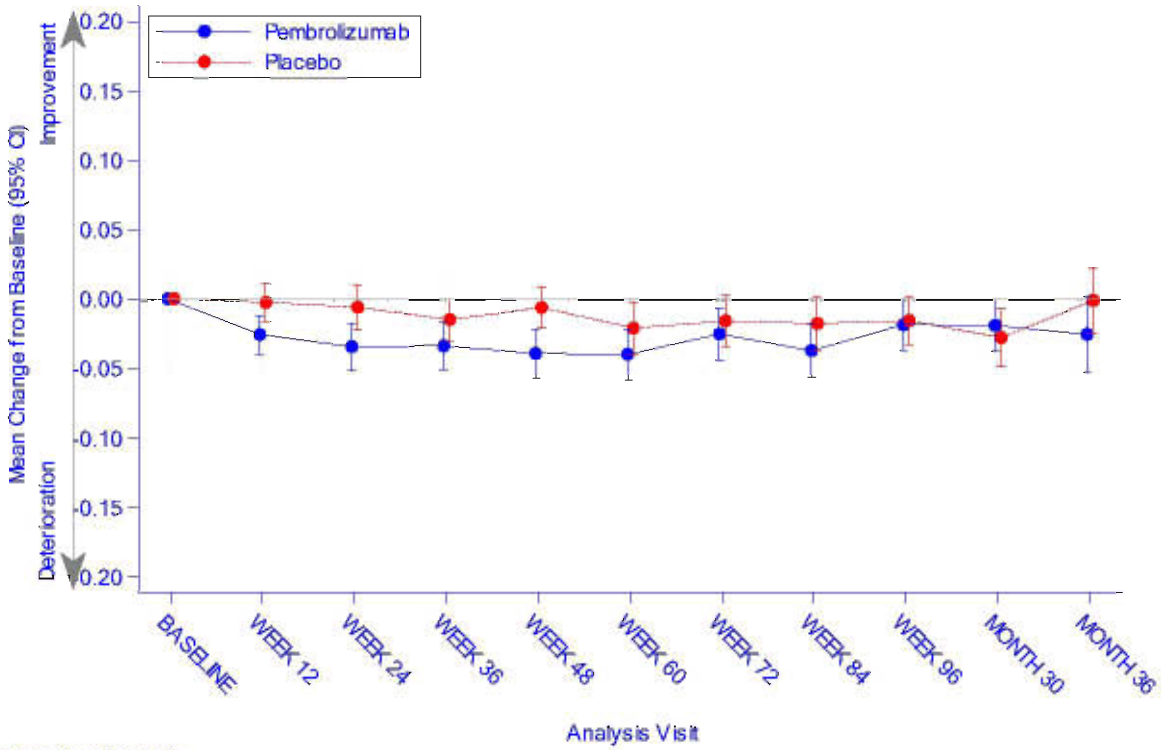
[a] Based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factor melanoma T stage (IIB T3b greater than 2.0-4.0 mm with ulceration vs. IIB T4a greater than 4.0 mm without ulceration vs. IIC T4b greater than 4.0 mm with ulceration) as covariate.

For baseline and Week 72, N is the number of subjects in each treatment group with non-missing assessments at the specific time point; for change from baseline, N is the number of subjects in the analysis population in each treatment group.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adpro]

Figure 14.2-28
Empirical Mean Change from Baseline and 95% CI for the EQ-5D-5L Index Score using the crosswalk method - United Kingdom - Over Time by Treatment Group
(PRO FAS Population)



Number of participants

Pembrolizumab	456	400	372	335	335	301	284	273	296	247	147
Placebo	466	423	384	363	365	294	278	264	290	245	141

Database Cutoff Date: 04JAN2023

14.3 Safety Data

14.3.1 Adverse Events

14.3.1.1 Pediatric Adverse Events

Table 14.3-1
Adverse Event Summary
(APaT Population - Pediatric Patients)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	1		1	
with one or more adverse events	1	(100.0)	0	(0.0)
with no adverse event	0	(0.0)	1	(100.0)
with drug-related[a] adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-2
Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Pediatric Patients)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	1		1	
with one or more adverse events	1	(100.0)	0	(0.0)
with no adverse events	0	(0.0)	1	(100.0)
[redacted]				

Redacted under section 40 of the FOI Act

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-3
Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Pediatric Patients)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	1		1	
with one or more adverse events	0	(0.0)	0	(0.0)
with no adverse events	1	(100.0)	1	(100.0)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-4
Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population - Pediatric Patients)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	1		1		1		1		1		1	
with one or more adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with no adverse events	1	(100.0)	1	(100.0)	1	(100.0)	1	(100.0)	1	(100.0)	1	(100.0)

Every participant is counted a single time for each applicable row and column.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.2 All Adverse Events

Table 14.3-5
Adverse Event Summary
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse event	22	(4.6)	40	(8.2)
with drug-related[a] adverse events	399	(82.6)	309	(63.6)
with toxicity grade 3-5 adverse events	137	(28.4)	98	(20.2)
with toxicity grade 3-5 drug-related adverse events	83	(17.2)	25	(5.1)
with serious adverse events	103	(21.3)	96	(19.8)
with serious drug-related adverse events	49	(10.1)	11	(2.3)
who died	1	(0.2)	5	(1.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	83	(17.2)	23	(4.7)
discontinued drug due to a drug-related adverse event	77	(15.9)	12	(2.5)
discontinued drug due to a serious adverse event	38	(7.9)	13	(2.7)
discontinued drug due to a serious drug-related adverse event	33	(6.8)	4	(0.8)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-6
Adverse Event Summary
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	6	(75.0)	54	(85.7)
with no adverse event	2	(25.0)	9	(14.3)
with drug-related[a] adverse events	4	(50.0)	36	(57.1)
with toxicity grade 3-5 adverse events	1	(12.5)	15	(23.8)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	6	(9.5)
with serious adverse events	1	(12.5)	10	(15.9)
with serious drug-related adverse events	0	(0.0)	3	(4.8)
who died	0	(0.0)	1	(1.6)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	10	(15.9)
discontinued drug due to a drug-related adverse event	0	(0.0)	8	(12.7)
discontinued drug due to a serious adverse event	0	(0.0)	5	(7.9)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	3	(4.8)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-7
Exposure-Adjusted Adverse Event Summary
(Including Multiple Occurrences of Events)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]			
	Pembrolizumab		Placebo	
Number of participants exposed	483		486	
Total exposure[b] in person-months	4945.05		5420.53	
Total events (rate)				
adverse events	4,192	(84.77)	3,200	(59.03)
drug-related[c] adverse events	1,900	(38.42)	1,090	(20.11)
toxicity grade 3-5 adverse events	199	(4.02)	139	(2.56)
toxicity grade 3-5 drug-related adverse events	114	(2.31)	30	(0.55)
serious adverse events	154	(3.11)	154	(2.84)
serious drug-related adverse events	59	(1.19)	11	(0.20)
adverse events leading to death	1	(0.02)	5	(0.09)
drug-related adverse events leading to death	0	(0.00)	0	(0.00)
adverse events resulting in drug discontinuation	90	(1.82)	28	(0.52)
drug-related adverse events resulting in drug discontinuation	84	(1.70)	16	(0.30)
serious adverse events resulting in drug discontinuation	38	(0.77)	13	(0.24)
serious drug-related adverse events resulting in drug discontinuation	33	(0.67)	4	(0.07)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

[c] Determined by the investigator to be related to the drug.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-8
Adverse Event Summary for Elderly Participants by Age
(APaT Population)

	Age (Years)							
	Pembrolizumab							
	< 65		65 - 74		75 - 84		85+	
	n	(%)	n	(%)	n	(%)	n	(%)
Participants in Population	299		132		52		0	
with one or more adverse events	285	(95.3)	124	(93.9)	52	(100.0)	0	(NA)
who died	0	(0.0)	0	(0.0)	1	(1.9)	0	(NA)
with serious adverse events	54	(18.1)	27	(20.5)	22	(42.3)	0	(NA)
discontinued due to an adverse event	46	(15.4)	25	(18.9)	12	(23.1)	0	(NA)
CNS (confusion/extrapyramidal)	17	(5.7)	2	(1.5)	1	(1.9)	0	(NA)
AE related to falling	23	(7.7)	9	(6.8)	5	(9.6)	0	(NA)
CV events	60	(20.1)	28	(21.2)	11	(21.2)	0	(NA)
Cerebrovascular events	0	(0.0)	1	(0.8)	1	(1.9)	0	(NA)
Infections	112	(37.5)	41	(31.1)	21	(40.4)	0	(NA)

Adverse Event Summary for Elderly Participants by Age
(APaT Population)

	Age (Years)							
	Placebo							
	< 65		65 - 74		75 - 84		85+	
	n	(%)	n	(%)	n	(%)	n	(%)
Participants in Population	295		134		55		2	
with one or more adverse events	273	(92.5)	123	(91.8)	48	(87.3)	2	(100.0)
who died	3	(1.0)	1	(0.7)	0	(0.0)	1	(50.0)
with serious adverse events	54	(18.3)	22	(16.4)	19	(34.5)	1	(50.0)
discontinued due to an adverse event	12	(4.1)	6	(4.5)	4	(7.3)	1	(50.0)
CNS (confusion/extrapyramidal)	10	(3.4)	5	(3.7)	5	(9.1)	0	(0.0)
AE related to falling	25	(8.5)	15	(11.2)	8	(14.5)	0	(0.0)
CV events	53	(18.0)	28	(20.9)	12	(21.8)	0	(0.0)
Cerebrovascular events	0	(0.0)	0	(0.0)	2	(3.6)	0	(0.0)
Infections	110	(37.3)	46	(34.3)	13	(23.6)	1	(50.0)

AEs were followed 30 days after last dose of study treatment; SAEs were followed 90 days after last dose of study treatment.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-9
Adverse Event Summary by Age (<65, ≥65)
(APaT Population)

	<65				≥65			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	299		295		184		191	
with one or more adverse events	285	(95.3)	273	(92.5)	176	(95.7)	173	(90.6)
with no adverse event	14	(4.7)	22	(7.5)	8	(4.3)	18	(9.4)
with drug-related[a] adverse events	252	(84.3)	197	(66.8)	147	(79.9)	112	(58.6)
with toxicity grade 3-5 adverse events	69	(23.1)	63	(21.4)	68	(37.0)	35	(18.3)
with toxicity grade 3-5 drug-related adverse events	41	(13.7)	16	(5.4)	42	(22.8)	9	(4.7)
with serious adverse events	54	(18.1)	54	(18.3)	49	(26.6)	42	(22.0)
with serious drug-related adverse events	26	(8.7)	7	(2.4)	23	(12.5)	4	(2.1)
who died	0	(0.0)	3	(1.0)	1	(0.5)	2	(1.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	46	(15.4)	12	(4.1)	37	(20.1)	11	(5.8)
discontinued drug due to a drug-related adverse event	41	(13.7)	6	(2.0)	36	(19.6)	6	(3.1)
discontinued drug due to a serious adverse event	22	(7.4)	7	(2.4)	16	(8.7)	6	(3.1)
discontinued drug due to a serious drug-related adverse event	17	(5.7)	3	(1.0)	16	(8.7)	1	(0.5)

[a] Determined by the investigator to be related to the drug.
Adverse events occurred after the first dose of second course are excluded.
Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-10
Adverse Event Summary by Age (<65 yrs; 65 to 74 yrs; 75 to 84 yrs; ≥85 yrs)
(APaT Population)

	< 65				65 - 74				75 - 84				85+			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	299		295		132		134		52		55		0		2	
with one or more adverse events	285	(95.3)	273	(92.5)	124	(93.9)	123	(91.8)	52	(100.0)	48	(87.3)	0	(0.0)	2	(100.0)
with no adverse event	14	(4.7)	22	(7.5)	8	(6.1)	11	(8.2)	0	(0.0)	7	(12.7)	0	(0.0)	0	(0.0)
with drug-related[a] adverse events	252	(84.3)	197	(66.8)	104	(78.8)	80	(59.7)	43	(82.7)	30	(54.5)	0	(0.0)	2	(100.0)
with toxicity grade 3-5 adverse events	69	(23.1)	63	(21.4)	46	(34.8)	24	(17.9)	22	(42.3)	10	(18.2)	0	(0.0)	1	(50.0)
with toxicity grade 3-5 drug-related adverse events	41	(13.7)	16	(5.4)	28	(21.2)	7	(5.2)	14	(26.9)	2	(3.6)	0	(0.0)	0	(0.0)
with serious adverse events	54	(18.1)	54	(18.3)	27	(20.5)	22	(16.4)	22	(42.3)	19	(34.5)	0	(0.0)	1	(50.0)
with serious drug-related adverse events	26	(8.7)	7	(2.4)	16	(12.1)	1	(0.7)	7	(13.5)	3	(5.5)	0	(0.0)	0	(0.0)
who died	0	(0.0)	3	(1.0)	0	(0.0)	1	(0.7)	1	(1.9)	0	(0.0)	0	(0.0)	1	(50.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	46	(15.4)	12	(4.1)	25	(18.9)	6	(4.5)	12	(23.1)	4	(7.3)	0	(0.0)	1	(50.0)
discontinued drug due to a drug-related adverse event	41	(13.7)	6	(2.0)	24	(18.2)	4	(3.0)	12	(23.1)	2	(3.6)	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	22	(7.4)	7	(2.4)	10	(7.6)	3	(2.2)	6	(11.5)	2	(3.6)	0	(0.0)	1	(50.0)

Adverse Event Summary by Age (<65 yrs; 65 to 74 yrs; 75 to 84 yrs; ≥85 yrs)
(APaT Population)

	< 65				65 - 74				75 - 84				85+			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued drug due to a serious drug-related adverse event	17	(5.7)	3	(1.0)	10	(7.6)	1	(0.7)	6	(11.5)	0	(0.0)	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.

MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-11
Adverse Event Summary by Sex (Male, Female)
(APaT Population)

	Male				Female			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	297		287		186		199	
with one or more adverse events	278	(93.6)	260	(90.6)	183	(98.4)	186	(93.5)
with no adverse event	19	(6.4)	27	(9.4)	3	(1.6)	13	(6.5)
with drug-related[a] adverse events	235	(79.1)	170	(59.2)	164	(88.2)	139	(69.8)
with toxicity grade 3-5 adverse events	94	(31.6)	65	(22.6)	43	(23.1)	33	(16.6)
with toxicity grade 3-5 drug-related adverse events	59	(19.9)	21	(7.3)	24	(12.9)	4	(2.0)
with serious adverse events	70	(23.6)	59	(20.6)	33	(17.7)	37	(18.6)
with serious drug-related adverse events	32	(10.8)	8	(2.8)	17	(9.1)	3	(1.5)
who died	1	(0.3)	4	(1.4)	0	(0.0)	1	(0.5)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	56	(18.9)	16	(5.6)	27	(14.5)	7	(3.5)
discontinued drug due to a drug-related adverse event	52	(17.5)	8	(2.8)	25	(13.4)	4	(2.0)
discontinued drug due to a serious adverse event	25	(8.4)	11	(3.8)	13	(7.0)	2	(1.0)
discontinued drug due to a serious drug-related adverse event	21	(7.1)	3	(1.0)	12	(6.5)	1	(0.5)

[a] Determined by the investigator to be related to the drug.
Adverse events occurred after the first dose of second course are excluded.
Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-12
Adverse Event Summary by Race (White, All Others)
(APaT Population)

	White				All Others				Null			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	432		438		9		4		42		44	
with one or more adverse events	410	(94.9)	398	(90.9)	9	(100.0)	4	(100.0)	42	(100.0)	44	(100.0)
with no adverse event	22	(5.1)	40	(9.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with drug-related[a] adverse events	352	(81.5)	274	(62.6)	7	(77.8)	3	(75.0)	40	(95.2)	32	(72.7)
with toxicity grade 3-5 adverse events	123	(28.5)	86	(19.6)	3	(33.3)	3	(75.0)	11	(26.2)	9	(20.5)
with toxicity grade 3-5 drug-related adverse events	73	(16.9)	20	(4.6)	1	(11.1)	1	(25.0)	9	(21.4)	4	(9.1)
with serious adverse events	92	(21.3)	90	(20.5)	3	(33.3)	1	(25.0)	8	(19.0)	5	(11.4)
with serious drug-related adverse events	41	(9.5)	8	(1.8)	1	(11.1)	1	(25.0)	7	(16.7)	2	(4.5)
who died	1	(0.2)	5	(1.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	70	(16.2)	19	(4.3)	2	(22.2)	1	(25.0)	11	(26.2)	3	(6.8)
discontinued drug due to a drug-related adverse event	65	(15.0)	9	(2.1)	1	(11.1)	1	(25.0)	11	(26.2)	2	(4.5)
discontinued drug due to a serious adverse event	30	(6.9)	11	(2.5)	2	(22.2)	1	(25.0)	6	(14.3)	1	(2.3)

Adverse Event Summary by Race (White, All Others)
(APaT Population)

	White				All Others				Null			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued drug due to a serious drug-related adverse event	26	(6.0)	2	(0.5)	1	(11.1)	1	(25.0)	6	(14.3)	1	(2.3)

[a] Determined by the investigator to be related to the drug.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.

MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-13
Adverse Event Summary by ECOG PS (0, 1, 2)
(APaT Population)

	0				1				2			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	450		449		32		35		0		1	
with one or more adverse events	430	(95.6)	415	(92.4)	30	(93.8)	30	(85.7)	0	(0.0)	1	(100.0)
with no adverse event	20	(4.4)	34	(7.6)	2	(6.3)	5	(14.3)	0	(0.0)	0	(0.0)
with drug-related[a] adverse events	374	(83.1)	288	(64.1)	25	(78.1)	21	(60.0)	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	129	(28.7)	90	(20.0)	8	(25.0)	8	(22.9)	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	78	(17.3)	22	(4.9)	5	(15.6)	3	(8.6)	0	(0.0)	0	(0.0)
with serious adverse events	94	(20.9)	88	(19.6)	9	(28.1)	7	(20.0)	0	(0.0)	1	(100.0)
with serious drug-related adverse events	46	(10.2)	9	(2.0)	3	(9.4)	2	(5.7)	0	(0.0)	0	(0.0)
who died	1	(0.2)	3	(0.7)	0	(0.0)	2	(5.7)	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	80	(17.8)	19	(4.2)	3	(9.4)	4	(11.4)	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	75	(16.7)	10	(2.2)	2	(6.3)	2	(5.7)	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	36	(8.0)	9	(2.0)	2	(6.3)	4	(11.4)	0	(0.0)	0	(0.0)

Adverse Event Summary by ECOG PS (0, 1, 2)
(APaT Population)

	0				1				2			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued drug due to a serious drug-related adverse event	32	(7.1)	2	(0.4)	1	(3.1)	2	(5.7)	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.

MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-14
Adverse Event Summary by Region (NA, EU, ROW)
(APaT Population)

	North America				European Union				Rest of the World			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	120		106		250		302		113		78	
with one or more adverse events	117	(97.5)	102	(96.2)	241	(96.4)	268	(88.7)	103	(91.2)	76	(97.4)
with no adverse event	3	(2.5)	4	(3.8)	9	(3.6)	34	(11.3)	10	(8.8)	2	(2.6)
with drug-related[a] adverse events	99	(82.5)	74	(69.8)	210	(84.0)	176	(58.3)	90	(79.6)	59	(75.6)
with toxicity grade 3-5 adverse events	42	(35.0)	25	(23.6)	62	(24.8)	51	(16.9)	33	(29.2)	22	(28.2)
with toxicity grade 3-5 drug-related adverse events	22	(18.3)	3	(2.8)	39	(15.6)	17	(5.6)	22	(19.5)	5	(6.4)
with serious adverse events	25	(20.8)	26	(24.5)	51	(20.4)	49	(16.2)	27	(23.9)	21	(26.9)
with serious drug-related adverse events	9	(7.5)	0	(0.0)	30	(12.0)	10	(3.3)	10	(8.8)	1	(1.3)
who died	0	(0.0)	0	(0.0)	0	(0.0)	3	(1.0)	1	(0.9)	2	(2.6)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	21	(17.5)	1	(0.9)	48	(19.2)	16	(5.3)	14	(12.4)	6	(7.7)
discontinued drug due to a drug-related adverse event	19	(15.8)	0	(0.0)	45	(18.0)	10	(3.3)	13	(11.5)	2	(2.6)
discontinued drug due to a serious adverse event	7	(5.8)	1	(0.9)	25	(10.0)	8	(2.6)	6	(5.3)	4	(5.1)

Adverse Event Summary by Region (NA, EU, ROW)
(APaT Population)

	North America				European Union				Rest of the World			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued drug due to a serious drug-related adverse event	5	(4.2)	0	(0.0)	22	(8.8)	3	(1.0)	6	(5.3)	1	(1.3)

[a] Determined by the investigator to be related to the drug.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.

MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.2.1 Most Frequently Reported Adverse Events

Table 14.3-15
Participants With Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse events	22	(4.6)	40	(8.2)
Fatigue	143	(29.6)	127	(26.1)
Diarrhoea	136	(28.2)	100	(20.6)
Pruritus	134	(27.7)	66	(13.6)
Arthralgia	114	(23.6)	85	(17.5)
Rash	91	(18.8)	42	(8.6)
Headache	83	(17.2)	55	(11.3)
Hypothyroidism	82	(17.0)	17	(3.5)
Nausea	67	(13.9)	56	(11.5)
Cough	61	(12.6)	58	(11.9)
Alanine aminotransferase increased	57	(11.8)	29	(6.0)
Asthenia	56	(11.6)	52	(10.7)
Hyperthyroidism	51	(10.6)	3	(0.6)
Myalgia	51	(10.6)	28	(5.8)
Hypertension	43	(8.9)	43	(8.8)
Rash maculo-papular	42	(8.7)	11	(2.3)
Back pain	41	(8.5)	39	(8.0)
Constipation	40	(8.3)	41	(8.4)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Dizziness	33	(6.8)	27	(5.6)
Pyrexia	33	(6.8)	26	(5.3)
Dry mouth	32	(6.6)	9	(1.9)
Vomiting	32	(6.6)	16	(3.3)
Abdominal pain	31	(6.4)	24	(4.9)
Decreased appetite	28	(5.8)	13	(2.7)
Oedema peripheral	28	(5.8)	24	(4.9)
Pain in extremity	28	(5.8)	28	(5.8)
Dyspnoea	22	(4.6)	27	(5.6)
Nasopharyngitis	21	(4.3)	30	(6.2)
Basal cell carcinoma	17	(3.5)	27	(5.6)

Participants With Adverse Events by Decreasing Incidence (Incidence ≥ 5% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hyperglycaemia	15	(3.1)	28	(5.8)

Every participant is counted a single time for each applicable row and column.

A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-16
Participants With Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	6	(75.0)	54	(85.7)
with no adverse events	2	(25.0)	9	(14.3)
Arthralgia	3	(37.5)	6	(9.5)
Asthenia	2	(25.0)	7	(11.1)
Fatigue	2	(25.0)	3	(4.8)
Alopecia	1	(12.5)	1	(1.6)
Animal bite	1	(12.5)	0	(0.0)
Arthritis	1	(12.5)	2	(3.2)
Back pain	1	(12.5)	3	(4.8)
Blood creatinine increased	1	(12.5)	0	(0.0)
Constipation	1	(12.5)	2	(3.2)
Device related infection	1	(12.5)	0	(0.0)
Diarrhoea	1	(12.5)	6	(9.5)
Dysphagia	1	(12.5)	0	(0.0)
Headache	1	(12.5)	8	(12.7)
IVth nerve paresis	1	(12.5)	0	(0.0)
Influenza like illness	1	(12.5)	1	(1.6)
Insomnia	1	(12.5)	5	(7.9)
Monoparesis	1	(12.5)	0	(0.0)
Myalgia	1	(12.5)	2	(3.2)
Odynophagia	1	(12.5)	0	(0.0)
Oedema	1	(12.5)	0	(0.0)
Paraesthesia	1	(12.5)	0	(0.0)
Pruritus	1	(12.5)	10	(15.9)
Sciatica	1	(12.5)	0	(0.0)
Seizure	1	(12.5)	0	(0.0)
Abdominal pain	0	(0.0)	5	(7.9)
Abdominal pain upper	0	(0.0)	1	(1.6)
Adrenal insufficiency	0	(0.0)	2	(3.2)
Alanine aminotransferase increased	0	(0.0)	6	(9.5)
Anaemia	0	(0.0)	3	(4.8)
Angiodysplasia	0	(0.0)	1	(1.6)
Angioedema	0	(0.0)	1	(1.6)
Anxiety	0	(0.0)	2	(3.2)
Appendicitis	0	(0.0)	1	(1.6)

Participants With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Aspartate aminotransferase increased	0	(0.0)	5	(7.9)
Asthma	0	(0.0)	1	(1.6)
Bacterial rhinitis	0	(0.0)	1	(1.6)
Balance disorder	0	(0.0)	1	(1.6)
Basal cell carcinoma	0	(0.0)	1	(1.6)
Benign prostatic hyperplasia	0	(0.0)	1	(1.6)
Blood albumin decreased	0	(0.0)	1	(1.6)
Blood alkaline phosphatase increased	0	(0.0)	1	(1.6)
Blood cholesterol increased	0	(0.0)	1	(1.6)
Blood creatine phosphokinase increased	0	(0.0)	1	(1.6)
Blood glucose increased	0	(0.0)	1	(1.6)
Blood magnesium decreased	0	(0.0)	1	(1.6)
Blood thyroid stimulating hormone increased	0	(0.0)	1	(1.6)
Bradycardia	0	(0.0)	1	(1.6)
Breast mass	0	(0.0)	1	(1.6)
Bronchitis	0	(0.0)	2	(3.2)
Burning sensation	0	(0.0)	1	(1.6)
COVID-19	0	(0.0)	2	(3.2)
Cardiac failure	0	(0.0)	1	(1.6)
Cardiac murmur	0	(0.0)	1	(1.6)
Cerebral ischaemia	0	(0.0)	1	(1.6)
Chalazion	0	(0.0)	1	(1.6)
Chest pain	0	(0.0)	1	(1.6)
Chills	0	(0.0)	2	(3.2)
Cholecystitis	0	(0.0)	1	(1.6)
Chronic gastritis	0	(0.0)	1	(1.6)
Conjunctivitis	0	(0.0)	1	(1.6)
Cough	0	(0.0)	3	(4.8)
Death	0	(0.0)	1	(1.6)
Decreased appetite	0	(0.0)	1	(1.6)
Dehydration	0	(0.0)	1	(1.6)
Dental caries	0	(0.0)	1	(1.6)
Dermatitis	0	(0.0)	1	(1.6)
Dizziness	0	(0.0)	5	(7.9)
Dry eye	0	(0.0)	1	(1.6)
Dry mouth	0	(0.0)	4	(6.3)
Dry skin	0	(0.0)	2	(3.2)

Participants With Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Dyspepsia	0	(0.0)	1	(1.6)
Dyspnoea	0	(0.0)	3	(4.8)
Dysuria	0	(0.0)	1	(1.6)
Ear pain	0	(0.0)	2	(3.2)
Eczema	0	(0.0)	1	(1.6)
Eczema eyelids	0	(0.0)	1	(1.6)
Embolism	0	(0.0)	1	(1.6)
Eosinophil count increased	0	(0.0)	1	(1.6)
Erectile dysfunction	0	(0.0)	1	(1.6)
Erythema	0	(0.0)	1	(1.6)
Erythema of eyelid	0	(0.0)	1	(1.6)
Eye pruritus	0	(0.0)	1	(1.6)
Eye swelling	0	(0.0)	1	(1.6)
Fibrin D dimer increased	0	(0.0)	1	(1.6)
Flatulence	0	(0.0)	1	(1.6)
Folate deficiency	0	(0.0)	1	(1.6)
Gastric ulcer	0	(0.0)	1	(1.6)
Gastroenteritis	0	(0.0)	1	(1.6)
Gastrooesophageal reflux disease	0	(0.0)	1	(1.6)
Gingival pain	0	(0.0)	1	(1.6)
Glossitis	0	(0.0)	1	(1.6)
Groin pain	0	(0.0)	1	(1.6)
Haemangioma of skin	0	(0.0)	1	(1.6)
Haematochezia	0	(0.0)	1	(1.6)
Haematoma	0	(0.0)	1	(1.6)
Haematuria	0	(0.0)	1	(1.6)
Hepatitis	0	(0.0)	1	(1.6)
Hepatotoxicity	0	(0.0)	1	(1.6)
Herpes simplex	0	(0.0)	1	(1.6)
Hot flush	0	(0.0)	1	(1.6)
Hyperglycaemia	0	(0.0)	2	(3.2)
Hyperhidrosis	0	(0.0)	1	(1.6)
Hyperkalaemia	0	(0.0)	1	(1.6)
Hypersensitivity	0	(0.0)	1	(1.6)
Hypertension	0	(0.0)	1	(1.6)
Hyperthyroidism	0	(0.0)	9	(14.3)
Hypertriglyceridaemia	0	(0.0)	1	(1.6)

Participants With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Hypokalaemia	0	(0.0)	1	(1.6)
Hypophosphataemia	0	(0.0)	4	(6.3)
Hypothyroidism	0	(0.0)	6	(9.5)
Incision site oedema	0	(0.0)	1	(1.6)
Incision site pain	0	(0.0)	2	(3.2)
Inflammatory pain	0	(0.0)	1	(1.6)
Infusion site extravasation	0	(0.0)	1	(1.6)
Inguinal mass	0	(0.0)	1	(1.6)
Intermenstrual bleeding	0	(0.0)	1	(1.6)
Intraocular pressure increased	0	(0.0)	1	(1.6)
Joint effusion	0	(0.0)	1	(1.6)
Lacrimation increased	0	(0.0)	1	(1.6)
Lichenoid keratosis	0	(0.0)	1	(1.6)
Limb injury	0	(0.0)	1	(1.6)
Lipase increased	0	(0.0)	2	(3.2)
Lung adenocarcinoma	0	(0.0)	1	(1.6)
Lymphadenopathy	0	(0.0)	1	(1.6)
Malaise	0	(0.0)	1	(1.6)
Memory impairment	0	(0.0)	1	(1.6)
Mucinous adenocarcinoma of appendix	0	(0.0)	1	(1.6)
Muscle atrophy	0	(0.0)	1	(1.6)
Muscle spasms	0	(0.0)	1	(1.6)
Musculoskeletal chest pain	0	(0.0)	1	(1.6)
Musculoskeletal pain	0	(0.0)	2	(3.2)
Musculoskeletal stiffness	0	(0.0)	1	(1.6)
Myasthenia gravis	0	(0.0)	2	(3.2)
Nasal congestion	0	(0.0)	2	(3.2)
Nasopharyngitis	0	(0.0)	2	(3.2)
Nausea	0	(0.0)	5	(7.9)
Nephrolithiasis	0	(0.0)	1	(1.6)
Occipital neuralgia	0	(0.0)	1	(1.6)
Oral candidiasis	0	(0.0)	2	(3.2)
Oral dysaesthesia	0	(0.0)	1	(1.6)
Osteoarthritis	0	(0.0)	1	(1.6)
Osteoporosis	0	(0.0)	2	(3.2)
Otitis media	0	(0.0)	1	(1.6)
Pain in extremity	0	(0.0)	1	(1.6)

Participants With Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Pancreatitis	0	(0.0)	1	(1.6)
Pelvic pain	0	(0.0)	1	(1.6)
Pharyngeal erythema	0	(0.0)	1	(1.6)
Phlebitis	0	(0.0)	1	(1.6)
Pneumonia	0	(0.0)	2	(3.2)
Pneumonitis	0	(0.0)	1	(1.6)
Pneumonitis aspiration	0	(0.0)	1	(1.6)
Pollakiuria	0	(0.0)	1	(1.6)
Poor dental condition	0	(0.0)	1	(1.6)
Postoperative wound infection	0	(0.0)	2	(3.2)
Procedural pain	0	(0.0)	1	(1.6)
Productive cough	0	(0.0)	1	(1.6)
Pyrexia	0	(0.0)	4	(6.3)
Rash	0	(0.0)	7	(11.1)
Rash maculo-papular	0	(0.0)	2	(3.2)
Rash pruritic	0	(0.0)	1	(1.6)
Renal colic	0	(0.0)	1	(1.6)
Respiratory tract infection	0	(0.0)	2	(3.2)
Retinal haemorrhage	0	(0.0)	1	(1.6)
Rib fracture	0	(0.0)	1	(1.6)
Scar pain	0	(0.0)	1	(1.6)
Seborrhoeic dermatitis	0	(0.0)	1	(1.6)
Seborrhoeic keratosis	0	(0.0)	1	(1.6)
Seminoma	0	(0.0)	1	(1.6)
Seroma	0	(0.0)	1	(1.6)
Skin exfoliation	0	(0.0)	1	(1.6)
Skin fissures	0	(0.0)	1	(1.6)
Skin lesion	0	(0.0)	2	(3.2)
Skin mass	0	(0.0)	1	(1.6)
Sleep disorder	0	(0.0)	1	(1.6)
Spinal compression fracture	0	(0.0)	1	(1.6)
Spinal fracture	0	(0.0)	2	(3.2)
Squamous cell carcinoma	0	(0.0)	1	(1.6)
Stomatitis	0	(0.0)	2	(3.2)
Stress	0	(0.0)	1	(1.6)
Suspected COVID-19	0	(0.0)	1	(1.6)
Swelling	0	(0.0)	1	(1.6)

Participants With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Tachycardia	0	(0.0)	1	(1.6)
Tendon disorder	0	(0.0)	1	(1.6)
Tendon rupture	0	(0.0)	1	(1.6)
Thyroiditis	0	(0.0)	1	(1.6)
Tinnitus	0	(0.0)	1	(1.6)
Tonsillar hypertrophy	0	(0.0)	1	(1.6)
Tonsillitis	0	(0.0)	1	(1.6)
Tooth abscess	0	(0.0)	2	(3.2)
Transaminases increased	0	(0.0)	1	(1.6)
Tricuspid valve incompetence	0	(0.0)	1	(1.6)
Upper respiratory tract infection	0	(0.0)	2	(3.2)
Upper-airway cough syndrome	0	(0.0)	1	(1.6)
Urinary tract infection	0	(0.0)	4	(6.3)
Urinary tract pain	0	(0.0)	1	(1.6)
Urticaria	0	(0.0)	1	(1.6)
Vaginal lesion	0	(0.0)	1	(1.6)
Vertigo	0	(0.0)	2	(3.2)
Vitamin D deficiency	0	(0.0)	1	(1.6)
Vitiligo	0	(0.0)	3	(4.8)
Vomiting	0	(0.0)	2	(3.2)
Vulval ulceration	0	(0.0)	1	(1.6)
Vulvovaginal candidiasis	0	(0.0)	1	(1.6)
Weight decreased	0	(0.0)	3	(4.8)
White blood cell count decreased	0	(0.0)	1	(1.6)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-17
Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse events	22	(4.6)	40	(8.2)
Blood and lymphatic system disorders	**40**	**(8.3)**	**31**	**(6.4)**
Anaemia	16	(3.3)	12	(2.5)
Eosinophilia	7	(1.4)	1	(0.2)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Iron deficiency anaemia	0	(0.0)	1	(0.2)
Leukocytosis	1	(0.2)	3	(0.6)
Leukopenia	2	(0.4)	2	(0.4)
Lymph node pain	1	(0.2)	2	(0.4)
Lymphadenopathy	4	(0.8)	2	(0.4)
Lymphocytosis	0	(0.0)	2	(0.4)
Lymphopenia	4	(0.8)	4	(0.8)
Macrocytosis	0	(0.0)	1	(0.2)
Monocytosis	0	(0.0)	1	(0.2)
Neutropenia	4	(0.8)	3	(0.6)
Normocytic anaemia	1	(0.2)	0	(0.0)
Splenomegaly	0	(0.0)	1	(0.2)
Thrombocytopenia	4	(0.8)	3	(0.6)
Cardiac disorders	**32**	**(6.6)**	**29**	**(6.0)**
Acute myocardial infarction	0	(0.0)	2	(0.4)
Angina pectoris	2	(0.4)	0	(0.0)
Atrial fibrillation	8	(1.7)	2	(0.4)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Bradycardia	2	(0.4)	4	(0.8)
Cardiac failure	0	(0.0)	1	(0.2)
Cardiomyopathy	1	(0.2)	0	(0.0)
Cardiovascular insufficiency	0	(0.0)	1	(0.2)
Coronary artery disease	0	(0.0)	2	(0.4)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Mitral valve prolapse	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Palpitations	6	(1.2)	7	(1.4)
Sinus bradycardia	2	(0.4)	2	(0.4)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cardiac disorders	**32**	**(6.6)**	**29**	**(6.0)**
Sinus tachycardia	3	(0.6)	4	(0.8)
Supraventricular extrasystoles	0	(0.0)	1	(0.2)
Tachycardia	8	(1.7)	2	(0.4)
Ventricular arrhythmia	0	(0.0)	1	(0.2)
Ventricular extrasystoles	2	(0.4)	1	(0.2)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**0**	**(0.0)**
Albinism	1	(0.2)	0	(0.0)
Gilbert's syndrome	1	(0.2)	0	(0.0)
Ear and labyrintb disorders	**23**	**(4.8)**	**25**	**(5.1)**
Chondrodermatitis nodularis chronica helicis	0	(0.0)	1	(0.2)
Deafness	1	(0.2)	1	(0.2)
Deafness neurosensory	1	(0.2)	0	(0.0)
Deafness unilateral	1	(0.2)	0	(0.0)
Ear congestion	2	(0.4)	0	(0.0)
Ear discomfort	1	(0.2)	0	(0.0)
Ear pain	2	(0.4)	3	(0.6)
Ear pruritus	2	(0.4)	1	(0.2)
Ear swelling	1	(0.2)	0	(0.0)
External ear inflammation	1	(0.2)	0	(0.0)
Hypoacusis	1	(0.2)	1	(0.2)
Tinnitus	4	(0.8)	4	(0.8)
Vertigo	9	(1.9)	16	(3.3)
Vertigo positional	0	(0.0)	1	(0.2)
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**
Adrenal insufficiency	13	(2.7)	0	(0.0)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Endocrine disorder	1	(0.2)	0	(0.0)
Goitre	2	(0.4)	2	(0.4)
Hyperparathyroidism primary	1	(0.2)	0	(0.0)
Hyperthyroidism	51	(10.6)	3	(0.6)
Hypophysitis	7	(1.4)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**
Hypothyroidism	82	(17.0)	17	(3.5)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Thyroid cyst	1	(0.2)	0	(0.0)
Thyroid mass	2	(0.4)	0	(0.0)
Thyroiditis	2	(0.4)	1	(0.2)
Thyroiditis subacute	1	(0.2)	0	(0.0)
Eye disorders	**55**	**(11.4)**	**30**	**(6.2)**
Asthenopia	0	(0.0)	1	(0.2)
Blepharitis	2	(0.4)	2	(0.4)
Blepharospasm	0	(0.0)	1	(0.2)
Cataract	2	(0.4)	1	(0.2)
Chalazion	2	(0.4)	1	(0.2)
Conjunctival hyperaemia	1	(0.2)	3	(0.6)
Conjunctival oedema	0	(0.0)	1	(0.2)
Conjunctivitis allergic	1	(0.2)	0	(0.0)
Dermatochalasis	1	(0.2)	0	(0.0)
Diplopia	0	(0.0)	1	(0.2)
Dry eye	14	(2.9)	6	(1.2)
Eczema eyelids	2	(0.4)	0	(0.0)
Erythema of eyelid	1	(0.2)	0	(0.0)
Eye inflammation	1	(0.2)	0	(0.0)
Eye irritation	3	(0.6)	2	(0.4)
Eye pain	1	(0.2)	1	(0.2)
Eye pruritus	3	(0.6)	2	(0.4)
Eyelid irritation	1	(0.2)	0	(0.0)
Eyelid myokymia	1	(0.2)	0	(0.0)
Eyelid oedema	3	(0.6)	0	(0.0)
Eyelid ptosis	1	(0.2)	0	(0.0)
Glaucoma	1	(0.2)	2	(0.4)
Iridocyclitis	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Lacrimation increased	6	(1.2)	3	(0.6)
Macular detachment	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Eye disorders	**55**	**(11.4)**	**30**	**(6.2)**
Myopia	1	(0.2)	0	(0.0)
Ocular hyperaemia	4	(0.8)	2	(0.4)
Ocular hypertension	0	(0.0)	1	(0.2)
Periorbital oedema	2	(0.4)	0	(0.0)
Periorbital swelling	1	(0.2)	0	(0.0)
Photophobia	1	(0.2)	0	(0.0)
Retinal artery occlusion	0	(0.0)	1	(0.2)
Retinal ischaemia	0	(0.0)	1	(0.2)
Scleritis	1	(0.2)	0	(0.0)
Vision blurred	11	(2.3)	3	(0.6)
Visual acuity reduced	1	(0.2)	1	(0.2)
Visual impairment	0	(0.0)	1	(0.2)
Vitreous detachment	0	(0.0)	1	(0.2)
Vitreous floaters	1	(0.2)	2	(0.4)
Vitreous haze	1	(0.2)	0	(0.0)
Xerophthalmia	3	(0.6)	0	(0.0)
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Abdominal discomfort	1	(0.2)	1	(0.2)
Abdominal distension	8	(1.7)	5	(1.0)
Abdominal pain	31	(6.4)	24	(4.9)
Abdominal pain lower	4	(0.8)	1	(0.2)
Abdominal pain upper	16	(3.3)	16	(3.3)
Abdominal tenderness	1	(0.2)	0	(0.0)
Aerophagia	0	(0.0)	1	(0.2)
Anal fistula	1	(0.2)	0	(0.0)
Anal haemorrhage	0	(0.0)	1	(0.2)
Anal incontinence	0	(0.0)	1	(0.2)
Anal inflammation	1	(0.2)	0	(0.0)
Anal pruritus	0	(0.0)	1	(0.2)
Anal ulcer	0	(0.0)	1	(0.2)
Angular cheilitis	1	(0.2)	0	(0.0)
Anorectal discomfort	1	(0.2)	0	(0.0)
Aphthous ulcer	2	(0.4)	1	(0.2)
Aptyalism	1	(0.2)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Bowel movement irregularity	0	(0.0)	1	(0.2)
Chapped lips	1	(0.2)	0	(0.0)
Cheilitis	2	(0.4)	0	(0.0)
Chronic gastritis	2	(0.4)	1	(0.2)
Colitis	16	(3.3)	5	(1.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Constipation	40	(8.3)	41	(8.4)
Diarrhoea	136	(28.2)	100	(20.6)
Diverticulum	1	(0.2)	3	(0.6)
Diverticulum intestinal	0	(0.0)	1	(0.2)
Dry mouth	32	(6.6)	9	(1.9)
Duodenal polyp	0	(0.0)	1	(0.2)
Dyschezia	1	(0.2)	0	(0.0)
Dyspepsia	13	(2.7)	10	(2.1)
Dysphagia	4	(0.8)	2	(0.4)
Enteritis	1	(0.2)	0	(0.0)
Erosive oesophagitis	1	(0.2)	0	(0.0)
Faeces soft	2	(0.4)	2	(0.4)
Flatulence	7	(1.4)	4	(0.8)
Frequent bowel movements	4	(0.8)	2	(0.4)
Gastritis	1	(0.2)	1	(0.2)
Gastrointestinal pain	1	(0.2)	2	(0.4)
Gastrointestinal sounds abnormal	0	(0.0)	1	(0.2)
Gastrooesophageal reflux disease	7	(1.4)	15	(3.1)
Gingival bleeding	1	(0.2)	0	(0.0)
Gingival pain	0	(0.0)	1	(0.2)
Gingival swelling	0	(0.0)	1	(0.2)
Glossitis	1	(0.2)	0	(0.0)
Glossodynia	2	(0.4)	1	(0.2)
Haematemesis	1	(0.2)	0	(0.0)
Haematochezia	3	(0.6)	1	(0.2)
Haemorrhoids	5	(1.0)	5	(1.0)
Hypoaesthesia oral	0	(0.0)	1	(0.2)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Inguinal hernia	1	(0.2)	1	(0.2)
Intestinal polyp	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Large intestine polyp	3	(0.6)	1	(0.2)
Lip dry	2	(0.4)	2	(0.4)
Lip oedema	1	(0.2)	0	(0.0)
Lip pain	0	(0.0)	1	(0.2)
Lip swelling	0	(0.0)	1	(0.2)
Mouth swelling	1	(0.2)	0	(0.0)
Mouth ulceration	1	(0.2)	5	(1.0)
Nausea	67	(13.9)	56	(11.5)
Noninfective gingivitis	0	(0.0)	1	(0.2)
Noninfective sialoadenitis	0	(0.0)	1	(0.2)
Odynophagia	4	(0.8)	1	(0.2)
Oral disorder	0	(0.0)	2	(0.4)
Oral dysaesthesia	3	(0.6)	0	(0.0)
Oral lichen planus	1	(0.2)	0	(0.0)
Oral lichenoid reaction	1	(0.2)	0	(0.0)
Oral mucosa erosion	1	(0.2)	0	(0.0)
Oral pain	2	(0.4)	1	(0.2)
Palatal oedema	1	(0.2)	0	(0.0)
Palatal swelling	0	(0.0)	1	(0.2)
Pancreatic cyst	0	(0.0)	1	(0.2)
Pancreatitis	2	(0.4)	0	(0.0)
Periodontal disease	2	(0.4)	0	(0.0)
Proctitis	3	(0.6)	0	(0.0)
Rectal haemorrhage	4	(0.8)	1	(0.2)
Retching	1	(0.2)	1	(0.2)
Salivary gland pain	0	(0.0)	1	(0.2)
Salivary hypersecretion	1	(0.2)	0	(0.0)
Stomatitis	17	(3.5)	3	(0.6)
Terminal ileitis	0	(0.0)	1	(0.2)
Tongue blistering	1	(0.2)	0	(0.0)
Tongue discolouration	1	(0.2)	0	(0.0)
Tongue ulceration	1	(0.2)	0	(0.0)
Tooth loss	1	(0.2)	0	(0.0)
Toothache	6	(1.2)	1	(0.2)
Vomiting	32	(6.6)	16	(3.3)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**234**	**(48.4)**	**220**	**(45.3)**
Asthenia	56	(11.6)	52	(10.7)
Axillary pain	3	(0.6)	5	(1.0)
Catheter site bruise	1	(0.2)	0	(0.0)
Catheter site haematoma	1	(0.2)	0	(0.0)
Catheter site pain	0	(0.0)	1	(0.2)
Catheter site rash	0	(0.0)	2	(0.4)
Chest discomfort	4	(0.8)	1	(0.2)
Chest pain	8	(1.7)	9	(1.9)
Chills	10	(2.1)	7	(1.4)
Chronic inflammatory response syndrome	0	(0.0)	1	(0.2)
Cyst	1	(0.2)	0	(0.0)
Discomfort	0	(0.0)	1	(0.2)
Extravasation	0	(0.0)	1	(0.2)
Face oedema	1	(0.2)	1	(0.2)
Fatigue	143	(29.6)	127	(26.1)
Feeling abnormal	1	(0.2)	0	(0.0)
Feeling cold	2	(0.4)	1	(0.2)
Fibrosis	0	(0.0)	1	(0.2)
Impaired healing	0	(0.0)	1	(0.2)
Implant site warmth	0	(0.0)	1	(0.2)
Influenza like illness	12	(2.5)	11	(2.3)
Infusion site urticaria	0	(0.0)	1	(0.2)
Injection site rash	0	(0.0)	1	(0.2)
Localised oedema	2	(0.4)	0	(0.0)
Malaise	1	(0.2)	2	(0.4)
Mass	1	(0.2)	0	(0.0)
Nodule	2	(0.4)	2	(0.4)
Non-cardiac chest pain	3	(0.6)	1	(0.2)
Oedema peripheral	28	(5.8)	24	(4.9)
Pain	6	(1.2)	4	(0.8)
Peripheral swelling	4	(0.8)	4	(0.8)
Pre-existing condition improved	0	(0.0)	1	(0.2)
Pyrexia	33	(6.8)	26	(5.3)
Soft tissue inflammation	1	(0.2)	0	(0.0)
Suprapubic pain	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**234**	**(48.4)**	**220**	**(45.3)**
Swelling	0	(0.0)	1	(0.2)
Swelling face	0	(0.0)	1	(0.2)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)
Temperature intolerance	1	(0.2)	0	(0.0)
Therapeutic response unexpected	0	(0.0)	1	(0.2)
Thirst	1	(0.2)	0	(0.0)
Xerosis	0	(0.0)	2	(0.4)
Hepatobiliary disorders	**24**	**(5.0)**	**16**	**(3.3)**
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Cholecystitis	1	(0.2)	0	(0.0)
Cholelithiasis	1	(0.2)	1	(0.2)
Cholestasis	1	(0.2)	2	(0.4)
Gallbladder obstruction	0	(0.0)	1	(0.2)
Hepatic cytolysis	1	(0.2)	5	(1.0)
Hepatic pain	1	(0.2)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.2)
Hepatitis	3	(0.6)	1	(0.2)
Hepatomegaly	1	(0.2)	0	(0.0)
Hepatotoxicity	2	(0.4)	1	(0.2)
Hyperbilirubinaemia	1	(0.2)	0	(0.0)
Hypertransaminasaemia	5	(1.0)	5	(1.0)
Jaundice	1	(0.2)	0	(0.0)
Immune system disorders	**10**	**(2.1)**	**9**	**(1.9)**
Contrast media allergy	2	(0.4)	1	(0.2)
Contrast media reaction	1	(0.2)	0	(0.0)
Drug hypersensitivity	1	(0.2)	2	(0.4)
Dust allergy	0	(0.0)	1	(0.2)
Hypersensitivity	0	(0.0)	1	(0.2)
Sarcoidosis	3	(0.6)	0	(0.0)
Seasonal allergy	3	(0.6)	4	(0.8)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Abdominal wall abscess	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Abscess soft tissue	1	(0.2)	0	(0.0)
Acarodermatitis	1	(0.2)	0	(0.0)
Anal abscess	0	(0.0)	1	(0.2)
Anorectal infection	1	(0.2)	0	(0.0)
Arthritis bacterial	1	(0.2)	0	(0.0)
Asymptomatic COVID-19	2	(0.4)	1	(0.2)
Asymptomatic bacteriuria	2	(0.4)	0	(0.0)
Atypical pneumonia	1	(0.2)	0	(0.0)
Bacteriuria	1	(0.2)	5	(1.0)
Beta haemolytic streptococcal infection	1	(0.2)	0	(0.0)
Body tinea	0	(0.0)	1	(0.2)
Bronchitis	5	(1.0)	11	(2.3)
COVID-19	4	(0.8)	7	(1.4)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Candida infection	2	(0.4)	0	(0.0)
Cellulitis	6	(1.2)	4	(0.8)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Chronic hepatitis B	0	(0.0)	1	(0.2)
Chronic sinusitis	1	(0.2)	0	(0.0)
Conjunctivitis	9	(1.9)	4	(0.8)
Cystitis	3	(0.6)	6	(1.2)
Dermatitis infected	0	(0.0)	1	(0.2)
Dermatophytosis	1	(0.2)	0	(0.0)
Dermo-hypodermitis	0	(0.0)	1	(0.2)
Diarrhoea infectious	0	(0.0)	1	(0.2)
Diverticulitis	2	(0.4)	2	(0.4)
Ear infection	3	(0.6)	8	(1.6)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Erysipelas	4	(0.8)	0	(0.0)
Escherichia urinary tract infection	1	(0.2)	1	(0.2)
Eyelid infection	1	(0.2)	0	(0.0)
Folliculitis	4	(0.8)	1	(0.2)
Fungal foot infection	3	(0.6)	1	(0.2)
Fungal infection	1	(0.2)	1	(0.2)
Fungal skin infection	0	(0.0)	2	(0.4)
Furuncle	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Gastroenteritis	3	(0.6)	6	(1.2)
Gastroenteritis viral	2	(0.4)	0	(0.0)
Gastrointestinal viral infection	1	(0.2)	0	(0.0)
Genital herpes	0	(0.0)	1	(0.2)
Gingivitis	1	(0.2)	3	(0.6)
Helicobacter infection	1	(0.2)	0	(0.0)
Herpes simplex	0	(0.0)	1	(0.2)
Herpes virus infection	1	(0.2)	2	(0.4)
Herpes zoster	4	(0.8)	1	(0.2)
Hordeolum	3	(0.6)	3	(0.6)
Infected bite	0	(0.0)	1	(0.2)
Infected dermal cyst	0	(0.0)	1	(0.2)
Infected seroma	0	(0.0)	1	(0.2)
Infective glossitis	1	(0.2)	0	(0.0)
Influenza	6	(1.2)	9	(1.9)
Laryngitis	0	(0.0)	2	(0.4)
Localised infection	0	(0.0)	2	(0.4)
Lower respiratory tract infection	3	(0.6)	0	(0.0)
Lymphangitis	0	(0.0)	1	(0.2)
Mastoiditis	1	(0.2)	0	(0.0)
Mucosal infection	1	(0.2)	0	(0.0)
Nail infection	1	(0.2)	0	(0.0)
Nasal herpes	1	(0.2)	0	(0.0)
Nasopharyngitis	21	(4.3)	30	(6.2)
Onychomycosis	3	(0.6)	2	(0.4)
Ophthalmic herpes zoster	0	(0.0)	1	(0.2)
Oral candidiasis	4	(0.8)	0	(0.0)
Oral fungal infection	1	(0.2)	0	(0.0)
Oral herpes	5	(1.0)	7	(1.4)
Oral infection	0	(0.0)	2	(0.4)
Otitis externa	2	(0.4)	0	(0.0)
Otitis media	1	(0.2)	3	(0.6)
Pantoea agglomerans infection	1	(0.2)	0	(0.0)
Paronychia	0	(0.0)	1	(0.2)
Periodontitis	1	(0.2)	0	(0.0)
Pharyngitis	3	(0.6)	4	(0.8)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Pharyngitis streptococcal	0	(0.0)	1	(0.2)
Phlebitis infective	1	(0.2)	0	(0.0)
Pneumonia	8	(1.7)	3	(0.6)
Post procedural infection	0	(0.0)	1	(0.2)
Postoperative wound infection	4	(0.8)	1	(0.2)
Pustule	2	(0.4)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.2)
Pyoderma	1	(0.2)	0	(0.0)
Pynria	1	(0.2)	1	(0.2)
Rash pustular	4	(0.8)	1	(0.2)
Respiratory tract infection	1	(0.2)	0	(0.0)
Rhinitis	11	(2.3)	8	(1.6)
Rhinovirus infection	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Sialoadenitis	0	(0.0)	1	(0.2)
Sinusitis	8	(1.7)	8	(1.6)
Skin infection	7	(1.4)	3	(0.6)
Soft tissue infection	1	(0.2)	0	(0.0)
Staphylococcal infection	1	(0.2)	1	(0.2)
Subcutaneous abscess	1	(0.2)	0	(0.0)
Superinfection	1	(0.2)	0	(0.0)
Tinea cruris	1	(0.2)	2	(0.4)
Tinea infection	1	(0.2)	0	(0.0)
Tinea pedis	1	(0.2)	1	(0.2)
Tonsillitis	1	(0.2)	1	(0.2)
Tooth abscess	1	(0.2)	0	(0.0)
Tooth infection	4	(0.8)	0	(0.0)
Trichomoniasis	0	(0.0)	1	(0.2)
Upper respiratory tract infection	19	(3.9)	19	(3.9)
Upper respiratory tract infection bacterial	1	(0.2)	0	(0.0)
Urinary tract infection	18	(3.7)	21	(4.3)
Vaginal infection	3	(0.6)	0	(0.0)
Viral infection	2	(0.4)	2	(0.4)
Viral pharyngitis	0	(0.0)	1	(0.2)
Viral rhinitis	0	(0.0)	2	(0.4)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Viral sinusitis	1	(0.2)	0	(0.0)
Viral upper respiratory tract infection	5	(1.0)	2	(0.4)
Vulvovaginal candidiasis	1	(0.2)	2	(0.4)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)
Wound infection	5	(1.0)	1	(0.2)
Injury, poisoning and procedural complications	**53**	**(11.0)**	**60**	**(12.3)**
Anastomotic leak	0	(0.0)	1	(0.2)
Animal bite	2	(0.4)	1	(0.2)
Ankle fracture	1	(0.2)	0	(0.0)
Arthropod bite	2	(0.4)	2	(0.4)
Arthropod sting	0	(0.0)	1	(0.2)
Concussion	0	(0.0)	1	(0.2)
Contusion	2	(0.4)	6	(1.2)
Eye contusion	0	(0.0)	1	(0.2)
Eyelid injury	1	(0.2)	0	(0.0)
Face injury	1	(0.2)	0	(0.0)
Facial bones fracture	1	(0.2)	0	(0.0)
Fall	12	(2.5)	10	(2.1)
Foot fracture	3	(0.6)	0	(0.0)
Foreign body	1	(0.2)	0	(0.0)
Hand fracture	0	(0.0)	2	(0.4)
Head injury	0	(0.0)	1	(0.2)
Humerus fracture	0	(0.0)	1	(0.2)
Iliotibial band syndrome	0	(0.0)	1	(0.2)
Incision site erythema	1	(0.2)	0	(0.0)
Incision site fibrosis	1	(0.2)	0	(0.0)
Incision site pain	1	(0.2)	0	(0.0)
Inflammation of wound	0	(0.0)	1	(0.2)
Infusion related reaction	2	(0.4)	4	(0.8)
Joint dislocation	0	(0.0)	2	(0.4)
Joint injury	1	(0.2)	2	(0.4)
Ligament rupture	1	(0.2)	1	(0.2)
Ligament sprain	0	(0.0)	2	(0.4)
Limb injury	3	(0.6)	4	(0.8)
Lisfranc fracture	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**53**	**(11.0)**	**60**	**(12.3)**
Lower limb fracture	0	(0.0)	1	(0.2)
Lumbar vertebral fracture	0	(0.0)	1	(0.2)
Meniscus injury	2	(0.4)	0	(0.0)
Muscle contusion	1	(0.2)	0	(0.0)
Muscle rupture	0	(0.0)	2	(0.4)
Nail injury	2	(0.4)	0	(0.0)
Neck injury	0	(0.0)	1	(0.2)
Patella fracture	1	(0.2)	0	(0.0)
Post procedural diarrhoea	0	(0.0)	1	(0.2)
Post procedural haemorrhage	0	(0.0)	1	(0.2)
Post vaccination syndrome	2	(0.4)	1	(0.2)
Procedural pain	2	(0.4)	1	(0.2)
Radius fracture	0	(0.0)	1	(0.2)
Rib fracture	3	(0.6)	2	(0.4)
Road traffic accident	0	(0.0)	1	(0.2)
Scar	2	(0.4)	0	(0.0)
Seroma	2	(0.4)	0	(0.0)
Skin abrasion	1	(0.2)	3	(0.6)
Skin injury	0	(0.0)	1	(0.2)
Skin laceration	0	(0.0)	2	(0.4)
Soft tissue injury	0	(0.0)	1	(0.2)
Synovial rupture	2	(0.4)	0	(0.0)
Tendon rupture	0	(0.0)	2	(0.4)
Thermal burn	1	(0.2)	2	(0.4)
Tooth fracture	1	(0.2)	1	(0.2)
Tooth injury	0	(0.0)	1	(0.2)
Traumatic haematoma	0	(0.0)	1	(0.2)
Upper limb fracture	0	(0.0)	2	(0.4)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)
Wound	1	(0.2)	1	(0.2)
Wound complication	0	(0.0)	1	(0.2)
Wound dehiscence	2	(0.4)	1	(0.2)
Wrist fracture	1	(0.2)	0	(0.0)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Alanine aminotransferase increased	57	(11.8)	29	(6.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Amylase decreased	1	(0.2)	0	(0.0)
Amylase increased	10	(2.1)	11	(2.3)
Antinuclear antibody positive	0	(0.0)	1	(0.2)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Bacterial test positive	2	(0.4)	1	(0.2)
Bilirubin conjugated increased	0	(0.0)	2	(0.4)
Blood alkaline phosphatase increased	15	(3.1)	7	(1.4)
Blood bilirubin increased	5	(1.0)	16	(3.3)
Blood bilirubin unconjugated increased	0	(0.0)	1	(0.2)
Blood calcium increased	1	(0.2)	1	(0.2)
Blood chloride increased	0	(0.0)	2	(0.4)
Blood cholesterol increased	4	(0.8)	3	(0.6)
Blood creatine increased	1	(0.2)	1	(0.2)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	13	(2.7)	8	(1.6)
Blood creatinine increased	15	(3.1)	12	(2.5)
Blood fibrinogen increased	1	(0.2)	0	(0.0)
Blood glucose increased	3	(0.6)	6	(1.2)
Blood lactate dehydrogenase increased	7	(1.4)	6	(1.2)
Blood luteinising hormone decreased	0	(0.0)	1	(0.2)
Blood magnesium decreased	0	(0.0)	1	(0.2)
Blood phosphorus decreased	3	(0.6)	3	(0.6)
Blood phosphorus increased	1	(0.2)	0	(0.0)
Blood potassium decreased	1	(0.2)	0	(0.0)
Blood potassium increased	1	(0.2)	3	(0.6)
Blood prolactin increased	0	(0.0)	1	(0.2)
Blood sodium decreased	2	(0.4)	1	(0.2)
Blood testosterone decreased	1	(0.2)	1	(0.2)
Blood thyroid stimulating hormone decreased	6	(1.2)	3	(0.6)
Blood thyroid stimulating hormone increased	13	(2.7)	12	(2.5)
Blood triglycerides increased	0	(0.0)	1	(0.2)
Blood urea increased	1	(0.2)	2	(0.4)
Blood uric acid increased	2	(0.4)	1	(0.2)
Body temperature increased	2	(0.4)	2	(0.4)
Borrelia test positive	1	(0.2)	0	(0.0)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
C-reactive protein increased	3	(0.6)	0	(0.0)
Carbon dioxide increased	0	(0.0)	1	(0.2)
Cortisol decreased	1	(0.2)	0	(0.0)
Electrocardiogram QT prolonged	0	(0.0)	1	(0.2)
Eosinophil count increased	2	(0.4)	0	(0.0)
Faecal elastase concentration decreased	2	(0.4)	0	(0.0)
Fibrin D dimer increased	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	4	(0.8)	9	(1.9)
Globulins decreased	1	(0.2)	1	(0.2)
Glomerular filtration rate decreased	3	(0.6)	0	(0.0)
Grip strength decreased	0	(0.0)	1	(0.2)
Haematocrit increased	1	(0.2)	0	(0.0)
Haemoglobin decreased	1	(0.2)	0	(0.0)
Haemoglobin increased	0	(0.0)	1	(0.2)
Heart rate increased	1	(0.2)	2	(0.4)
Influenza virus test positive	1	(0.2)	0	(0.0)
Interleukin level increased	1	(0.2)	0	(0.0)
International normalised ratio increased	0	(0.0)	1	(0.2)
Limb girth increased	0	(0.0)	1	(0.2)
Lipase increased	15	(3.1)	13	(2.7)
Lymphocyte count decreased	7	(1.4)	4	(0.8)
Lymphocyte count increased	1	(0.2)	0	(0.0)
Neutrophil count decreased	3	(0.6)	2	(0.4)
Neutrophil count increased	1	(0.2)	1	(0.2)
Pancreatic enzymes increased	0	(0.0)	1	(0.2)
Platelet count decreased	8	(1.7)	7	(1.4)
Prostatic specific antigen abnormal	0	(0.0)	1	(0.2)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)
Protein total decreased	1	(0.2)	0	(0.0)
Red blood cell count decreased	0	(0.0)	1	(0.2)
Red blood cell sedimentation rate increased	1	(0.2)	0	(0.0)
SARS-CoV-2 antibody test positive	1	(0.2)	0	(0.0)
SARS-CoV-2 test positive	1	(0.2)	3	(0.6)
Serum ferritin decreased	1	(0.2)	0	(0.0)
Thyroxine free decreased	1	(0.2)	1	(0.2)
Thyroxine free increased	1	(0.2)	3	(0.6)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Transaminases increased	1	(0.2)	1	(0.2)
Tri-iodothyronine decreased	1	(0.2)	1	(0.2)
Tri-iodothyronine free decreased	0	(0.0)	3	(0.6)
Tri-iodothyronine free increased	0	(0.0)	2	(0.4)
Troponin I increased	1	(0.2)	0	(0.0)
Troponin T increased	1	(0.2)	0	(0.0)
Troponin increased	0	(0.0)	1	(0.2)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Urinary occult blood positive	1	(0.2)	0	(0.0)
Urinary sediment present	1	(0.2)	1	(0.2)
Urine ketone body present	0	(0.0)	1	(0.2)
Weight decreased	14	(2.9)	5	(1.0)
Weight increased	3	(0.6)	9	(1.9)
White blood cell count decreased	2	(0.4)	2	(0.4)
White blood cell count increased	1	(0.2)	1	(0.2)
White blood cells urine positive	1	(0.2)	1	(0.2)
Metabolism and nutrition disorders	**101**	**(20.9)**	**88**	**(18.1)**
Acidosis	0	(0.0)	1	(0.2)
Decreased appetite	28	(5.8)	13	(2.7)
Dehydration	7	(1.4)	2	(0.4)
Diabetes mellitus	0	(0.0)	1	(0.2)
Diabetes mellitus inadequate control	1	(0.2)	0	(0.0)
Diabetic metabolic decompensation	1	(0.2)	0	(0.0)
Dyslipidaemia	2	(0.4)	0	(0.0)
Gout	5	(1.0)	0	(0.0)
Hyperamylasaemia	0	(0.0)	3	(0.6)
Hypercalcaemia	5	(1.0)	3	(0.6)
Hyperchloraemia	1	(0.2)	0	(0.0)
Hypercholesterolaemia	2	(0.4)	2	(0.4)
Hyperglycaemia	15	(3.1)	28	(5.8)
Hyperkalaemia	7	(1.4)	9	(1.9)
Hyperlipasaemia	0	(0.0)	1	(0.2)
Hypermagnesaemia	0	(0.0)	1	(0.2)
Hypernatraemia	1	(0.2)	0	(0.0)
Hyperphosphataemia	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Metabolism and nutrition disorders	**101**	**(20.9)**	**88**	**(18.1)**
Hypertriglyceridaemia	1	(0.2)	2	(0.4)
Hyperuricaemia	2	(0.4)	0	(0.0)
Hypoalbuminaemia	1	(0.2)	1	(0.2)
Hypocalcaemia	4	(0.8)	2	(0.4)
Hypoglycaemia	1	(0.2)	1	(0.2)
Hypokalaemia	9	(1.9)	6	(1.2)
Hypomagnesaemia	5	(1.0)	3	(0.6)
Hyponatraemia	8	(1.7)	5	(1.0)
Hypophosphataemia	12	(2.5)	17	(3.5)
Hypovitaminosis	1	(0.2)	0	(0.0)
Increased appetite	2	(0.4)	0	(0.0)
Iron deficiency	2	(0.4)	3	(0.6)
Malnutrition	1	(0.2)	0	(0.0)
Refeeding syndrome	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	5	(1.0)	6	(1.2)
Underweight	1	(0.2)	0	(0.0)
Vitamin B12 deficiency	1	(0.2)	0	(0.0)
Vitamin D deficiency	4	(0.8)	2	(0.4)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	114	(23.6)	85	(17.5)
Arthritis	6	(1.2)	5	(1.0)
Axillary mass	0	(0.0)	1	(0.2)
Back pain	41	(8.5)	39	(8.0)
Bone disorder	0	(0.0)	1	(0.2)
Bone pain	3	(0.6)	0	(0.0)
Bursitis	0	(0.0)	1	(0.2)
Cervical spinal stenosis	1	(0.2)	0	(0.0)
Chest wall haematoma	1	(0.2)	0	(0.0)
Coccydynia	1	(0.2)	1	(0.2)
Compartment syndrome	1	(0.2)	0	(0.0)
Exostosis	1	(0.2)	0	(0.0)
Fibromyalgia	0	(0.0)	1	(0.2)
Flank pain	2	(0.4)	4	(0.8)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Foot deformity	1	(0.2)	0	(0.0)
Groin pain	3	(0.6)	2	(0.4)
Haemarthrosis	1	(0.2)	1	(0.2)
Hypercreatinaemia	0	(0.0)	1	(0.2)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Intervertebral disc protrusion	2	(0.4)	1	(0.2)
Joint effusion	1	(0.2)	1	(0.2)
Joint range of motion decreased	0	(0.0)	3	(0.6)
Joint stiffness	4	(0.8)	2	(0.4)
Joint swelling	3	(0.6)	4	(0.8)
Limb discomfort	0	(0.0)	2	(0.4)
Limb mass	2	(0.4)	0	(0.0)
Mandibular mass	1	(0.2)	0	(0.0)
Muscle atrophy	1	(0.2)	0	(0.0)
Muscle contracture	2	(0.4)	0	(0.0)
Muscle hypertrophy	0	(0.0)	1	(0.2)
Muscle rigidity	1	(0.2)	0	(0.0)
Muscle spasms	9	(1.9)	9	(1.9)
Muscle tightness	0	(0.0)	1	(0.2)
Muscle twitching	1	(0.2)	0	(0.0)
Muscular weakness	6	(1.2)	0	(0.0)
Musculoskeletal chest pain	5	(1.0)	5	(1.0)
Musculoskeletal discomfort	1	(0.2)	1	(0.2)
Musculoskeletal pain	6	(1.2)	8	(1.6)
Musculoskeletal stiffness	5	(1.0)	3	(0.6)
Myalgia	51	(10.6)	28	(5.8)
Myopathy	2	(0.4)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Neck pain	12	(2.5)	9	(1.9)
Osteoarthritis	4	(0.8)	1	(0.2)
Osteopenia	0	(0.0)	1	(0.2)
Osteoporosis	2	(0.4)	1	(0.2)
Pain in extremity	28	(5.8)	28	(5.8)
Pain in jaw	3	(0.6)	2	(0.4)
Plantar fasciitis	0	(0.0)	1	(0.2)
Polyarthritis	2	(0.4)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Polymyalgia rheumatica	2	(0.4)	0	(0.0)
Pseudarthrosis	0	(0.0)	1	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Rotator cuff syndrome	1	(0.2)	1	(0.2)
Sacral pain	0	(0.0)	1	(0.2)
Sjogren's syndrome	1	(0.2)	1	(0.2)
Spinal osteoarthritis	1	(0.2)	1	(0.2)
Spinal pain	6	(1.2)	4	(0.8)
Spinal stenosis	1	(0.2)	0	(0.0)
Synovial cyst	5	(1.0)	0	(0.0)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)
Tendon pain	2	(0.4)	0	(0.0)
Tendonitis	4	(0.8)	0	(0.0)
Torticollis	1	(0.2)	1	(0.2)
Trigger finger	1	(0.2)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**64**	**(13.3)**	**68**	**(14.0)**
Acrochordon	1	(0.2)	0	(0.0)
Adenoma benign	1	(0.2)	0	(0.0)
Basal cell carcinoma	17	(3.5)	27	(5.6)
Bladder cancer	1	(0.2)	0	(0.0)
Bowen's disease	1	(0.2)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)
Chronic lymphocytic leukaemia	1	(0.2)	0	(0.0)
Dysplastic naevus	1	(0.2)	2	(0.4)
Haemangioma	1	(0.2)	2	(0.4)
Haemangioma of liver	1	(0.2)	1	(0.2)
Haemangioma of skin	1	(0.2)	0	(0.0)
Keratoacanthoma	0	(0.0)	4	(0.8)
Lentigo maligna	0	(0.0)	1	(0.2)
Lipoma	2	(0.4)	2	(0.4)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Lymphoma	1	(0.2)	0	(0.0)
Malignant melanoma	4	(0.8)	5	(1.0)
Malignant melanoma in situ	5	(1.0)	6	(1.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**64**	**(13.3)**	**68**	**(14.0)**
Melanocytic naevus	8	(1.7)	4	(0.8)
Meningioma	1	(0.2)	0	(0.0)
Neoplasm	1	(0.2)	0	(0.0)
Neurofibroma	1	(0.2)	0	(0.0)
Neuroma	1	(0.2)	0	(0.0)
Papilloma	1	(0.2)	0	(0.0)
Parathyroid tumour benign	0	(0.0)	1	(0.2)
Prostate cancer	2	(0.4)	1	(0.2)
Recurrent cancer	1	(0.2)	3	(0.6)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Seborrhoeic keratosis	14	(2.9)	6	(1.2)
Second primary malignancy	0	(0.0)	1	(0.2)
Skin papilloma	6	(1.2)	0	(0.0)
Squamous cell carcinoma of skin	5	(1.0)	14	(2.9)
Sweat gland tumour	0	(0.0)	1	(0.2)
Thyroid adenoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)
Uterine leiomyoma	0	(0.0)	1	(0.2)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Ageusia	0	(0.0)	1	(0.2)
Amnesia	2	(0.4)	2	(0.4)
Anosmia	1	(0.2)	2	(0.4)
Aphasia	1	(0.2)	0	(0.0)
Autonomic neuropathy	1	(0.2)	0	(0.0)
Balance disorder	1	(0.2)	1	(0.2)
Burning sensation	0	(0.0)	1	(0.2)
Carotid arteriosclerosis	0	(0.0)	1	(0.2)
Carotid artery stenosis	0	(0.0)	1	(0.2)
Carpal tunnel syndrome	1	(0.2)	1	(0.2)
Cervical radiculopathy	1	(0.2)	0	(0.0)
Cervicobrachial syndrome	0	(0.0)	1	(0.2)
Cervicogenic headache	1	(0.2)	0	(0.0)
Cognitive disorder	2	(0.4)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Disturbance in attention	2	(0.4)	2	(0.4)
Dizziness	33	(6.8)	27	(5.6)
Dizziness postural	2	(0.4)	1	(0.2)
Dysaesthesia	1	(0.2)	1	(0.2)
Dysgeusia	11	(2.3)	6	(1.2)
Facial paralysis	1	(0.2)	1	(0.2)
Headache	83	(17.2)	55	(11.3)
Hemiparesis	1	(0.2)	0	(0.0)
Hyperaesthesia	0	(0.0)	1	(0.2)
Hypoaesthesia	3	(0.6)	7	(1.4)
Hyposmia	1	(0.2)	0	(0.0)
Intercostal neuralgia	0	(0.0)	1	(0.2)
Lethargy	2	(0.4)	1	(0.2)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Memory impairment	2	(0.4)	3	(0.6)
Meningorrhagia	0	(0.0)	1	(0.2)
Migraine	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Nerve compression	0	(0.0)	1	(0.2)
Neuralgia	3	(0.6)	4	(0.8)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Neuropathy peripheral	5	(1.0)	6	(1.2)
Ophthalmic migraine	0	(0.0)	1	(0.2)
Paraesthesia	23	(4.8)	19	(3.9)
Parkinsonism	0	(0.0)	1	(0.2)
Peripheral motor neuropathy	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	3	(0.6)	3	(0.6)
Polyneuropathy	0	(0.0)	1	(0.2)
Post herpetic neuralgia	1	(0.2)	0	(0.0)
Presyncope	1	(0.2)	2	(0.4)
Radiculopathy	1	(0.2)	0	(0.0)
Restless legs syndrome	1	(0.2)	0	(0.0)
Sciatica	4	(0.8)	6	(1.2)
Seizure	0	(0.0)	1	(0.2)
Sensory loss	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Somnolence	2	(0.4)	1	(0.2)
Syncope	3	(0.6)	5	(1.0)
Taste disorder	4	(0.8)	0	(0.0)
Tremor	3	(0.6)	2	(0.4)
Trigeminal nerve disorder	0	(0.0)	1	(0.2)
Psychiatric disorders	**41**	**(8.5)**	**37**	**(7.6)**
Affective disorder	1	(0.2)	0	(0.0)
Agitation	1	(0.2)	1	(0.2)
Alcoholism	0	(0.0)	1	(0.2)
Anxiety	7	(1.4)	8	(1.6)
Anxiety disorder	1	(0.2)	0	(0.0)
Completed suicide	0	(0.0)	1	(0.2)
Delirium	1	(0.2)	0	(0.0)
Depressed mood	1	(0.2)	2	(0.4)
Depression	5	(1.0)	1	(0.2)
Depressive symptom	0	(0.0)	1	(0.2)
Emotional distress	1	(0.2)	0	(0.0)
Initial insomnia	0	(0.0)	1	(0.2)
Insomnia	20	(4.1)	22	(4.5)
Irritability	2	(0.4)	1	(0.2)
Libido decreased	2	(0.4)	0	(0.0)
Mania	0	(0.0)	1	(0.2)
Mood altered	1	(0.2)	2	(0.4)
Sleep disorder	2	(0.4)	0	(0.0)
Stress	1	(0.2)	0	(0.0)
Suicidal ideation	0	(0.0)	2	(0.4)
Tearfulness	1	(0.2)	0	(0.0)
Renal and urinary disorders	**50**	**(10.4)**	**30**	**(6.2)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Calculus urinary	1	(0.2)	0	(0.0)
Chromaturia	3	(0.6)	0	(0.0)
Chronic kidney disease	2	(0.4)	0	(0.0)
Dysuria	8	(1.7)	3	(0.6)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Renal and urinary disorders	**50**	**(10.4)**	**30**	**(6.2)**
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Glycosuria	2	(0.4)	2	(0.4)
Haematuria	6	(1.2)	5	(1.0)
Hydronephrosis	0	(0.0)	1	(0.2)
Leukocyturia	3	(0.6)	5	(1.0)
Micturition urgency	1	(0.2)	0	(0.0)
Nephritis	3	(0.6)	0	(0.0)
Nephrolithiasis	1	(0.2)	1	(0.2)
Nocturia	4	(0.8)	1	(0.2)
Pollakiuria	8	(1.7)	4	(0.8)
Polyuria	2	(0.4)	1	(0.2)
Proteinuria	3	(0.6)	7	(1.4)
Renal cyst	0	(0.0)	1	(0.2)
Renal failure	3	(0.6)	0	(0.0)
Renal impairment	1	(0.2)	1	(0.2)
Renal pain	0	(0.0)	1	(0.2)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Urge incontinence	1	(0.2)	0	(0.0)
Urinary hesitation	1	(0.2)	0	(0.0)
Urinary retention	2	(0.4)	1	(0.2)
Urinary straining	1	(0.2)	0	(0.0)
Urine abnormality	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**33**	**(6.8)**	**31**	**(6.4)**
Amenorrhoea	2	(0.4)	0	(0.0)
Balanoposthitis	1	(0.2)	0	(0.0)
Bartholin's cyst	1	(0.2)	0	(0.0)
Benign prostatic hyperplasia	1	(0.2)	3	(0.6)
Breast cyst	0	(0.0)	1	(0.2)
Breast discomfort	0	(0.0)	1	(0.2)
Breast haematoma	0	(0.0)	1	(0.2)
Breast mass	1	(0.2)	2	(0.4)
Breast pain	3	(0.6)	5	(1.0)
Dysmenorrhoea	2	(0.4)	0	(0.0)
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Erectile dysfunction	1	(0.2)	2	(0.4)

Participants With Adverse Events
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Reproductive system and breast disorders	**33**	**(6.8)**	**31**	**(6.4)**
Galactorrhoea	0	(0.0)	1	(0.2)
Genital cyst	1	(0.2)	0	(0.0)
Genital erythema	2	(0.4)	0	(0.0)
Genital lesion	1	(0.2)	0	(0.0)
Genital paraesthesia	1	(0.2)	0	(0.0)
Genital rash	1	(0.2)	1	(0.2)
Gynaecomastia	1	(0.2)	2	(0.4)
Intermenstrual bleeding	0	(0.0)	3	(0.6)
Menopausal symptoms	0	(0.0)	1	(0.2)
Menstruation delayed	0	(0.0)	1	(0.2)
Menstruation irregular	1	(0.2)	0	(0.0)
Nipple pain	1	(0.2)	0	(0.0)
Oligomenorrhoea	0	(0.0)	1	(0.2)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Pelvic pain	2	(0.4)	1	(0.2)
Penile erythema	1	(0.2)	0	(0.0)
Perineal pain	1	(0.2)	0	(0.0)
Prostatitis	3	(0.6)	0	(0.0)
Prostatomegaly	1	(0.2)	1	(0.2)
Pruritus genital	0	(0.0)	1	(0.2)
Scrotal pain	1	(0.2)	0	(0.0)
Testicular pain	0	(0.0)	1	(0.2)
Uterine haemorrhage	0	(0.0)	1	(0.2)
Vaginal discharge	1	(0.2)	1	(0.2)
Vaginal haemorrhage	1	(0.2)	2	(0.4)
Vaginal prolapse	0	(0.0)	1	(0.2)
Vulva cyst	0	(0.0)	1	(0.2)
Vulvovaginal burning sensation	1	(0.2)	0	(0.0)
Vulvovaginal dryness	1	(0.2)	2	(0.4)
Vulvovaginal inflammation	1	(0.2)	0	(0.0)
Vulvovaginal pruritus	1	(0.2)	2	(0.4)
Respiratory, tboracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Allergic sinusitis	1	(0.2)	0	(0.0)
Aphonia	1	(0.2)	0	(0.0)

Participants With Adverse Events
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Asthma	1	(0.2)	2	(0.4)
Asthma exercise induced	1	(0.2)	0	(0.0)
Asthmatic crisis	1	(0.2)	0	(0.0)
Atelectasis	1	(0.2)	0	(0.0)
Bronchial hyperreactivity	0	(0.0)	1	(0.2)
Bronchial obstruction	1	(0.2)	0	(0.0)
Catarrh	1	(0.2)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	2	(0.4)
Cough	61	(12.6)	58	(11.9)
Dysphonia	0	(0.0)	2	(0.4)
Dyspnoea	22	(4.6)	27	(5.6)
Dyspnoea exertional	9	(1.9)	8	(1.6)
Epistaxis	5	(1.0)	1	(0.2)
Haemoptysis	1	(0.2)	0	(0.0)
Hiccups	1	(0.2)	0	(0.0)
Hypoxia	0	(0.0)	1	(0.2)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Laryngeal dysplasia	1	(0.2)	0	(0.0)
Lower respiratory tract congestion	0	(0.0)	4	(0.8)
Lung infiltration	1	(0.2)	0	(0.0)
Nasal congestion	16	(3.3)	12	(2.5)
Nasal discomfort	1	(0.2)	0	(0.0)
Nasal polyps	0	(0.0)	1	(0.2)
Obstructive sleep apnoea syndrome	2	(0.4)	2	(0.4)
Oropharyngeal pain	13	(2.7)	8	(1.6)
Pharyngeal erythema	0	(0.0)	1	(0.2)
Pharyngeal hypertrophy	1	(0.2)	0	(0.0)
Pickwickian syndrome	1	(0.2)	0	(0.0)
Pleural effusion	2	(0.4)	2	(0.4)
Pleural thickening	0	(0.0)	1	(0.2)
Pleuritic pain	2	(0.4)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Productive cough	0	(0.0)	1	(0.2)
Pulmonary embolism	2	(0.4)	3	(0.6)
Pulmonary oedema	0	(0.0)	1	(0.2)

Participants With Adverse Events
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(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Reflux laryngitis	1	(0.2)	0	(0.0)
Respiratory symptom	1	(0.2)	0	(0.0)
Rhinalgia	0	(0.0)	1	(0.2)
Rhinitis allergic	3	(0.6)	3	(0.6)
Rhinorrhoea	4	(0.8)	3	(0.6)
Sinus congestion	0	(0.0)	4	(0.8)
Sinus polyp	1	(0.2)	0	(0.0)
Sneezing	1	(0.2)	0	(0.0)
Sputum discoloured	2	(0.4)	0	(0.0)
Throat irritation	2	(0.4)	0	(0.0)
Tonsillar hypertrophy	0	(0.0)	1	(0.2)
Upper-airway cough syndrome	1	(0.2)	1	(0.2)
Wheezing	2	(0.4)	0	(0.0)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Acne	1	(0.2)	2	(0.4)
Actinic elastosis	0	(0.0)	2	(0.4)
Actinic keratosis	18	(3.7)	16	(3.3)
Alopecia	8	(1.7)	8	(1.6)
Angioedema	3	(0.6)	0	(0.0)
Angiokeratoma	1	(0.2)	0	(0.0)
Blister	1	(0.2)	0	(0.0)
Chronic cutaneous lupus erythematosus	0	(0.0)	1	(0.2)
Cold sweat	1	(0.2)	1	(0.2)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Dermal cyst	3	(0.6)	5	(1.0)
Dermatitis	7	(1.4)	7	(1.4)
Dermatitis acneiform	5	(1.0)	2	(0.4)
Dermatitis allergic	4	(0.8)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Dermatitis contact	1	(0.2)	1	(0.2)
Dermatitis psoriasiform	3	(0.6)	0	(0.0)
Dry skin	19	(3.9)	21	(4.3)
Dyshidrotic eczema	1	(0.2)	0	(0.0)
Ecchymosis	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Eczema	13	(2.7)	10	(2.1)
Eczema nummular	1	(0.2)	3	(0.6)
Erythema	14	(2.9)	9	(1.9)
Erythema multiforme	1	(0.2)	0	(0.0)
Granulomatous dermatitis	1	(0.2)	0	(0.0)
Hair colour changes	1	(0.2)	0	(0.0)
Hidradenitis	1	(0.2)	0	(0.0)
Hyperhidrosis	2	(0.4)	1	(0.2)
Hyperkeratosis	5	(1.0)	4	(0.8)
Hypertrophic scar	1	(0.2)	1	(0.2)
Ingrowing nail	0	(0.0)	1	(0.2)
Intertrigo	4	(0.8)	3	(0.6)
Itching scar	1	(0.2)	1	(0.2)
Lentigo	1	(0.2)	1	(0.2)
Leukoplakia	2	(0.4)	0	(0.0)
Lichen planus	4	(0.8)	0	(0.0)
Lichen sclerosus	1	(0.2)	0	(0.0)
Lichenification	1	(0.2)	0	(0.0)
Lichenoid keratosis	3	(0.6)	0	(0.0)
Macule	1	(0.2)	3	(0.6)
Melanocytic hyperplasia	0	(0.0)	1	(0.2)
Miliaria	1	(0.2)	0	(0.0)
Nail disorder	1	(0.2)	1	(0.2)
Nail dystrophy	1	(0.2)	0	(0.0)
Nail pigmentation	1	(0.2)	0	(0.0)
Neurodermatitis	1	(0.2)	0	(0.0)
Night sweats	1	(0.2)	4	(0.8)
Onychoclasis	1	(0.2)	0	(0.0)
Onycholysis	0	(0.0)	1	(0.2)
Pain of skin	1	(0.2)	1	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)
Papule	3	(0.6)	2	(0.4)
Pemphigoid	1	(0.2)	0	(0.0)
Photosensitivity reaction	2	(0.4)	2	(0.4)
Precancerous skin lesion	0	(0.0)	1	(0.2)
Prurigo	1	(0.2)	0	(0.0)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Pruritus	134	(27.7)	66	(13.6)
Psoriasis	3	(0.6)	2	(0.4)
Purpura	1	(0.2)	0	(0.0)
Purpura senile	1	(0.2)	0	(0.0)
Rash	91	(18.8)	42	(8.6)
Rash erythematous	4	(0.8)	3	(0.6)
Rash follicular	1	(0.2)	0	(0.0)
Rash macular	4	(0.8)	1	(0.2)
Rash maculo-papular	42	(8.7)	11	(2.3)
Rash papular	3	(0.6)	1	(0.2)
Rash pruritic	7	(1.4)	4	(0.8)
Rash vesicular	0	(0.0)	1	(0.2)
Rosacea	2	(0.4)	1	(0.2)
Scar pain	1	(0.2)	1	(0.2)
Sebaceous adenitis	1	(0.2)	0	(0.0)
Sebaceous hyperplasia	0	(0.0)	1	(0.2)
Seborrhoeic dermatitis	5	(1.0)	4	(0.8)
Skin depigmentation	1	(0.2)	0	(0.0)
Skin disorder	1	(0.2)	0	(0.0)
Skin erosion	0	(0.0)	1	(0.2)
Skin exfoliation	7	(1.4)	0	(0.0)
Skin fissures	4	(0.8)	0	(0.0)
Skin hyperpigmentation	1	(0.2)	0	(0.0)
Skin hypopigmentation	1	(0.2)	0	(0.0)
Skin irritation	1	(0.2)	1	(0.2)
Skin lesion	17	(3.5)	10	(2.1)
Skin mass	3	(0.6)	4	(0.8)
Skin plaque	1	(0.2)	0	(0.0)
Skin reaction	1	(0.2)	0	(0.0)
Skin toxicity	1	(0.2)	1	(0.2)
Skin ulcer	5	(1.0)	1	(0.2)
Stasis dermatitis	1	(0.2)	0	(0.0)
Sticky skin	1	(0.2)	0	(0.0)
Superficial inflammatory dermatosis	0	(0.0)	1	(0.2)
Telangiectasia	1	(0.2)	0	(0.0)
Umbilical discharge	0	(0.0)	1	(0.2)

Participants With Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Urticaria	4	(0.8)	3	(0.6)
Vitiligo	7	(1.4)	9	(1.9)
Xeroderma	3	(0.6)	0	(0.0)
Vascular disorders	**74**	**(15.3)**	**72**	**(14.8)**
Axillary vein thrombosis	0	(0.0)	1	(0.2)
Cyanosis	1	(0.2)	0	(0.0)
Deep vein thrombosis	1	(0.2)	0	(0.0)
Diastolic hypertension	0	(0.0)	1	(0.2)
Embolism	0	(0.0)	1	(0.2)
Flushing	2	(0.4)	1	(0.2)
Haematoma	2	(0.4)	4	(0.8)
Hot flush	11	(2.3)	12	(2.5)
Hypertension	43	(8.9)	43	(8.8)
Hypertensive crisis	2	(0.4)	0	(0.0)
Hypotension	10	(2.1)	3	(0.6)
Jugular vein thrombosis	0	(0.0)	1	(0.2)
Lymphocele	0	(0.0)	1	(0.2)
Lymphoedema	5	(1.0)	3	(0.6)
Peripheral arterial occlusive disease	0	(0.0)	1	(0.2)
Peripheral coldness	2	(0.4)	0	(0.0)
Phlebitis	0	(0.0)	1	(0.2)
Thrombophlebitis	0	(0.0)	1	(0.2)
Varicose vein	0	(0.0)	1	(0.2)
Venous thrombosis	1	(0.2)	0	(0.0)
White coat hypertension	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Recurrent Cancer: recurrence of disease under the study

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-18
Participants With Adverse Events
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
with no adverse events	22	(4.6)	40	(8.2)
Blood and lymphatic system disorders	**40**	**(8.3)**	**31**	**(6.4)**
Cardiac disorders	**32**	**(6.6)**	**29**	**(6.0)**
Ear and labyrinth disorders	**23**	**(4.8)**	**25**	**(5.1)**
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**
Hyperthyroidism	51	(10.6)	3	(0.6)
Hypothyroidism	82	(17.0)	17	(3.5)
Eye disorders	**55**	**(11.4)**	**30**	**(6.2)**
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Abdominal pain	31	(6.4)	24	(4.9)
Constipation	40	(8.3)	41	(8.4)
Diarrhoea	136	(28.2)	100	(20.6)
Dry mouth	32	(6.6)	9	(1.9)
Nausea	67	(13.9)	56	(11.5)
Vomiting	32	(6.6)	16	(3.3)
General disorders and administration site conditions	**234**	**(48.4)**	**220**	**(45.3)**
Asthenia	56	(11.6)	52	(10.7)
Fatigue	143	(29.6)	127	(26.1)
Oedema peripheral	28	(5.8)	24	(4.9)
Pyrexia	33	(6.8)	26	(5.3)
Hepatobiliary disorders	**24**	**(5.0)**	**16**	**(3.3)**
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Nasopharyngitis	21	(4.3)	30	(6.2)
Injury, poisoning and procedural complications	**53**	**(11.0)**	**60**	**(12.3)**

Participants With Adverse Events
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Alanine aminotransferase increased	57	(11.8)	29	(6.0)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Metabolism and nutrition disorders	**101**	**(20.9)**	**88**	**(18.1)**
Decreased appetite	28	(5.8)	13	(2.7)
Hyperglycaemia	15	(3.1)	28	(5.8)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Arthralgia	114	(23.6)	85	(17.5)
Back pain	41	(8.5)	39	(8.0)
Myalgia	51	(10.6)	28	(5.8)
Pain in extremity	28	(5.8)	28	(5.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**64**	**(13.3)**	**68**	**(14.0)**
Basal cell carcinoma	17	(3.5)	27	(5.6)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Dizziness	33	(6.8)	27	(5.6)
Headache	83	(17.2)	55	(11.3)
Psychiatric disorders	**41**	**(8.5)**	**37**	**(7.6)**
Renal and urinary disorders	**50**	**(10.4)**	**30**	**(6.2)**
Reproductive system and breast disorders	**33**	**(6.8)**	**31**	**(6.4)**
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Cough	61	(12.6)	58	(11.9)
Dyspnoea	22	(4.6)	27	(5.6)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Pruritus	134	(27.7)	66	(13.6)
Rash	91	(18.8)	42	(8.6)
Rash maculo-papular	42	(8.7)	11	(2.3)

Participants With Adverse Events
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vascular disorders	**74**	**(15.3)**	**72**	**(14.8)**
Hypertension	43	(8.9)	43	(8.8)

Every participant is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-19
Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
Grade 1	97	(20.1)	154	(31.7)
Grade 2	227	(47.0)	194	(39.9)
Grade 3	120	(24.8)	83	(17.1)
Grade 4	16	(3.3)	10	(2.1)
Grade 5	1	(0.2)	5	(1.0)
with no adverse events	22	(4.6)	40	(8.2)
Blood and lymphatic system disorders	**40**	**(8.3)**	**31**	**(6.4)**
Grade 1	35	(7.2)	25	(5.1)
Grade 2	5	(1.0)	5	(1.0)
Grade 3	0	(0.0)	1	(0.2)
Anaemia	16	(3.3)	12	(2.5)
Grade 1	15	(3.1)	10	(2.1)
Grade 2	1	(0.2)	2	(0.4)
Eosinophilia	7	(1.4)	1	(0.2)
Grade 1	7	(1.4)	1	(0.2)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Iron deficiency anaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Leukocytosis	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	2	(0.4)
Leukopenia	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Lymph node pain	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Lymphadenopathy	4	(0.8)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Lymphocytosis	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lymphopenia	4	(0.8)	4	(0.8)
Grade 1	2	(0.4)	3	(0.6)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lymphopenia	4	(0.8)	4	(0.8)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Macrocytosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Monocytosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Neutropenia	4	(0.8)	3	(0.6)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Normocytic anaemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Splenomegaly	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Thrombocytopenia	4	(0.8)	3	(0.6)
Grade 1	4	(0.8)	3	(0.6)
Cardiac disorders	**32**	**(6.6)**	**29**	**(6.0)**
Grade 1	22	(4.6)	16	(3.3)
Grade 2	6	(1.2)	6	(1.2)
Grade 3	3	(0.6)	5	(1.0)
Grade 4	1	(0.2)	2	(0.4)
Acute myocardial infarction	0	(0.0)	2	(0.4)
Grade 3	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Angina pectoris	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Atrial fibrillation	8	(1.7)	2	(0.4)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	4	(0.8)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Bradycardia	2	(0.4)	4	(0.8)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cardiac failure	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Cardiomyopathy	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Cardiovascular insufficiency	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Coronary artery disease	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	2	(0.4)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Mitral valve prolapse	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Palpitations	6	(1.2)	7	(1.4)
Grade 1	6	(1.2)	7	(1.4)
Sinus bradycardia	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Sinus tachycardia	3	(0.6)	4	(0.8)
Grade 1	3	(0.6)	4	(0.8)
Supraventricular extrasystoles	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Tachycardia	8	(1.7)	2	(0.4)
Grade 1	6	(1.2)	2	(0.4)
Grade 2	2	(0.4)	0	(0.0)
Ventricular arrhythmia	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Ventricular extrasystoles	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**0**	**(0.0)**
Grade 1	2	(0.4)	0	(0.0)
Albinism	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Gilbert's syndrome	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Ear and labyrintb disorders	**23**	**(4.8)**	**25**	**(5.1)**
Grade 1	21	(4.3)	16	(3.3)
Grade 2	2	(0.4)	9	(1.9)
Chondrodermatitis nodularis chronica helicis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Deafness	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Deafness neurosensory	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Deafness unilateral	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Ear congestion	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Ear discomfort	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ear pain	2	(0.4)	3	(0.6)
Grade 1	2	(0.4)	3	(0.6)
Ear pruritus	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Ear swelling	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
External ear inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hypoacusis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tinnitus	4	(0.8)	4	(0.8)
Grade 1	4	(0.8)	3	(0.6)
Grade 2	0	(0.0)	1	(0.2)
Vertigo	9	(1.9)	16	(3.3)
Grade 1	8	(1.7)	9	(1.9)
Grade 2	1	(0.2)	7	(1.4)
Vertigo positional	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**
Grade 1	35	(7.2)	17	(3.5)
Grade 2	82	(17.0)	7	(1.4)
Grade 3	10	(2.1)	0	(0.0)
Adrenal insufficiency	13	(2.7)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	5	(1.0)	0	(0.0)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	3	(0.6)	1	(0.2)
Endocrine disorder	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Goitre	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Hyperparathyroidism primary	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperthyroidism	51	(10.6)	3	(0.6)
Grade 1	35	(7.2)	3	(0.6)
Grade 2	15	(3.1)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypophysitis	7	(1.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	5	(1.0)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Hypothyroidism	82	(17.0)	17	(3.5)
Grade 1	27	(5.6)	12	(2.5)
Grade 2	55	(11.4)	5	(1.0)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Thyroid cyst	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Thyroid mass	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Thyroiditis	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Thyroiditis subacute	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Eye disorders	**55**	**(11.4)**	**30**	**(6.2)**
Grade 1	42	(8.7)	27	(5.6)
Grade 2	12	(2.5)	2	(0.4)
Grade 3	1	(0.2)	1	(0.2)
Asthenopia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blepharitis	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Blepharospasm	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Cataract	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Chalazion	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Conjunctival hyperaemia	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Conjunctival oedema	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Conjunctivitis allergic	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Dermatochalasis	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Dermatochalasis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Diplopia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Dry eye	14	(2.9)	6	(1.2)
Grade 1	14	(2.9)	4	(0.8)
Grade 2	0	(0.0)	2	(0.4)
Eczema eyelids	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Erythema of eyelid	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eye inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eye irritation	3	(0.6)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Eye pain	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Eye pruritus	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Eyelid irritation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eyelid myokymia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eyelid oedema	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Eyelid ptosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Glaucoma	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	1	(0.2)
Iridocyclitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lacrimation increased	6	(1.2)	3	(0.6)
Grade 1	5	(1.0)	3	(0.6)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lacrimation increased	6	(1.2)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Myopia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ocular hyperaemia	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Ocular hypertension	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Periorbital oedema	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Periorbital swelling	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Photophobia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Retinal artery occlusion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Retinal ischaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Scleritis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vision blurred	11	(2.3)	3	(0.6)
Grade 1	9	(1.9)	3	(0.6)
Grade 2	2	(0.4)	0	(0.0)
Visual acuity reduced	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Visual impairment	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Vitreous detachment	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Vitreous floaters	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Vitreous haze	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Xerophthalmia	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Grade 1	171	(35.4)	164	(33.7)
Grade 2	76	(15.7)	33	(6.8)
Grade 3	23	(4.8)	1	(0.2)
Abdominal discomfort	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Abdominal distension	8	(1.7)	5	(1.0)
Grade 1	6	(1.2)	5	(1.0)
Grade 2	2	(0.4)	0	(0.0)
Abdominal pain	31	(6.4)	24	(4.9)
Grade 1	28	(5.8)	21	(4.3)
Grade 2	3	(0.6)	3	(0.6)
Abdominal pain lower	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Abdominal pain upper	16	(3.3)	16	(3.3)
Grade 1	12	(2.5)	15	(3.1)
Grade 2	4	(0.8)	1	(0.2)
Abdominal tenderness	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Aerophagia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Anal fistula	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Anal haemorrhage	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Anal incontinence	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Anal inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Anal pruritus	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Anal ulcer	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Angular cheilitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Anorectal discomfort	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Aphthous ulcer	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Aptyalism	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Bowel movement irregularity	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Chapped lips	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Cheilitis	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Chronic gastritis	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Colitis	16	(3.3)	5	(1.0)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	7	(1.4)	3	(0.6)
Grade 3	5	(1.0)	0	(0.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Constipation	40	(8.3)	41	(8.4)
Grade 1	33	(6.8)	39	(8.0)
Grade 2	7	(1.4)	2	(0.4)
Diarrhoea	136	(28.2)	100	(20.6)
Grade 1	101	(20.9)	89	(18.3)
Grade 2	27	(5.6)	10	(2.1)
Grade 3	8	(1.7)	1	(0.2)
Diverticulum	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Diverticulum intestinal	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Dry mouth	32	(6.6)	9	(1.9)
Grade 1	28	(5.8)	9	(1.9)
Grade 2	4	(0.8)	0	(0.0)
Duodenal polyp	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Dyschezia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Dyspepsia	13	(2.7)	10	(2.1)
Grade 1	12	(2.5)	8	(1.6)
Grade 2	1	(0.2)	2	(0.4)
Dysphagia	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Enteritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Erosive oesophagitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Faeces soft	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Flatulence	7	(1.4)	4	(0.8)
Grade 1	7	(1.4)	4	(0.8)
Frequent bowel movements	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Gastritis	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Gastrointestinal pain	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Gastrointestinal sounds abnormal	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Gastrooesophageal reflux disease	7	(1.4)	15	(3.1)
Grade 1	5	(1.0)	13	(2.7)
Grade 2	2	(0.4)	2	(0.4)
Gingival bleeding	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Gingival pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Gingival swelling	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Glossitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Glossodynia	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Haematemesis	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Haematemesis	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Haematochezia	3	(0.6)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Haemorrhoids	5	(1.0)	5	(1.0)
Grade 1	3	(0.6)	4	(0.8)
Grade 2	2	(0.4)	1	(0.2)
Hypoaesthesia oral	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Inguinal hernia	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Intestinal polyp	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Large intestine polyp	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Lip dry	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Lip oedema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Lip pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Lip swelling	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Mouth swelling	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Mouth ulceration	1	(0.2)	5	(1.0)
Grade 1	1	(0.2)	5	(1.0)
Nausea	67	(13.9)	56	(11.5)
Grade 1	57	(11.8)	52	(10.7)
Grade 2	10	(2.1)	4	(0.8)
Noninfective gingivitis	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Noninfective gingivitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Noninfective sialoadenitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Odynophagia	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Oral disorder	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Oral dysaesthesia	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Oral lichen planus	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral lichenoid reaction	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Oral mucosa erosion	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral pain	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Palatal oedema	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Palatal swelling	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pancreatic cyst	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pancreatitis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Periodontal disease	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Proctitis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Rectal haemorrhage	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Retching	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Salivary gland pain	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Salivary gland pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Salivary hypersecretion	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Stomatitis	17	(3.5)	3	(0.6)
Grade 1	12	(2.5)	2	(0.4)
Grade 2	5	(1.0)	1	(0.2)
Terminal ileitis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Tongue blistering	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tongue discolouration	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tongue ulceration	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tooth loss	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Toothache	6	(1.2)	1	(0.2)
Grade 1	5	(1.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Vomiting	32	(6.6)	16	(3.3)
Grade 1	30	(6.2)	14	(2.9)
Grade 2	2	(0.4)	2	(0.4)
General disorders and administration site conditions	**234**	**(48.4)**	**220**	**(45.3)**
Grade 1	167	(34.6)	187	(38.5)
Grade 2	63	(13.0)	31	(6.4)
Grade 3	4	(0.8)	2	(0.4)
Asthenia	56	(11.6)	52	(10.7)
Grade 1	37	(7.7)	45	(9.3)
Grade 2	18	(3.7)	7	(1.4)
Grade 3	1	(0.2)	0	(0.0)
Axillary pain	3	(0.6)	5	(1.0)
Grade 1	2	(0.4)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Catheter site bruise	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Catheter site bruise	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Catheter site haematoma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Catheter site pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Catheter site rash	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Chest discomfort	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Chest pain	8	(1.7)	9	(1.9)
Grade 1	8	(1.7)	7	(1.4)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Chills	10	(2.1)	7	(1.4)
Grade 1	9	(1.9)	7	(1.4)
Grade 2	1	(0.2)	0	(0.0)
Chronic inflammatory response syndrome	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Cyst	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Discomfort	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Extravasation	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Face oedema	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Fatigue	143	(29.6)	127	(26.1)
Grade 1	115	(23.8)	110	(22.6)
Grade 2	26	(5.4)	16	(3.3)
Grade 3	2	(0.4)	1	(0.2)
Feeling abnormal	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Feeling cold	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Fibrosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Impaired healing	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Impaired healing	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Implant site warmth	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Influenza like illness	12	(2.5)	11	(2.3)
Grade 1	6	(1.2)	10	(2.1)
Grade 2	6	(1.2)	1	(0.2)
Infusion site urticaria	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Injection site rash	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Localised oedema	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Malaise	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Mass	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nodule	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Non-cardiac chest pain	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Oedema peripheral	28	(5.8)	24	(4.9)
Grade 1	21	(4.3)	23	(4.7)
Grade 2	7	(1.4)	1	(0.2)
Pain	6	(1.2)	4	(0.8)
Grade 1	5	(1.0)	4	(0.8)
Grade 2	1	(0.2)	0	(0.0)
Peripheral swelling	4	(0.8)	4	(0.8)
Grade 1	4	(0.8)	4	(0.8)
Pre-existing condition improved	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pyrexia	33	(6.8)	26	(5.3)
Grade 1	26	(5.4)	23	(4.7)
Grade 2	7	(1.4)	3	(0.6)
Soft tissue inflammation	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Suprapubic pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Swelling	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Swelling face	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Temperature intolerance	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Therapeutic response unexpected	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Thirst	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Xerosis	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Hepatobiliary disorders	**24**	**(5.0)**	**16**	**(3.3)**
Grade 1	8	(1.7)	8	(1.6)
Grade 2	5	(1.0)	6	(1.2)
Grade 3	11	(2.3)	2	(0.4)
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	7	(1.4)	2	(0.4)
Cholecystitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Cholelithiasis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Cholestasis	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Gallbladder obstruction	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hepatic cytolysis	1	(0.2)	5	(1.0)
Grade 1	1	(0.2)	4	(0.8)
Grade 2	0	(0.0)	1	(0.2)
Hepatic pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hepatic steatosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hepatitis	3	(0.6)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Hepatomegaly	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hepatotoxicity	2	(0.4)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Hyperbilirubinaemia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hypertransaminasaemia	5	(1.0)	5	(1.0)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	3	(0.6)	3	(0.6)
Jaundice	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Immune system disorders	**10**	**(2.1)**	**9**	**(1.9)**
Grade 1	6	(1.2)	7	(1.4)
Grade 2	4	(0.8)	2	(0.4)
Contrast media allergy	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Contrast media reaction	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Drug hypersensitivity	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Dust allergy	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hypersensitivity	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Sarcoidosis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Seasonal allergy	3	(0.6)	4	(0.8)
Grade 1	3	(0.6)	4	(0.8)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Grade 1	79	(16.4)	100	(20.6)
Grade 2	81	(16.8)	60	(12.3)
Grade 3	11	(2.3)	8	(1.6)
Grade 4	2	(0.4)	0	(0.0)
Grade 5	1	(0.2)	2	(0.4)
Abdominal wall abscess	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Abscess soft tissue	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Acarodermatitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Anal abscess	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Anorectal infection	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Arthritis bacterial	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Asymptomatic COVID-19	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Asymptomatic bacteriuria	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Atypical pneumonia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Bacteriuria	1	(0.2)	5	(1.0)
Grade 1	1	(0.2)	4	(0.8)
Grade 2	0	(0.0)	1	(0.2)
Beta haemolytic streptococcal infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Body tinea	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Bronchitis	5	(1.0)	11	(2.3)
Grade 1	2	(0.4)	4	(0.8)
Grade 2	3	(0.6)	7	(1.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
COVID-19	4	(0.8)	7	(1.4)
Grade 1	2	(0.4)	5	(1.0)
Grade 2	2	(0.4)	2	(0.4)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Grade 3	1	(0.2)	2	(0.4)
Grade 5	1	(0.2)	1	(0.2)
Candida infection	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Cellulitis	6	(1.2)	4	(0.8)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	3	(0.6)
Grade 3	3	(0.6)	1	(0.2)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Chronic hepatitis B	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Chronic sinusitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Conjunctivitis	9	(1.9)	4	(0.8)
Grade 1	7	(1.4)	3	(0.6)
Grade 2	2	(0.4)	1	(0.2)
Cystitis	3	(0.6)	6	(1.2)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	2	(0.4)	3	(0.6)
Dermatitis infected	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Dermatophytosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Dermo-hypodermitis	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Diarrhoea infectious	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Diverticulitis	2	(0.4)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	2	(0.4)	0	(0.0)
Ear infection	3	(0.6)	8	(1.6)
Grade 1	2	(0.4)	4	(0.8)
Grade 2	1	(0.2)	4	(0.8)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Erysipelas	4	(0.8)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Escherichia urinary tract infection	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Eyelid infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Folliculitis	4	(0.8)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Fungal foot infection	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Fungal infection	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Fungal skin infection	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Furuncle	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Gastroenteritis	3	(0.6)	6	(1.2)
Grade 1	2	(0.4)	6	(1.2)
Grade 2	1	(0.2)	0	(0.0)
Gastroenteritis viral	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Gastrointestinal viral infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Genital herpes	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Gingivitis	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Helicobacter infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Herpes simplex	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Herpes virus infection	1	(0.2)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Herpes virus infection	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Herpes zoster	4	(0.8)	1	(0.2)
Grade 2	4	(0.8)	1	(0.2)
Hordeolum	3	(0.6)	3	(0.6)
Grade 1	2	(0.4)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Infected bite	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Infected dermal cyst	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Infected seroma	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Infective glossitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Influenza	6	(1.2)	9	(1.9)
Grade 1	5	(1.0)	8	(1.6)
Grade 2	1	(0.2)	1	(0.2)
Laryngitis	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Localised infection	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lower respiratory tract infection	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Lymphangitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Mastoiditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Mucosal infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Nail infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Nasal herpes	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nasopharyngitis	21	(4.3)	30	(6.2)
Grade 1	18	(3.7)	28	(5.8)
Grade 2	3	(0.6)	2	(0.4)
Onychomycosis	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Ophthalmic herpes zoster	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Oral candidiasis	4	(0.8)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral fungal infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral herpes	5	(1.0)	7	(1.4)
Grade 1	5	(1.0)	6	(1.2)
Grade 2	0	(0.0)	1	(0.2)
Oral infection	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Otitis externa	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Otitis media	1	(0.2)	3	(0.6)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	2	(0.4)
Pantoea agglomerans infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Paronychia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Periodontitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pharyngitis	3	(0.6)	4	(0.8)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	2	(0.4)	2	(0.4)
Pharyngitis streptococcal	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Phlebitis infective	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pneumonia	8	(1.7)	3	(0.6)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pneumonia	8	(1.7)	3	(0.6)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	4	(0.8)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Grade 5	0	(0.0)	1	(0.2)
Post procedural infection	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Postoperative wound infection	4	(0.8)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Pustule	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Pyoderma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pyuria	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Rash pustular	4	(0.8)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Respiratory tract infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Rhinitis	11	(2.3)	8	(1.6)
Grade 1	10	(2.1)	8	(1.6)
Grade 2	1	(0.2)	0	(0.0)
Rhinovirus infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Sialoadenitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Sinusitis	8	(1.7)	8	(1.6)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	5	(1.0)	6	(1.2)
Skin infection	7	(1.4)	3	(0.6)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	4	(0.8)	1	(0.2)
Soft tissue infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Staphylococcal infection	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Subcutaneous abscess	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Superinfection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Tinea cruris	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Tinea infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tinea pedis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tonsillitis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Tooth abscess	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Tooth infection	4	(0.8)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Trichomoniasis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Upper respiratory tract infection	19	(3.9)	19	(3.9)
Grade 1	8	(1.7)	14	(2.9)
Grade 2	11	(2.3)	5	(1.0)
Upper respiratory tract infection bacterial	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Urinary tract infection	18	(3.7)	21	(4.3)
Grade 1	1	(0.2)	11	(2.3)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Urinary tract infection	18	(3.7)	21	(4.3)
Grade 2	17	(3.5)	9	(1.9)
Grade 3	0	(0.0)	1	(0.2)
Vaginal infection	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Viral infection	2	(0.4)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Viral pharyngitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Viral rhinitis	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Viral sinusitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Viral upper respiratory tract infection	5	(1.0)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	2	(0.4)	0	(0.0)
Vulvovaginal candidiasis	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Wound infection	5	(1.0)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	4	(0.8)	1	(0.2)
Injury, poisoning and procedural complications	**53**	**(11.0)**	**60**	**(12.3)**
Grade 1	36	(7.5)	39	(8.0)
Grade 2	12	(2.5)	15	(3.1)
Grade 3	5	(1.0)	5	(1.0)
Grade 4	0	(0.0)	1	(0.2)
Anastomotic leak	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Animal bite	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Ankle fracture	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Ankle fracture	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Arthropod bite	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Arthropod sting	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Concussion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Contusion	2	(0.4)	6	(1.2)
Grade 1	2	(0.4)	6	(1.2)
Eye contusion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Eyelid injury	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Face injury	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Facial bones fracture	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Fall	12	(2.5)	10	(2.1)
Grade 1	10	(2.1)	8	(1.6)
Grade 2	2	(0.4)	2	(0.4)
Foot fracture	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Foreign body	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hand fracture	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	2	(0.4)
Head injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Humerus fracture	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Iliotibial band syndrome	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Incision site erythema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Incision site fibrosis	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Incision site fibrosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Incision site pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Inflammation of wound	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Infusion related reaction	2	(0.4)	4	(0.8)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	3	(0.6)
Joint dislocation	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	2	(0.4)
Joint injury	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Ligament rupture	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Ligament sprain	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Limb injury	3	(0.6)	4	(0.8)
Grade 1	2	(0.4)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Lisfranc fracture	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lower limb fracture	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Lumbar vertebral fracture	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Meniscus injury	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Muscle contusion	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Muscle rupture	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Nail injury	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Neck injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Patella fracture	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Patella fracture	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Post procedural diarrhoea	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Post procedural haemorrhage	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Post vaccination syndrome	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Procedural pain	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Radius fracture	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Rib fracture	3	(0.6)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Road traffic accident	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Scar	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Seroma	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Skin abrasion	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Skin injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Skin laceration	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Soft tissue injury	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Synovial rupture	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Tendon rupture	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Thermal burn	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Tooth fracture	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tooth injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Traumatic haematoma	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Upper limb fracture	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Wound	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Wound complication	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Wound dehiscence	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Wrist fracture	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Grade 1	116	(24.0)	101	(20.8)
Grade 2	23	(4.8)	25	(5.1)
Grade 3	14	(2.9)	16	(3.3)
Grade 4	6	(1.2)	3	(0.6)
Alanine aminotransferase increased	57	(11.8)	29	(6.0)
Grade 1	46	(9.5)	28	(5.8)
Grade 2	6	(1.2)	0	(0.0)
Grade 3	5	(1.0)	1	(0.2)
Amylase decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Amylase increased	10	(2.1)	11	(2.3)
Grade 1	6	(1.2)	6	(1.2)
Grade 2	1	(0.2)	3	(0.6)
Grade 3	2	(0.4)	1	(0.2)
Grade 4	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Antinuclear antibody positive	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Grade 1	27	(5.6)	17	(3.5)
Grade 2	8	(1.7)	0	(0.0)
Grade 3	3	(0.6)	3	(0.6)
Bacterial test positive	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Bilirubin conjugated increased	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	2	(0.4)
Blood alkaline phosphatase increased	15	(3.1)	7	(1.4)
Grade 1	14	(2.9)	7	(1.4)
Grade 3	1	(0.2)	0	(0.0)
Blood bilirubin increased	5	(1.0)	16	(3.3)
Grade 1	3	(0.6)	12	(2.5)
Grade 2	2	(0.4)	4	(0.8)
Blood bilirubin unconjugated increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood calcium increased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Blood chloride increased	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Blood cholesterol increased	4	(0.8)	3	(0.6)
Grade 1	2	(0.4)	3	(0.6)
Grade 2	2	(0.4)	0	(0.0)
Blood creatine increased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	13	(2.7)	8	(1.6)
Grade 1	6	(1.2)	4	(0.8)
Grade 2	3	(0.6)	0	(0.0)
Grade 3	3	(0.6)	3	(0.6)
Grade 4	1	(0.2)	1	(0.2)
Blood creatinine increased	15	(3.1)	12	(2.5)
Grade 1	12	(2.5)	9	(1.9)
Grade 2	3	(0.6)	3	(0.6)
Blood fibrinogen increased	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Blood fibrinogen increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Blood glucose increased	3	(0.6)	6	(1.2)
Grade 1	3	(0.6)	5	(1.0)
Grade 2	0	(0.0)	1	(0.2)
Blood lactate dehydrogenase increased	7	(1.4)	6	(1.2)
Grade 1	7	(1.4)	6	(1.2)
Blood luteinising hormone decreased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood magnesium decreased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood phosphorus decreased	3	(0.6)	3	(0.6)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Blood phosphorus increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Blood potassium decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Blood potassium increased	1	(0.2)	3	(0.6)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Blood prolactin increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood sodium decreased	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Blood testosterone decreased	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Blood thyroid stimulating hormone decreased	6	(1.2)	3	(0.6)
Grade 1	5	(1.0)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Blood thyroid stimulating hormone increased	13	(2.7)	12	(2.5)
Grade 1	12	(2.5)	11	(2.3)
Grade 2	1	(0.2)	1	(0.2)
Blood triglycerides increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood urea increased	1	(0.2)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Blood urea increased	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Blood uric acid increased	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Body temperature increased	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Borrelia test positive	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
C-reactive protein increased	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Carbon dioxide increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Cortisol decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Electrocardiogram QT prolonged	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Eosinophil count increased	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Faecal elastase concentration decreased	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Fibrin D dimer increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	4	(0.8)	9	(1.9)
Grade 1	1	(0.2)	7	(1.4)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Globulins decreased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Glomerular filtration rate decreased	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grip strength decreased	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Haematocrit increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Haemoglobin decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Haemoglobin increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Heart rate increased	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Influenza virus test positive	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Interleukin level increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
International normalised ratio increased	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Limb girth increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Lipase increased	15	(3.1)	13	(2.7)
Grade 1	9	(1.9)	3	(0.6)
Grade 2	1	(0.2)	2	(0.4)
Grade 3	1	(0.2)	6	(1.2)
Grade 4	4	(0.8)	2	(0.4)
Lymphocyte count decreased	7	(1.4)	4	(0.8)
Grade 1	5	(1.0)	3	(0.6)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Lymphocyte count increased	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Neutrophil count decreased	3	(0.6)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Neutrophil count increased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Pancreatic enzymes increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Platelet count decreased	8	(1.7)	7	(1.4)
Grade 1	8	(1.7)	7	(1.4)
Prostatic specific antigen abnormal	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Protein total decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Red blood cell count decreased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Red blood cell sedimentation rate increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
SARS-CoV-2 antibody test positive	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
SARS-CoV-2 test positive	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Serum ferritin decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Thyroxine free decreased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Thyroxine free increased	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Transaminases increased	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Tri-iodothyronine decreased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tri-iodothyronine free decreased	0	(0.0)	3	(0.6)
Grade 1	0	(0.0)	3	(0.6)
Tri-iodothyronine free increased	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Troponin I increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Troponin T increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Troponin increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Urinary occult blood positive	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Urinary sediment present	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Urinary sediment present	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Urine ketone body present	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Weight decreased	14	(2.9)	5	(1.0)
Grade 1	10	(2.1)	4	(0.8)
Grade 2	4	(0.8)	1	(0.2)
Weight increased	3	(0.6)	9	(1.9)
Grade 1	3	(0.6)	7	(1.4)
Grade 2	0	(0.0)	2	(0.4)
White blood cell count decreased	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
White blood cell count increased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
White blood cells urine positive	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Metabolism and nutrition disorders	**101**	**(20.9)**	**88**	**(18.1)**
Grade 1	70	(14.5)	65	(13.4)
Grade 2	19	(3.9)	14	(2.9)
Grade 3	11	(2.3)	7	(1.4)
Grade 4	1	(0.2)	2	(0.4)
Acidosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Decreased appetite	28	(5.8)	13	(2.7)
Grade 1	23	(4.8)	11	(2.3)
Grade 2	3	(0.6)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Dehydration	7	(1.4)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	4	(0.8)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Diabetes mellitus	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Diabetes mellitus inadequate control	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Diabetic metabolic decompensation	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dyslipidaemia	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Gout	5	(1.0)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Hyperamylasaemia	0	(0.0)	3	(0.6)
Grade 1	0	(0.0)	3	(0.6)
Hypercalcaemia	5	(1.0)	3	(0.6)
Grade 1	5	(1.0)	3	(0.6)
Hyperchloraemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hypercholesterolaemia	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Hyperglycaemia	15	(3.1)	28	(5.8)
Grade 1	11	(2.3)	24	(4.9)
Grade 2	2	(0.4)	3	(0.6)
Grade 3	2	(0.4)	0	(0.0)
Grade 4	0	(0.0)	1	(0.2)
Hyperkalaemia	7	(1.4)	9	(1.9)
Grade 1	4	(0.8)	8	(1.6)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Hyperlipasaemia	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Hypermagnesaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hypernatraemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperphosphataemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hypertriglyceridaemia	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Hyperuricaemia	2	(0.4)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hyperuricaemia	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Hypoalbuminaemia	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Hypocalcaemia	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Hypoglycaemia	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Hypokalaemia	9	(1.9)	6	(1.2)
Grade 1	8	(1.7)	6	(1.2)
Grade 3	1	(0.2)	0	(0.0)
Hypomagnesaemia	5	(1.0)	3	(0.6)
Grade 1	5	(1.0)	3	(0.6)
Hyponatraemia	8	(1.7)	5	(1.0)
Grade 1	8	(1.7)	5	(1.0)
Hypophosphataemia	12	(2.5)	17	(3.5)
Grade 1	7	(1.4)	11	(2.3)
Grade 2	2	(0.4)	3	(0.6)
Grade 3	3	(0.6)	3	(0.6)
Hypovitaminosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Increased appetite	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Iron deficiency	2	(0.4)	3	(0.6)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Malnutrition	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Refeeding syndrome	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	5	(1.0)	6	(1.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	3	(0.6)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Type 2 diabetes mellitus	5	(1.0)	6	(1.2)
Grade 3	2	(0.4)	4	(0.8)
Underweight	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Vitamin B12 deficiency	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vitamin D deficiency	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	0	(0.0)
Grade 2	0	(0.0)	2	(0.4)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Grade 1	124	(25.7)	143	(29.4)
Grade 2	80	(16.6)	34	(7.0)
Grade 3	12	(2.5)	6	(1.2)
Grade 4	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Arthralgia	114	(23.6)	85	(17.5)
Grade 1	75	(15.5)	70	(14.4)
Grade 2	38	(7.9)	13	(2.7)
Grade 3	1	(0.2)	2	(0.4)
Arthritis	6	(1.2)	5	(1.0)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	3	(0.6)	3	(0.6)
Grade 3	1	(0.2)	0	(0.0)
Axillary mass	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Back pain	41	(8.5)	39	(8.0)
Grade 1	25	(5.2)	34	(7.0)
Grade 2	14	(2.9)	5	(1.0)
Grade 3	2	(0.4)	0	(0.0)
Bone disorder	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Bone pain	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Bursitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cervical spinal stenosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Chest wall haematoma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Coccydynia	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Compartment syndrome	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Exostosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Fibromyalgia	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Flank pain	2	(0.4)	4	(0.8)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Foot deformity	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Groin pain	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Haemarthrosis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Hypercreatinaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Intervertebral disc protrusion	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Joint effusion	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Joint range of motion decreased	0	(0.0)	3	(0.6)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Joint stiffness	4	(0.8)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Joint stiffness	4	(0.8)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Joint swelling	3	(0.6)	4	(0.8)
Grade 1	1	(0.2)	4	(0.8)
Grade 2	2	(0.4)	0	(0.0)
Limb discomfort	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Limb mass	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Mandibular mass	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Muscle atrophy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Muscle contracture	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Muscle hypertrophy	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Muscle rigidity	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Muscle spasms	9	(1.9)	9	(1.9)
Grade 1	8	(1.7)	8	(1.6)
Grade 2	1	(0.2)	1	(0.2)
Muscle tightness	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Muscle twitching	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Muscular weakness	6	(1.2)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Musculoskeletal chest pain	5	(1.0)	5	(1.0)
Grade 1	4	(0.8)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Musculoskeletal discomfort	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Musculoskeletal pain	6	(1.2)	8	(1.6)
Grade 1	5	(1.0)	4	(0.8)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal pain	6	(1.2)	8	(1.6)
Grade 2	1	(0.2)	4	(0.8)
Musculoskeletal stiffness	5	(1.0)	3	(0.6)
Grade 1	4	(0.8)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Myalgia	51	(10.6)	28	(5.8)
Grade 1	41	(8.5)	26	(5.3)
Grade 2	8	(1.7)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Myopathy	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Neck pain	12	(2.5)	9	(1.9)
Grade 1	10	(2.1)	7	(1.4)
Grade 2	2	(0.4)	2	(0.4)
Osteoarthritis	4	(0.8)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Osteopenia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Osteoporosis	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Pain in extremity	28	(5.8)	28	(5.8)
Grade 1	21	(4.3)	23	(4.7)
Grade 2	7	(1.4)	4	(0.8)
Grade 3	0	(0.0)	1	(0.2)
Pain in jaw	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Plantar fasciitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Polyarthritis	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Polymyalgia rheumatica	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pseudarthrosis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Rotator cuff syndrome	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Sacral pain	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Sjogren's syndrome	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Spinal osteoarthritis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Spinal pain	6	(1.2)	4	(0.8)
Grade 1	5	(1.0)	4	(0.8)
Grade 2	1	(0.2)	0	(0.0)
Spinal stenosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Synovial cyst	5	(1.0)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Tendon pain	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Tendonitis	4	(0.8)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Torticollis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Trigger finger	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**64**	**(13.3)**	**68**	**(14.0)**
Grade 1	30	(6.2)	14	(2.9)
Grade 2	29	(6.0)	44	(9.1)
Grade 3	5	(1.0)	8	(1.6)
Grade 5	0	(0.0)	2	(0.4)
Acrochordon	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Adenoma benign	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Basal cell carcinoma	17	(3.5)	27	(5.6)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	17	(3.5)	23	(4.7)
Grade 3	0	(0.0)	2	(0.4)
Bladder cancer	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Bowen's disease	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Chronic lymphocytic leukaemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Dysplastic naevus	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Haemangioma	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Haemangioma of liver	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Haemangioma of skin	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Keratoacanthoma	0	(0.0)	4	(0.8)
Grade 1	0	(0.0)	3	(0.6)
Grade 2	0	(0.0)	1	(0.2)
Lentigo maligna	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lipoma	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Grade 5	0	(0.0)	1	(0.2)
Lymphoma	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Malignant melanoma	4	(0.8)	5	(1.0)
Grade 2	4	(0.8)	4	(0.8)
Grade 3	0	(0.0)	1	(0.2)
Malignant melanoma in situ	5	(1.0)	6	(1.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	5	(1.0)	5	(1.0)
Melanocytic naevus	8	(1.7)	4	(0.8)
Grade 1	7	(1.4)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Meningioma	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Neoplasm	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Neurofibroma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Neuroma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Papilloma	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Parathyroid tumour benign	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Prostate cancer	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	1	(0.2)
Recurrent cancer	1	(0.2)	3	(0.6)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	1	(0.2)
Grade 5	0	(0.0)	1	(0.2)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Seborrhoeic keratosis	14	(2.9)	6	(1.2)
Grade 1	11	(2.3)	4	(0.8)
Grade 2	3	(0.6)	2	(0.4)
Second primary malignancy	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Second primary malignancy	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Skin papilloma	6	(1.2)	0	(0.0)
Grade 1	5	(1.0)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Squamous cell carcinoma of skin	5	(1.0)	14	(2.9)
Grade 2	5	(1.0)	14	(2.9)
Sweat gland tumour	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Thyroid adenoma	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Uterine leiomyoma	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Grade 1	107	(22.2)	91	(18.7)
Grade 2	30	(6.2)	25	(5.1)
Grade 3	8	(1.7)	6	(1.2)
Ageusia	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Amnesia	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Anosmia	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Aphasia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Autonomic neuropathy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Balance disorder	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Burning sensation	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Carotid arteriosclerosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Carotid artery stenosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Carpal tunnel syndrome	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Cervical radiculopathy	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Cervicobrachial syndrome	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Cervicogenic headache	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Cognitive disorder	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Disturbance in attention	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Dizziness	33	(6.8)	27	(5.6)
Grade 1	30	(6.2)	23	(4.7)
Grade 2	3	(0.6)	4	(0.8)
Dizziness postural	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Dysaesthesia	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Dysgeusia	11	(2.3)	6	(1.2)
Grade 1	11	(2.3)	6	(1.2)
Facial paralysis	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Headache	83	(17.2)	55	(11.3)
Grade 1	68	(14.1)	50	(10.3)
Grade 2	15	(3.1)	5	(1.0)
Hemiparesis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperaesthesia	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hyperaesthesia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hypoaesthesia	3	(0.6)	7	(1.4)
Grade 1	3	(0.6)	5	(1.0)
Grade 2	0	(0.0)	2	(0.4)
Hyposmia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Intercostal neuralgia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Lethargy	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Memory impairment	2	(0.4)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Meningorrhagia	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Migraine	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Nerve compression	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Neuralgia	3	(0.6)	4	(0.8)
Grade 1	2	(0.4)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Neuropathy peripheral	5	(1.0)	6	(1.2)
Grade 1	4	(0.8)	1	(0.2)
Grade 2	1	(0.2)	5	(1.0)
Ophthalmic migraine	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Paraesthesia	23	(4.8)	19	(3.9)
Grade 1	21	(4.3)	18	(3.7)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Paraesthesia	23	(4.8)	19	(3.9)
Grade 2	2	(0.4)	1	(0.2)
Parkinsonism	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Peripheral motor neuropathy	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	3	(0.6)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Polyneuropathy	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Post herpetic neuralgia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Presyncope	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Radiculopathy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Restless legs syndrome	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sciatica	4	(0.8)	6	(1.2)
Grade 1	3	(0.6)	3	(0.6)
Grade 2	1	(0.2)	3	(0.6)
Seizure	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Sensory loss	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Somnolence	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Syncope	3	(0.6)	5	(1.0)
Grade 1	1	(0.2)	3	(0.6)
Grade 3	2	(0.4)	2	(0.4)
Taste disorder	4	(0.8)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Tremor	3	(0.6)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Tremor	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Trigeminal nerve disorder	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Psychiatric disorders	**41**	**(8.5)**	**37**	**(7.6)**
Grade 1	31	(6.4)	24	(4.9)
Grade 2	9	(1.9)	9	(1.9)
Grade 3	0	(0.0)	1	(0.2)
Grade 4	1	(0.2)	2	(0.4)
Grade 5	0	(0.0)	1	(0.2)
Affective disorder	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Agitation	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Alcoholism	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Anxiety	7	(1.4)	8	(1.6)
Grade 1	5	(1.0)	3	(0.6)
Grade 2	2	(0.4)	4	(0.8)
Grade 3	0	(0.0)	1	(0.2)
Anxiety disorder	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Completed suicide	0	(0.0)	1	(0.2)
Grade 5	0	(0.0)	1	(0.2)
Delirium	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Depressed mood	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Depression	5	(1.0)	1	(0.2)
Grade 1	4	(0.8)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Depressive symptom	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Emotional distress	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Emotional distress	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Initial insomnia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Insomnia	20	(4.1)	22	(4.5)
Grade 1	16	(3.3)	16	(3.3)
Grade 2	4	(0.8)	6	(1.2)
Irritability	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Libido decreased	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Mania	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Mood altered	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Sleep disorder	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Stress	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Suicidal ideation	0	(0.0)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Grade 4	0	(0.0)	1	(0.2)
Tearfulness	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Renal and urinary disorders	**50**	**(10.4)**	**30**	**(6.2)**
Grade 1	35	(7.2)	21	(4.3)
Grade 2	8	(1.7)	7	(1.4)
Grade 3	6	(1.2)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)
Acute kidney injury	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Calculus urinary	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Chromaturia	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Chronic kidney disease	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Dysuria	8	(1.7)	3	(0.6)
Grade 1	6	(1.2)	3	(0.6)
Grade 2	2	(0.4)	0	(0.0)
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Glycosuria	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Haematuria	6	(1.2)	5	(1.0)
Grade 1	6	(1.2)	4	(0.8)
Grade 3	0	(0.0)	1	(0.2)
Hydronephrosis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Leukocyturia	3	(0.6)	5	(1.0)
Grade 1	2	(0.4)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Micturition urgency	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nephritis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Nephrolithiasis	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	1	(0.2)
Nocturia	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Pollakiuria	8	(1.7)	4	(0.8)
Grade 1	8	(1.7)	4	(0.8)
Polyuria	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Proteinuria	3	(0.6)	7	(1.4)
Grade 1	3	(0.6)	3	(0.6)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Proteinuria	3	(0.6)	7	(1.4)
Grade 2	0	(0.0)	4	(0.8)
Renal cyst	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Renal failure	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Renal impairment	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Renal pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Urge incontinence	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Urinary hesitation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Urinary retention	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Urinary straining	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Urine abnormality	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**33**	**(6.8)**	**31**	**(6.4)**
Grade 1	23	(4.8)	21	(4.3)
Grade 2	9	(1.9)	8	(1.6)
Grade 3	0	(0.0)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)
Amenorrhoea	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Balanoposthitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Bartholin's cyst	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Bartholin's cyst	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Benign prostatic hyperplasia	1	(0.2)	3	(0.6)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Breast cyst	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Breast discomfort	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Breast haematoma	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Breast mass	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Breast pain	3	(0.6)	5	(1.0)
Grade 1	3	(0.6)	3	(0.6)
Grade 2	0	(0.0)	2	(0.4)
Dysmenorrhoea	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Erectile dysfunction	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Galactorrhoea	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Genital cyst	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Genital erythema	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Genital lesion	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Genital paraesthesia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Genital rash	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Gynaecomastia	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Intermenstrual bleeding	0	(0.0)	3	(0.6)
Grade 1	0	(0.0)	3	(0.6)
Menopausal symptoms	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Menstruation delayed	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Menstruation irregular	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nipple pain	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oligomenorrhoea	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Pelvic pain	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Penile erythema	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Perineal pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Prostatitis	3	(0.6)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Prostatomegaly	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Pruritus genital	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Scrotal pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Testicular pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Uterine haemorrhage	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Vaginal discharge	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Vaginal haemorrhage	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Vaginal prolapse	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vulva cyst	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Vulvovaginal burning sensation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vulvovaginal dryness	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Vulvovaginal inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vulvovaginal pruritus	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	2	(0.4)
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Grade 1	82	(17.0)	94	(19.3)
Grade 2	35	(7.2)	15	(3.1)
Grade 3	3	(0.6)	5	(1.0)
Grade 4	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Allergic sinusitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Aphonia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Asthma	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Asthma exercise induced	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Asthmatic crisis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Atelectasis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Bronchial hyperreactivity	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Bronchial obstruction	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Catarrh	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Chronic obstructive pulmonary disease	0	(0.0)	2	(0.4)
Grade 3	0	(0.0)	2	(0.4)
Cough	61	(12.6)	58	(11.9)
Grade 1	52	(10.8)	53	(10.9)
Grade 2	9	(1.9)	5	(1.0)
Dysphonia	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Dyspnoea	22	(4.6)	27	(5.6)
Grade 1	19	(3.9)	21	(4.3)
Grade 2	3	(0.6)	6	(1.2)
Dyspnoea exertional	9	(1.9)	8	(1.6)
Grade 1	7	(1.4)	8	(1.6)
Grade 2	2	(0.4)	0	(0.0)
Epistaxis	5	(1.0)	1	(0.2)
Grade 1	5	(1.0)	1	(0.2)
Haemoptysis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hiccups	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hypoxia	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Laryngeal dysplasia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Lower respiratory tract congestion	0	(0.0)	4	(0.8)
Grade 1	0	(0.0)	4	(0.8)
Lung infiltration	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nasal congestion	16	(3.3)	12	(2.5)
Grade 1	14	(2.9)	10	(2.1)
Grade 2	2	(0.4)	2	(0.4)
Nasal discomfort	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nasal discomfort	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nasal polyps	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Obstructive sleep apnoea syndrome	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Oropharyngeal pain	13	(2.7)	8	(1.6)
Grade 1	13	(2.7)	7	(1.4)
Grade 2	0	(0.0)	1	(0.2)
Pharyngeal erythema	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pharyngeal hypertrophy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pickwickian syndrome	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pleural effusion	2	(0.4)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Pleural thickening	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pleuritic pain	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Grade 1	5	(1.0)	3	(0.6)
Grade 2	4	(0.8)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Productive cough	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pulmonary embolism	2	(0.4)	3	(0.6)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	0	(0.0)	2	(0.4)
Pulmonary oedema	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Reflux laryngitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Respiratory symptom	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Rhinalgia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Rhinitis allergic	3	(0.6)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	2	(0.4)	1	(0.2)
Rhinorrhoea	4	(0.8)	3	(0.6)
Grade 1	4	(0.8)	3	(0.6)
Sinus congestion	0	(0.0)	4	(0.8)
Grade 1	0	(0.0)	4	(0.8)
Sinus polyp	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Sneezing	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sputum discoloured	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Throat irritation	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Tonsillar hypertrophy	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Upper-airway cough syndrome	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Wheezing	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Grade 1	204	(42.2)	167	(34.4)
Grade 2	59	(12.2)	26	(5.3)
Grade 3	14	(2.9)	3	(0.6)
Grade 4	1	(0.2)	0	(0.0)
Acne	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Actinic elastosis	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Actinic keratosis	18	(3.7)	16	(3.3)
Grade 1	13	(2.7)	10	(2.1)
Grade 2	5	(1.0)	6	(1.2)
Alopecia	8	(1.7)	8	(1.6)
Grade 1	8	(1.7)	8	(1.6)
Angioedema	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Angiokeratoma	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Blister	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Chronic cutaneous lupus erythematosus	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Cold sweat	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dermal cyst	3	(0.6)	5	(1.0)
Grade 1	3	(0.6)	4	(0.8)
Grade 2	0	(0.0)	1	(0.2)
Dermatitis	7	(1.4)	7	(1.4)
Grade 1	6	(1.2)	5	(1.0)
Grade 2	1	(0.2)	2	(0.4)
Dermatitis acneiform	5	(1.0)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	2	(0.4)	0	(0.0)
Dermatitis allergic	4	(0.8)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Dermatitis contact	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Dermatitis psoriasiform	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dry skin	19	(3.9)	21	(4.3)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Dry skin	19	(3.9)	21	(4.3)
Grade 1	19	(3.9)	21	(4.3)
Dyshidrotic eczema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ecchymosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eczema	13	(2.7)	10	(2.1)
Grade 1	12	(2.5)	7	(1.4)
Grade 2	1	(0.2)	3	(0.6)
Eczema nummular	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Erythema	14	(2.9)	9	(1.9)
Grade 1	14	(2.9)	9	(1.9)
Erythema multiforme	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Granulomatous dermatitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hair colour changes	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hidradenitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperhidrosis	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Hyperkeratosis	5	(1.0)	4	(0.8)
Grade 1	4	(0.8)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Hypertrophic scar	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Ingrowing nail	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Intertrigo	4	(0.8)	3	(0.6)
Grade 1	3	(0.6)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Itching scar	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Lentigo	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lentigo	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Leukoplakia	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lichen planus	4	(0.8)	0	(0.0)
Grade 2	4	(0.8)	0	(0.0)
Lichen sclerosus	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Lichenification	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lichenoid keratosis	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Macule	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Melanocytic hyperplasia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Miliaria	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nail disorder	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Nail dystrophy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nail pigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Neurodermatitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Night sweats	1	(0.2)	4	(0.8)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	0	(0.0)	1	(0.2)
Onychoclasis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Onycholysis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pain of skin	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Papule	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Pemphigoid	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Photosensitivity reaction	2	(0.4)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Precancerous skin lesion	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Prurigo	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pruritus	134	(27.7)	66	(13.6)
Grade 1	113	(23.4)	64	(13.2)
Grade 2	18	(3.7)	2	(0.4)
Grade 3	3	(0.6)	0	(0.0)
Psoriasis	3	(0.6)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Purpura	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Purpura senile	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Rash	91	(18.8)	42	(8.6)
Grade 1	71	(14.7)	37	(7.6)
Grade 2	13	(2.7)	3	(0.6)
Grade 3	7	(1.4)	2	(0.4)
Rash erythematous	4	(0.8)	3	(0.6)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Rash follicular	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Rash macular	4	(0.8)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Rash maculo-papular	42	(8.7)	11	(2.3)
Grade 1	29	(6.0)	9	(1.9)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Rash maculo-papular	42	(8.7)	11	(2.3)
Grade 2	11	(2.3)	1	(0.2)
Grade 3	2	(0.4)	1	(0.2)
Rash papular	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Rash pruritic	7	(1.4)	4	(0.8)
Grade 1	3	(0.6)	3	(0.6)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Rash vesicular	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Rosacea	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Scar pain	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Sebaceous adenitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sebaceous hyperplasia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Seborrhoeic dermatitis	5	(1.0)	4	(0.8)
Grade 1	5	(1.0)	4	(0.8)
Skin depigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin disorder	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin erosion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Skin exfoliation	7	(1.4)	0	(0.0)
Grade 1	6	(1.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Skin fissures	4	(0.8)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Skin hyperpigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin hypopigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin irritation	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Skin lesion	17	(3.5)	10	(2.1)
Grade 1	14	(2.9)	9	(1.9)
Grade 2	3	(0.6)	1	(0.2)
Skin mass	3	(0.6)	4	(0.8)
Grade 1	3	(0.6)	4	(0.8)
Skin plaque	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin reaction	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin toxicity	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Skin ulcer	5	(1.0)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Stasis dermatitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sticky skin	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Superficial inflammatory dermatosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Telangiectasia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Umbilical discharge	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Urticaria	4	(0.8)	3	(0.6)
Grade 1	4	(0.8)	3	(0.6)
Vitiligo	7	(1.4)	9	(1.9)
Grade 1	7	(1.4)	9	(1.9)
Xeroderma	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Vascular disorders	**74**	**(15.3)**	**72**	**(14.8)**
Grade 1	36	(7.5)	29	(6.0)
Grade 2	21	(4.3)	24	(4.9)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vascular disorders	**74**	**(15.3)**	**72**	**(14.8)**
Grade 3	17	(3.5)	19	(3.9)
Axillary vein thrombosis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Cyanosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Deep vein thrombosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Diastolic hypertension	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Embolism	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Flushing	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Haematoma	2	(0.4)	4	(0.8)
Grade 1	1	(0.2)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Hot flush	11	(2.3)	12	(2.5)
Grade 1	11	(2.3)	12	(2.5)
Hypertension	43	(8.9)	43	(8.8)
Grade 1	12	(2.5)	7	(1.4)
Grade 2	15	(3.1)	19	(3.9)
Grade 3	16	(3.3)	17	(3.5)
Hypertensive crisis	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Hypotension	10	(2.1)	3	(0.6)
Grade 1	6	(1.2)	3	(0.6)
Grade 2	3	(0.6)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Jugular vein thrombosis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lymphocele	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Lymphoedema	5	(1.0)	3	(0.6)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)

Participants With Adverse Events by SOC and PT by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Peripheral arterial occlusive disease	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Peripheral coldness	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Phlebitis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Thrombophlebitis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Varicose vein	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Venous thrombosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
White coat hypertension	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a system organ class is counted a single time for that system organ class.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

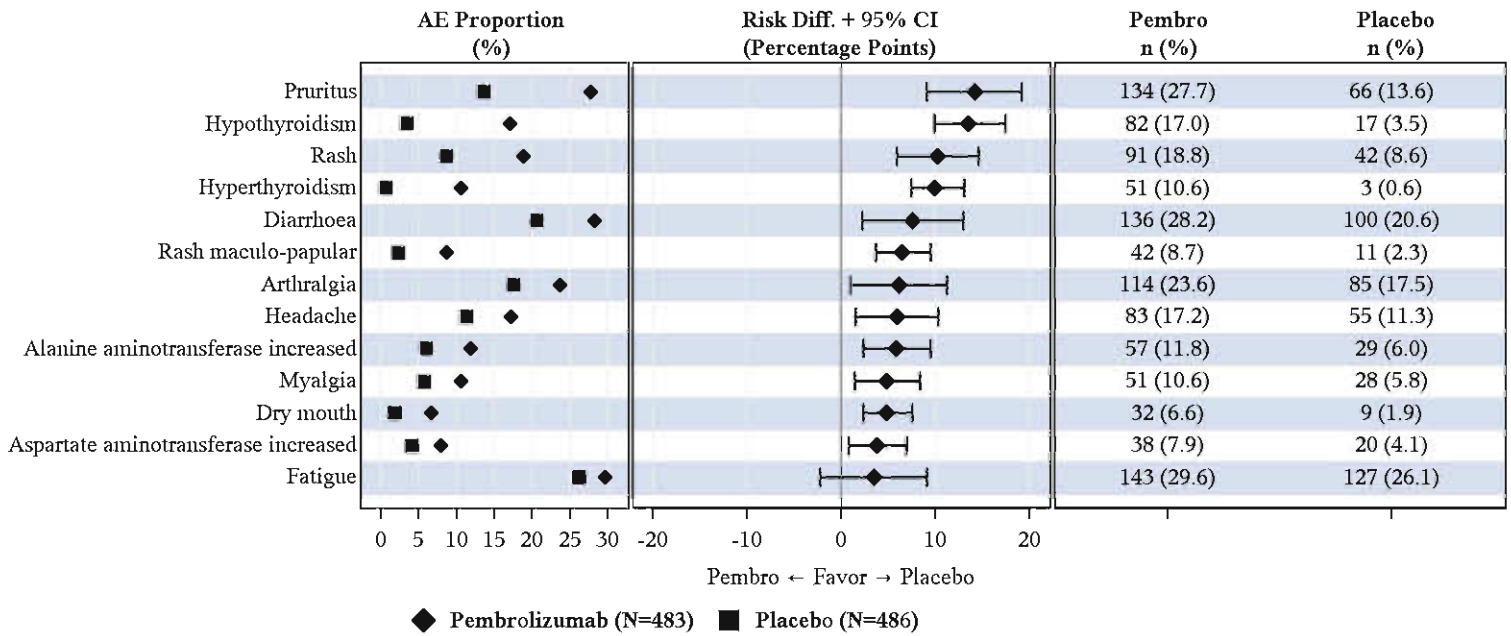
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Recurrent Cancer: recurrence of disease under the study

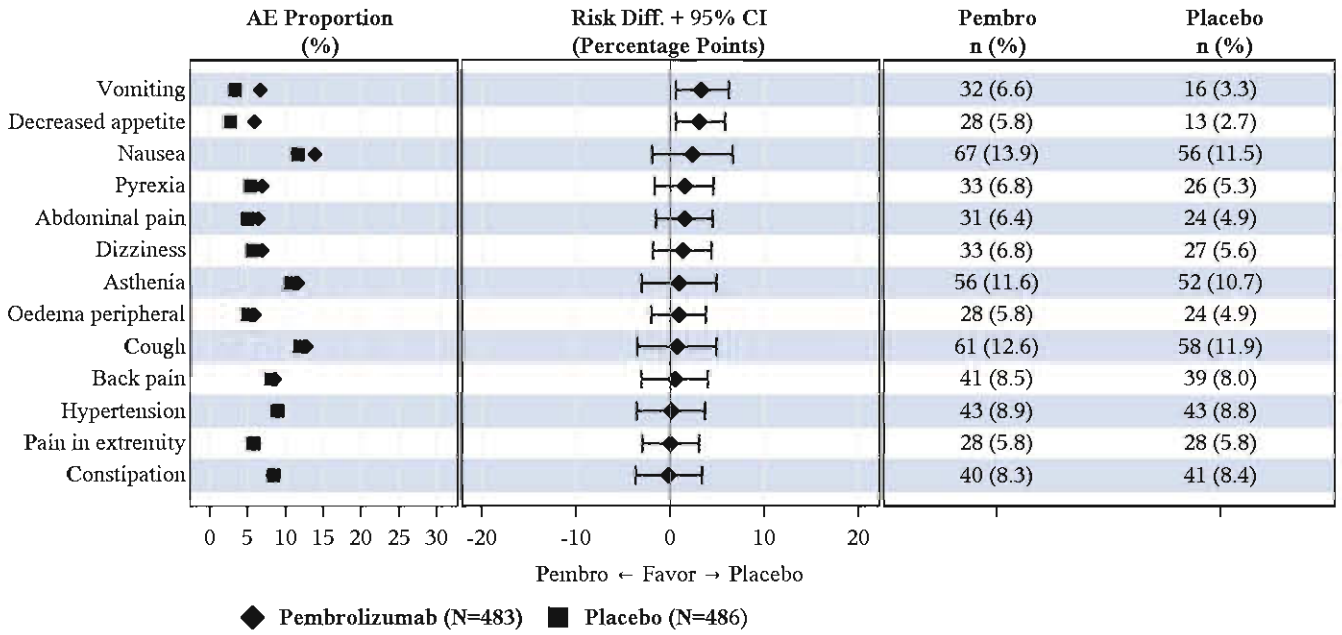
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

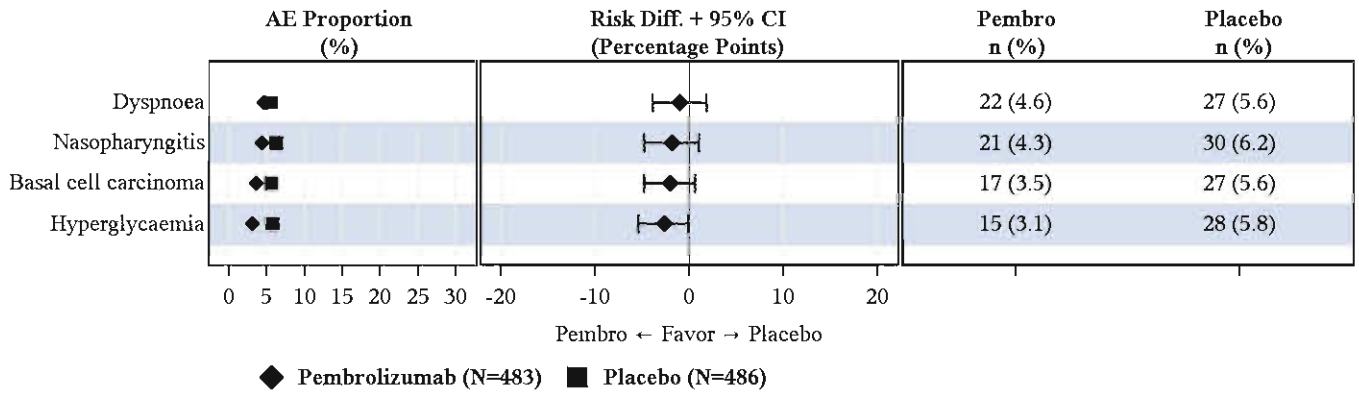
Figure 14.3-1
Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)



Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population) (Continued)



Rainfall Plot for Specific Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population) (Continued)



Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-20
Exposure-Adjusted Adverse Events
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Number of participants exposed	483	486
Total exposure[b] in person-months	4945.05	5420.53
Blood and lympbatic system disorders	**50 (1.01)**	**42 (0.77)**
Cardiac disorders	**36 (0.73)**	**36 (0.66)**
Ear and labyrintb disorders	**27 (0.55)**	**33 (0.61)**
Endocrine disorders	**179 (3.62)**	**28 (0.52)**
Hyperthyroidism	51 (1.03)	4 (0.07)
Hypothyroidism	84 (1.70)	19 (0.35)
Eye disorders	**82 (1.66)**	**40 (0.74)**
Gastrointestinal disorders	**673 (13.61)**	**509 (9.39)**
Abdominal pain	38 (0.77)	29 (0.54)
Constipation	46 (0.93)	46 (0.85)
Diarrhoea	223 (4.51)	190 (3.51)
Dry mouth	34 (0.69)	10 (0.18)
Nausea	99 (2.00)	90 (1.66)
Vomiting	41 (0.83)	18 (0.33)
General disorders and administration site conditions	**389 (7.87)**	**358 (6.60)**
Asthenia	79 (1.60)	79 (1.46)
Fatigue	164 (3.32)	153 (2.82)
Oedema peripheral	34 (0.69)	25 (0.46)
Pyrexia	35 (0.71)	27 (0.50)
Hepatobiliary disorders	**28 (0.57)**	**24 (0.44)**
Infections and infestations	**281 (5.68)**	**265 (4.89)**
Nasopharyngitis	26 (0.53)	36 (0.66)
Injury, poisoning and procedural complications	**65 (1.31)**	**84 (1.55)**
Investigations	**341 (6.90)**	**290 (5.35)**
Alanine aminotransferase increased	65 (1.31)	39 (0.72)
Aspartate aminotransferase increased	44 (0.89)	25 (0.46)
Metabolism and nutrition disorders	**168 (3.40)**	**130 (2.40)**
Decreased appetite	34 (0.69)	16 (0.30)

Exposure-Adjusted Adverse Events
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Metabolism and nutrition disorders	**168 (3.40)**	**130 (2.40)**
Hyperglycaemia	18 (0.36)	36 (0.66)
Musculoskeletal and connective tissue disorders	**432 (8.74)**	**311 (5.74)**
Arthralgia	158 (3.20)	110 (2.03)
Back pain	45 (0.91)	40 (0.74)
Myalgia	56 (1.13)	29 (0.54)
Pain in extremity	31 (0.63)	32 (0.59)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**95 (1.92)**	**125 (2.31)**
Basal cell carcinoma	23 (0.47)	57 (1.05)
Nervous system disorders	**252 (5.10)**	**196 (3.62)**
Dizziness	39 (0.79)	30 (0.55)
Headache	105 (2.12)	69 (1.27)
Psycbiatric disorders	**48 (0.97)**	**48 (0.89)**
Renal and urinary disorders	**66 (1.33)**	**36 (0.66)**
Reproductive system and breast disorders	**38 (0.77)**	**41 (0.76)**
Respiratory, tboracic and mediastinal disorders	**201 (4.06)**	**172 (3.17)**
Cough	71 (1.44)	66 (1.22)
Dyspnoea	22 (0.44)	33 (0.61)
Skin and subcutaneous tissue disorders	**636 (12.86)**	**330 (6.09)**
Pruritus	179 (3.62)	84 (1.55)
Rash	119 (2.41)	54 (1.00)
Rash maculo-papular	54 (1.09)	15 (0.28)
Vascular disorders	**93 (1.88)**	**93 (1.72)**

Exposure-Adjusted Adverse Events
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Vascular disorders	**93 (1.88)**	**93 (1.72)**
Hypertension	52 (1.05)	60 (1.11)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-21
Exposure-Adjusted Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	483	444	397	310
Total exposure[c] in person-months	1397.3	1262.2	2112.7	172.9
Endocrine disorders	**81(29.0)**	**32(31.9)**	**20(50.5)**	**2(111.7)**
Hyperthyroidism	48(70.5)	1(11.8)	2(363.2)	0(0.0)
Hypothyroidism	33(15.6)	31(33.7)	18(46.1)	2(111.7)
Gastrointestinal disorders	**200(17.8)**	**129(20.3)**	**144(38.4)**	**8(176.3)**
Abdominal pain	10(10.1)	10(14.5)	18(33.5)	0(0.0)
Constipation	27(28.0)	8(17.4)	11(41.5)	0(0.0)
Diarrhoea	92(17.4)	59(19.7)	67(37.4)	5(164.0)
Dry mouth	15(18.4)	13(43.6)	6(100.2)	0(0.0)
Nausea	40(18.5)	28(21.3)	28(34.9)	3(201.7)
Vomiting	16(16.1)	11(18.1)	14(47.3)	0(0.0)
General disorders and administration site conditions	**170(27.7)**	**69(22.0)**	**70(37.7)**	**3(560.9)**
Asthenia	37(20.7)	18(18.1)	24(38.2)	0(0.0)
Fatigue	105(38.1)	32(26.0)	26(37.2)	1(4006.9)
Oedema peripheral	17(24.0)	9(25.4)	8(56.0)	0(0.0)
Pyrexia	11(12.4)	10(17.9)	12(30.9)	2(392.2)
Infections and infestations	**6(8.9)**	**10(26.3)**	**10(36.0)**	**0(0.0)**
Nasopharyngitis	6(8.9)	10(26.3)	10(36.0)	0(0.0)
Investigations	**36(13.9)**	**30(16.8)**	**38(28.2)**	**5(80.6)**
Alanine aminotransferase increased	23(15.2)	16(15.5)	24(30.6)	2(77.5)
Aspartate aminotransferase increased	13(12.0)	14(18.5)	14(24.8)	3(82.8)
Metabolism and nutrition disorders	**20(16.5)**	**14(20.2)**	**17(27.9)**	**1(4006.9)**
Decreased appetite	16(22.1)	10(27.5)	8(38.7)	0(0.0)
Hyperglycaemia	4(8.2)	4(12.2)	9(22.3)	1(4006.9)
Musculoskeletal and connective tissue disorders	**112(16.7)**	**72(17.2)**	**104(38.4)**	**2(4006.9)**
Arthralgia	65(18.3)	41(19.2)	52(35.6)	0(0.0)
Back pain	16(15.1)	10(15.0)	18(43.1)	1(4006.9)
Myalgia	20(14.9)	12(13.5)	23(42.8)	1(4006.9)
Pain in extremity	11(14.7)	9(18.6)	11(37.6)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**8(14.3)**	**8(25.7)**	**7(49.2)**	**0(0.0)**

Exposure-Adjusted Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	486	471	443	350
Total exposure[c] in person-months	1435.9	1370.6	2437.4	176.7
Endocrine disorders	**11(21.1)**	**5(16.3)**	**6(28.6)**	**1(238.5)**
Hyperthyroidism	1(10.3)	0(0.0)	3(27.3)	0(0.0)
Hypothyroidism	10(23.6)	5(23.0)	3(30.1)	1(238.5)
Gastrointestinal disorders	**162(18.4)**	**90(17.1)**	**127(35.5)**	**4(152.1)**
Abdominal pain	11(14.7)	10(28.4)	7(27.8)	1(206.2)
Constipation	25(26.1)	7(14.1)	14(36.1)	0(0.0)
Diarrhoea	68(15.0)	47(15.6)	74(38.9)	1(282.9)
Dry mouth	6(33.3)	1(9.2)	3(33.7)	0(0.0)
Nausea	42(21.0)	21(18.8)	25(29.5)	2(111.7)
Vomiting	10(27.3)	4(23.5)	4(40.5)	0(0.0)
General disorders and administration site conditions	**150(26.7)**	**60(19.3)**	**69(32.3)**	**5(325.2)**
Asthenia	43(26.5)	12(13.4)	22(32.1)	2(181.6)
Fatigue	92(33.5)	35(26.6)	26(39.6)	0(0.0)
Oedema peripheral	8(13.4)	7(17.8)	9(26.9)	1(347.5)
Pyrexia	7(10.7)	6(12.0)	12(26.3)	2(1347.0)
Infections and infestations	**11(12.4)**	**9(15.1)**	**16(45.5)**	**0(0.0)**
Nasopharyngitis	11(12.4)	9(15.1)	16(45.5)	0(0.0)
Investigations	**17(10.3)**	**12(10.0)**	**32(29.3)**	**3(68.5)**
Alanine aminotransferase increased	11(11.0)	7(9.8)	19(30.0)	2(86.3)
Aspartate aminotransferase increased	6(9.1)	5(10.4)	13(28.2)	1(48.5)
Metabolism and nutrition disorders	**21(16.4)**	**8(9.8)**	**22(37.0)**	**1(82.8)**
Decreased appetite	6(14.7)	4(17.0)	5(24.1)	1(82.8)
Hyperglycaemia	15(17.2)	4(6.9)	17(43.9)	0(0.0)
Musculoskeletal and connective tissue disorders	**73(14.2)**	**41(11.7)**	**92(32.0)**	**5(165.8)**
Arthralgia	40(15.3)	16(8.7)	49(28.0)	5(165.8)
Back pain	14(13.9)	11(18.0)	15(34.2)	0(0.0)
Myalgia	13(19.9)	5(13.6)	11(42.6)	0(0.0)
Pain in extremity	6(7.0)	9(13.2)	17(39.4)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**20(14.3)**	**11(10.9)**	**20(22.5)**	**6(113.7)**

Exposure-Adjusted Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**8(14.3)**	**8(25.7)**	**7(49.2)**	**0(0.0)**
Basal cell carcinoma	8(14.3)	8(25.7)	7(49.2)	0(0.0)
Nervous system disorders	**53(16.2)**	**35(15.7)**	**52(32.6)**	**4(128.1)**
Dizziness	16(19.0)	10(17.3)	11(27.6)	2(270.3)
Headache	37(15.2)	25(15.1)	41(34.3)	2(83.9)
Respiratory, tboracic and mediastinal disorders	**34(15.3)**	**22(15.9)**	**32(25.6)**	**5(107.3)**
Cough	25(14.3)	16(14.7)	25(24.8)	5(107.3)
Dyspnoea	9(18.8)	6(20.5)	7(28.7)	0(0.0)
Skin and subcutaneous tissue disorders	**188(26.0)**	**86(24.2)**	**74(36.2)**	**4(132.3)**
Pruritus	97(27.1)	37(20.0)	44(37.1)	1(72.9)
Rash	60(23.3)	33(25.6)	24(36.4)	2(258.8)
Rash maculo-papular	31(28.7)	16(39.3)	6(30.3)	1(113.7)
Vascular disorders	**31(28.3)**	**11(24.4)**	**8(29.0)**	**2(154.0)**
Hypertension	31(28.3)	11(24.4)	8(29.0)	2(154.0)

Exposure-Adjusted Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**20(14.3)**	**11(10.9)**	**20(22.5)**	**6(113.7)**
Basal cell carcinoma	20(14.3)	11(10.9)	20(22.5)	6(113.7)
Nervous system disorders	**53(25.8)**	**24(24.2)**	**20(34.8)**	**2(1102.9)**
Dizziness	16(25.3)	5(13.0)	7(19.3)	2(1102.9)
Headache	37(26.1)	19(31.3)	13(61.4)	0(0.0)
Respiratory, tboracic and mediastinal disorders	**37(15.7)**	**27(18.4)**	**31(31.7)**	**4(125.5)**
Cough	26(17.3)	15(15.2)	22(32.5)	3(291.9)
Dyspnoea	11(13.0)	12(24.9)	9(30.0)	1(46.3)
Skin and subcutaneous tissue disorders	**77(23.7)**	**35(20.9)**	**39(42.8)**	**2(162.2)**
Pruritus	46(26.2)	20(25.5)	17(38.1)	1(193.1)
Rash	24(20.5)	11(14.8)	18(43.1)	1(139.9)
Rash maculo-papular	7(21.8)	4(26.6)	4(84.8)	0(0.0)
Vascular disorders	**22(14.9)**	**21(25.6)**	**17(36.3)**	**0(0.0)**
Hypertension	22(14.9)	21(25.6)	17(36.3)	0(0.0)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Number of subjects exposed to drug at the start of indicated time interval.

[c] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-22
Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	461	(95.4)	446	(91.8)
Grade 1	97	(20.1)	154	(31.7)
Grade 2	227	(47.0)	194	(39.9)
Grade 3	120	(24.8)	83	(17.1)
Grade 4	16	(3.3)	10	(2.1)
Grade 5	1	(0.2)	5	(1.0)
with no adverse events	22	(4.6)	40	(8.2)
Blood and lymphatic system disorders	**40**	**(8.3)**	**31**	**(6.4)**
Grade 1	35	(7.2)	25	(5.1)
Grade 2	5	(1.0)	5	(1.0)
Grade 3	0	(0.0)	1	(0.2)
Cardiac disorders	**32**	**(6.6)**	**29**	**(6.0)**
Grade 1	22	(4.6)	16	(3.3)
Grade 2	6	(1.2)	6	(1.2)
Grade 3	3	(0.6)	5	(1.0)
Grade 4	1	(0.2)	2	(0.4)
Ear and labyrinth disorders	**23**	**(4.8)**	**25**	**(5.1)**
Grade 1	21	(4.3)	16	(3.3)
Grade 2	2	(0.4)	9	(1.9)
Endocrine disorders	**127**	**(26.3)**	**24**	**(4.9)**
Grade 1	35	(7.2)	17	(3.5)
Grade 2	82	(17.0)	7	(1.4)
Grade 3	10	(2.1)	0	(0.0)
Hypothyroidism	82	(17.0)	17	(3.5)
Grade 1	27	(5.6)	12	(2.5)
Grade 2	55	(11.4)	5	(1.0)
Hyperthyroidism	51	(10.6)	3	(0.6)
Grade 1	35	(7.2)	3	(0.6)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hyperthyroidism	51	(10.6)	3	(0.6)
Grade 2	15	(3.1)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Eye disorders	**55**	**(11.4)**	**30**	**(6.2)**
Grade 1	42	(8.7)	27	(5.6)
Grade 2	12	(2.5)	2	(0.4)
Grade 3	1	(0.2)	1	(0.2)
Gastrointestinal disorders	**270**	**(55.9)**	**198**	**(40.7)**
Grade 1	171	(35.4)	164	(33.7)
Grade 2	76	(15.7)	33	(6.8)
Grade 3	23	(4.8)	1	(0.2)
Diarrhoea	136	(28.2)	100	(20.6)
Grade 1	101	(20.9)	89	(18.3)
Grade 2	27	(5.6)	10	(2.1)
Grade 3	8	(1.7)	1	(0.2)
Nausea	67	(13.9)	56	(11.5)
Grade 1	57	(11.8)	52	(10.7)
Grade 2	10	(2.1)	4	(0.8)
Constipation	40	(8.3)	41	(8.4)
Grade 1	33	(6.8)	39	(8.0)
Grade 2	7	(1.4)	2	(0.4)
Dry mouth	32	(6.6)	9	(1.9)
Grade 1	28	(5.8)	9	(1.9)
Grade 2	4	(0.8)	0	(0.0)
Vomiting	32	(6.6)	16	(3.3)
Grade 1	30	(6.2)	14	(2.9)
Grade 2	2	(0.4)	2	(0.4)
Abdominal pain	31	(6.4)	24	(4.9)
Grade 1	28	(5.8)	21	(4.3)
Grade 2	3	(0.6)	3	(0.6)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**234**	**(48.4)**	**220**	**(45.3)**
Grade 1	167	(34.6)	187	(38.5)
Grade 2	63	(13.0)	31	(6.4)
Grade 3	4	(0.8)	2	(0.4)
Fatigue	143	(29.6)	127	(26.1)
Grade 1	115	(23.8)	110	(22.6)
Grade 2	26	(5.4)	16	(3.3)
Grade 3	2	(0.4)	1	(0.2)
Asthenia	56	(11.6)	52	(10.7)
Grade 1	37	(7.7)	45	(9.3)
Grade 2	18	(3.7)	7	(1.4)
Grade 3	1	(0.2)	0	(0.0)
Pyrexia	33	(6.8)	26	(5.3)
Grade 1	26	(5.4)	23	(4.7)
Grade 2	7	(1.4)	3	(0.6)
Oedema peripheral	28	(5.8)	24	(4.9)
Grade 1	21	(4.3)	23	(4.7)
Grade 2	7	(1.4)	1	(0.2)
Hepatobiliary disorders	**24**	**(5.0)**	**16**	**(3.3)**
Grade 1	8	(1.7)	8	(1.6)
Grade 2	5	(1.0)	6	(1.2)
Grade 3	11	(2.3)	2	(0.4)
Infections and infestations	**174**	**(36.0)**	**170**	**(35.0)**
Grade 1	79	(16.4)	100	(20.6)
Grade 2	81	(16.8)	60	(12.3)
Grade 3	11	(2.3)	8	(1.6)
Grade 4	2	(0.4)	0	(0.0)
Grade 5	1	(0.2)	2	(0.4)
Nasopharyngitis	21	(4.3)	30	(6.2)
Grade 1	18	(3.7)	28	(5.8)
Grade 2	3	(0.6)	2	(0.4)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**53**	**(11.0)**	**60**	**(12.3)**
Grade 1	36	(7.5)	39	(8.0)
Grade 2	12	(2.5)	15	(3.1)
Grade 3	5	(1.0)	5	(1.0)
Grade 4	0	(0.0)	1	(0.2)
Investigations	**159**	**(32.9)**	**145**	**(29.8)**
Grade 1	116	(24.0)	101	(20.8)
Grade 2	23	(4.8)	25	(5.1)
Grade 3	14	(2.9)	16	(3.3)
Grade 4	6	(1.2)	3	(0.6)
Alanine aminotransferase increased	57	(11.8)	29	(6.0)
Grade 1	46	(9.5)	28	(5.8)
Grade 2	6	(1.2)	0	(0.0)
Grade 3	5	(1.0)	1	(0.2)
Aspartate aminotransferase increased	38	(7.9)	20	(4.1)
Grade 1	27	(5.6)	17	(3.5)
Grade 2	8	(1.7)	0	(0.0)
Grade 3	3	(0.6)	3	(0.6)
Metabolism and nutrition disorders	**101**	**(20.9)**	**88**	**(18.1)**
Grade 1	70	(14.5)	65	(13.4)
Grade 2	19	(3.9)	14	(2.9)
Grade 3	11	(2.3)	7	(1.4)
Grade 4	1	(0.2)	2	(0.4)
Decreased appetite	28	(5.8)	13	(2.7)
Grade 1	23	(4.8)	11	(2.3)
Grade 2	3	(0.6)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Hyperglycaemia	15	(3.1)	28	(5.8)
Grade 1	11	(2.3)	24	(4.9)
Grade 2	2	(0.4)	3	(0.6)
Grade 3	2	(0.4)	0	(0.0)
Grade 4	0	(0.0)	1	(0.2)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**217**	**(44.9)**	**183**	**(37.7)**
Grade 1	124	(25.7)	143	(29.4)
Grade 2	80	(16.6)	34	(7.0)
Grade 3	12	(2.5)	6	(1.2)
Grade 4	1	(0.2)	0	(0.0)
Arthralgia	114	(23.6)	85	(17.5)
Grade 1	75	(15.5)	70	(14.4)
Grade 2	38	(7.9)	13	(2.7)
Grade 3	1	(0.2)	2	(0.4)
Myalgia	51	(10.6)	28	(5.8)
Grade 1	41	(8.5)	26	(5.3)
Grade 2	8	(1.7)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Back pain	41	(8.5)	39	(8.0)
Grade 1	25	(5.2)	34	(7.0)
Grade 2	14	(2.9)	5	(1.0)
Grade 3	2	(0.4)	0	(0.0)
Pain in extremity	28	(5.8)	28	(5.8)
Grade 1	21	(4.3)	23	(4.7)
Grade 2	7	(1.4)	4	(0.8)
Grade 3	0	(0.0)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**64**	**(13.3)**	**68**	**(14.0)**
Grade 1	30	(6.2)	14	(2.9)
Grade 2	29	(6.0)	44	(9.1)
Grade 3	5	(1.0)	8	(1.6)
Grade 5	0	(0.0)	2	(0.4)
Basal cell carcinoma	17	(3.5)	27	(5.6)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	17	(3.5)	23	(4.7)
Grade 3	0	(0.0)	2	(0.4)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**145**	**(30.0)**	**122**	**(25.1)**
Grade 1	107	(22.2)	91	(18.7)
Grade 2	30	(6.2)	25	(5.1)
Grade 3	8	(1.7)	6	(1.2)
Headache	83	(17.2)	55	(11.3)
Grade 1	68	(14.1)	50	(10.3)
Grade 2	15	(3.1)	5	(1.0)
Dizziness	33	(6.8)	27	(5.6)
Grade 1	30	(6.2)	23	(4.7)
Grade 2	3	(0.6)	4	(0.8)
Psychiatric disorders	**41**	**(8.5)**	**37**	**(7.6)**
Grade 1	31	(6.4)	24	(4.9)
Grade 2	9	(1.9)	9	(1.9)
Grade 3	0	(0.0)	1	(0.2)
Grade 4	1	(0.2)	2	(0.4)
Grade 5	0	(0.0)	1	(0.2)
Renal and urinary disorders	**50**	**(10.4)**	**30**	**(6.2)**
Grade 1	35	(7.2)	21	(4.3)
Grade 2	8	(1.7)	7	(1.4)
Grade 3	6	(1.2)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**33**	**(6.8)**	**31**	**(6.4)**
Grade 1	23	(4.8)	21	(4.3)
Grade 2	9	(1.9)	8	(1.6)
Grade 3	0	(0.0)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Grade 1	82	(17.0)	94	(19.3)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**121**	**(25.1)**	**114**	**(23.5)**
Grade 2	35	(7.2)	15	(3.1)
Grade 3	3	(0.6)	5	(1.0)
Grade 4	1	(0.2)	0	(0.0)
Cough	61	(12.6)	58	(11.9)
Grade 1	52	(10.8)	53	(10.9)
Grade 2	9	(1.9)	5	(1.0)
Dyspnoea	22	(4.6)	27	(5.6)
Grade 1	19	(3.9)	21	(4.3)
Grade 2	3	(0.6)	6	(1.2)
Skin and subcutaneous tissue disorders	**278**	**(57.6)**	**196**	**(40.3)**
Grade 1	204	(42.2)	167	(34.4)
Grade 2	59	(12.2)	26	(5.3)
Grade 3	14	(2.9)	3	(0.6)
Grade 4	1	(0.2)	0	(0.0)
Pruritus	134	(27.7)	66	(13.6)
Grade 1	113	(23.4)	64	(13.2)
Grade 2	18	(3.7)	2	(0.4)
Grade 3	3	(0.6)	0	(0.0)
Rash	91	(18.8)	42	(8.6)
Grade 1	71	(14.7)	37	(7.6)
Grade 2	13	(2.7)	3	(0.6)
Grade 3	7	(1.4)	2	(0.4)
Rash maculo-papular	42	(8.7)	11	(2.3)
Grade 1	29	(6.0)	9	(1.9)
Grade 2	11	(2.3)	1	(0.2)
Grade 3	2	(0.4)	1	(0.2)
Vascular disorders	**74**	**(15.3)**	**72**	**(14.8)**
Grade 1	36	(7.5)	29	(6.0)
Grade 2	21	(4.3)	24	(4.9)
Grade 3	17	(3.5)	19	(3.9)
Hypertension	43	(8.9)	43	(8.8)

Participants With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence ≥ 5% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hypertension	43	(8.9)	43	(8.8)
Grade 1	12	(2.5)	7	(1.4)
Grade 2	15	(3.1)	19	(3.9)
Grade 3	16	(3.3)	17	(3.5)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a system organ class is counted a single time for that system organ class.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.2.2 Adverse Events Related to Study Intervention

Table 14.3-23
Participants With Drug-Related Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	399	(82.6)	309	(63.6)
with no adverse events	84	(17.4)	177	(36.4)
Pruritus	119	(24.6)	52	(10.7)
Fatigue	104	(21.5)	93	(19.1)
Diarrhoea	90	(18.6)	56	(11.5)
Arthralgia	79	(16.4)	39	(8.0)
Rash	78	(16.1)	34	(7.0)
Hypothyroidism	77	(15.9)	13	(2.7)
Hyperthyroidism	49	(10.1)	3	(0.6)
Asthenia	47	(9.7)	40	(8.2)
Alanine aminotransferase increased	39	(8.1)	22	(4.5)
Nausea	37	(7.7)	33	(6.8)
Rash maculo-papular	36	(7.5)	9	(1.9)
Myalgia	32	(6.6)	16	(3.3)
Aspartate aminotransferase increased	31	(6.4)	11	(2.3)

Every participant is counted a single time for each applicable row and column.
A specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-24
Participants With Drug-Related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	4	(50.0)	36	(57.1)
with no adverse events	4	(50.0)	27	(42.9)
Arthralgia	3	(37.5)	2	(3.2)
Asthenia	2	(25.0)	5	(7.9)
Arthritis	1	(12.5)	1	(1.6)
Back pain	1	(12.5)	0	(0.0)
Constipation	1	(12.5)	1	(1.6)
Diarrhoea	1	(12.5)	5	(7.9)
Fatigue	1	(12.5)	1	(1.6)
Insomnia	1	(12.5)	1	(1.6)
Myalgia	1	(12.5)	1	(1.6)
Paraesthesia	1	(12.5)	0	(0.0)
Pruritus	1	(12.5)	5	(7.9)
Abdominal pain upper	0	(0.0)	1	(1.6)
Adrenal insufficiency	0	(0.0)	1	(1.6)
Alanine aminotransferase increased	0	(0.0)	3	(4.8)
Angioedema	0	(0.0)	1	(1.6)
Aspartate aminotransferase increased	0	(0.0)	3	(4.8)
Bacterial rhinitis	0	(0.0)	1	(1.6)
Blood alkaline phosphatase increased	0	(0.0)	1	(1.6)
Blood glucose increased	0	(0.0)	1	(1.6)
Blood thyroid stimulating hormone increased	0	(0.0)	1	(1.6)
Bradycardia	0	(0.0)	1	(1.6)
Burning sensation	0	(0.0)	1	(1.6)
Chills	0	(0.0)	2	(3.2)
Cholecystitis	0	(0.0)	1	(1.6)
Chronic gastritis	0	(0.0)	1	(1.6)
Conjunctivitis	0	(0.0)	1	(1.6)
Cough	0	(0.0)	1	(1.6)
Dehydration	0	(0.0)	1	(1.6)
Dermatitis	0	(0.0)	1	(1.6)
Dizziness	0	(0.0)	1	(1.6)
Dry eye	0	(0.0)	1	(1.6)
Dry mouth	0	(0.0)	3	(4.8)
Dry skin	0	(0.0)	1	(1.6)

Participants With Drug-Related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Eczema	0	(0.0)	1	(1.6)
Eczema eyelids	0	(0.0)	1	(1.6)
Eosinophil count increased	0	(0.0)	1	(1.6)
Erythema of eyelid	0	(0.0)	1	(1.6)
Headache	0	(0.0)	2	(3.2)
Hepatitis	0	(0.0)	1	(1.6)
Hepatotoxicity	0	(0.0)	1	(1.6)
Hyperglycaemia	0	(0.0)	1	(1.6)
Hyperthyroidism	0	(0.0)	7	(11.1)
Hypothyroidism	0	(0.0)	4	(6.3)
Lichenoid keratosis	0	(0.0)	1	(1.6)
Lipase increased	0	(0.0)	1	(1.6)
Musculoskeletal pain	0	(0.0)	2	(3.2)
Myasthenia gravis	0	(0.0)	2	(3.2)
Nausea	0	(0.0)	2	(3.2)
Oral candidiasis	0	(0.0)	1	(1.6)
Pancreatitis	0	(0.0)	1	(1.6)
Pneumonia	0	(0.0)	1	(1.6)
Pneumonitis	0	(0.0)	1	(1.6)
Pyrexia	0	(0.0)	1	(1.6)
Rash	0	(0.0)	7	(11.1)
Rash maculo-papular	0	(0.0)	2	(3.2)
Rash pruritic	0	(0.0)	1	(1.6)
Skin fissures	0	(0.0)	1	(1.6)
Sleep disorder	0	(0.0)	1	(1.6)
Stomatitis	0	(0.0)	2	(3.2)
Tachycardia	0	(0.0)	1	(1.6)
Thyroiditis	0	(0.0)	1	(1.6)
Transaminases increased	0	(0.0)	1	(1.6)
Urticaria	0	(0.0)	1	(1.6)
Vitiligo	0	(0.0)	2	(3.2)
Vomiting	0	(0.0)	1	(1.6)

Participants With Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Weight decreased	0	(0.0)	3	(4.8)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-25
Participants With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	399	(82.6)	309	(63.6)
Grade 1	135	(28.0)	206	(42.4)
Grade 2	181	(37.5)	78	(16.0)
Grade 3	71	(14.7)	23	(4.7)
Grade 4	12	(2.5)	2	(0.4)
with no adverse events	84	(17.4)	177	(36.4)
Endocrine disorders	**118**	**(24.4)**	**17**	**(3.5)**
Grade 1	29	(6.0)	12	(2.5)
Grade 2	79	(16.4)	5	(1.0)
Grade 3	10	(2.1)	0	(0.0)
Hypothyroidism	77	(15.9)	13	(2.7)
Grade 1	25	(5.2)	9	(1.9)
Grade 2	52	(10.8)	4	(0.8)
Hyperthyroidism	49	(10.1)	3	(0.6)
Grade 1	34	(7.0)	3	(0.6)
Grade 2	14	(2.9)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**174**	**(36.0)**	**107**	**(22.0)**
Grade 1	109	(22.6)	89	(18.3)
Grade 2	49	(10.1)	17	(3.5)
Grade 3	16	(3.3)	1	(0.2)
Diarrhoea	90	(18.6)	56	(11.5)
Grade 1	65	(13.5)	48	(9.9)
Grade 2	20	(4.1)	7	(1.4)
Grade 3	5	(1.0)	1	(0.2)
Nausea	37	(7.7)	33	(6.8)
Grade 1	31	(6.4)	29	(6.0)
Grade 2	6	(1.2)	4	(0.8)
General disorders and administration site conditions	**161**	**(33.3)**	**141**	**(29.0)**

Participants With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**161**	**(33.3)**	**141**	**(29.0)**
Grade 1	117	(24.2)	121	(24.9)
Grade 2	42	(8.7)	19	(3.9)
Grade 3	2	(0.4)	1	(0.2)
Fatigue	104	(21.5)	93	(19.1)
Grade 1	79	(16.4)	81	(16.7)
Grade 2	24	(5.0)	11	(2.3)
Grade 3	1	(0.2)	1	(0.2)
Asthenia	47	(9.7)	40	(8.2)
Grade 1	32	(6.6)	35	(7.2)
Grade 2	14	(2.9)	5	(1.0)
Grade 3	1	(0.2)	0	(0.0)
Investigations	**93**	**(19.3)**	**68**	**(14.0)**
Grade 1	65	(13.5)	47	(9.7)
Grade 2	12	(2.5)	8	(1.6)
Grade 3	10	(2.1)	11	(2.3)
Grade 4	6	(1.2)	2	(0.4)
Alanine aminotransferase increased	39	(8.1)	22	(4.5)
Grade 1	31	(6.4)	21	(4.3)
Grade 2	4	(0.8)	0	(0.0)
Grade 3	4	(0.8)	1	(0.2)
Aspartate aminotransferase increased	31	(6.4)	11	(2.3)
Grade 1	23	(4.8)	10	(2.1)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	1	(0.2)	1	(0.2)
Metabolism and nutrition disorders	**34**	**(7.0)**	**21**	**(4.3)**
Grade 1	21	(4.3)	18	(3.7)
Grade 2	8	(1.7)	1	(0.2)
Grade 3	4	(0.8)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**119**	**(24.6)**	**62**	**(12.8)**
Grade 1	60	(12.4)	49	(10.1)
Grade 2	50	(10.4)	12	(2.5)
Grade 3	8	(1.7)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Arthralgia	79	(16.4)	39	(8.0)
Grade 1	45	(9.3)	33	(6.8)
Grade 2	33	(6.8)	6	(1.2)
Grade 3	1	(0.2)	0	(0.0)
Myalgia	32	(6.6)	16	(3.3)
Grade 1	25	(5.2)	14	(2.9)
Grade 2	5	(1.0)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Nervous system disorders	**60**	**(12.4)**	**41**	**(8.4)**
Grade 1	44	(9.1)	30	(6.2)
Grade 2	12	(2.5)	9	(1.9)
Grade 3	4	(0.8)	2	(0.4)
Respiratory, thoracic and mediastinal disorders	**35**	**(7.2)**	**17**	**(3.5)**
Grade 1	19	(3.9)	16	(3.3)
Grade 2	13	(2.7)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Skin and subcutaneous tissue disorders	**223**	**(46.2)**	**125**	**(25.7)**
Grade 1	167	(34.6)	115	(23.7)
Grade 2	42	(8.7)	9	(1.9)
Grade 3	13	(2.7)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Pruritus	119	(24.6)	52	(10.7)
Grade 1	98	(20.3)	50	(10.3)
Grade 2	18	(3.7)	2	(0.4)

Participants With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pruritus	119	(24.6)	52	(10.7)
Grade 3	3	(0.6)	0	(0.0)
Rash	78	(16.1)	34	(7.0)
Grade 1	58	(12.0)	31	(6.4)
Grade 2	13	(2.7)	2	(0.4)
Grade 3	7	(1.4)	1	(0.2)
Rash maculo-papular	36	(7.5)	9	(1.9)
Grade 1	26	(5.4)	8	(1.6)
Grade 2	8	(1.7)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a system organ class is counted a single time for that system organ class.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-26
Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	399	(82.6)	309	(63.6)
with no adverse events	84	(17.4)	177	(36.4)
Blood and lymphatic system disorders	**17**	**(3.5)**	**10**	**(2.1)**
Anaemia	6	(1.2)	2	(0.4)
Eosinophilia	4	(0.8)	1	(0.2)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Leukopenia	1	(0.2)	2	(0.4)
Lymph node pain	1	(0.2)	0	(0.0)
Lymphadenopathy	0	(0.0)	1	(0.2)
Lymphocytosis	0	(0.0)	1	(0.2)
Lymphopenia	3	(0.6)	3	(0.6)
Neutropenia	2	(0.4)	1	(0.2)
Thrombocytopenia	1	(0.2)	2	(0.4)
Cardiac disorders	**4**	**(0.8)**	**4**	**(0.8)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Palpitations	1	(0.2)	0	(0.0)
Sinus bradycardia	0	(0.0)	1	(0.2)
Sinus tachycardia	1	(0.2)	0	(0.0)
Tachycardia	2	(0.4)	1	(0.2)
Congenital, familial and genetic disorders	**1**	**(0.2)**	**0**	**(0.0)**
Albinism	1	(0.2)	0	(0.0)
Ear and lahyrinth disorders	**5**	**(1.0)**	**6**	**(1.2)**
Ear pain	1	(0.2)	0	(0.0)
Ear pruritus	1	(0.2)	0	(0.0)
Tinnitus	1	(0.2)	0	(0.0)
Vertigo	2	(0.4)	6	(1.2)
Endocrine disorders	**118**	**(24.4)**	**17**	**(3.5)**
Adrenal insufficiency	13	(2.7)	0	(0.0)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Endocrine disorders	**118**	**(24.4)**	**17**	**(3.5)**
Endocrine disorder	1	(0.2)	0	(0.0)
Goitre	1	(0.2)	0	(0.0)
Hyperthyroidism	49	(10.1)	3	(0.6)
Hypophysitis	7	(1.4)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)
Hypothyroidism	77	(15.9)	13	(2.7)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Thyroiditis	2	(0.4)	0	(0.0)
Thyroiditis subacute	1	(0.2)	0	(0.0)
Eye disorders	**18**	**(3.7)**	**10**	**(2.1)**
Blepharitis	1	(0.2)	1	(0.2)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)
Conjunctival oedema	0	(0.0)	1	(0.2)
Diplopia	0	(0.0)	1	(0.2)
Dry eye	7	(1.4)	5	(1.0)
Eczema eyelids	1	(0.2)	0	(0.0)
Erythema of eyelid	1	(0.2)	0	(0.0)
Eye inflammation	1	(0.2)	0	(0.0)
Eye irritation	2	(0.4)	2	(0.4)
Eyelid irritation	1	(0.2)	0	(0.0)
Eyelid oedema	2	(0.4)	0	(0.0)
Eyelid ptosis	1	(0.2)	0	(0.0)
Iridocyclitis	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Lacrimation increased	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Myopia	1	(0.2)	0	(0.0)
Ocular hyperaemia	1	(0.2)	0	(0.0)
Periorbital oedema	1	(0.2)	0	(0.0)
Scleritis	1	(0.2)	0	(0.0)
Vision blurred	3	(0.6)	1	(0.2)
Xerophthalmia	3	(0.6)	0	(0.0)
Gastrointestinal disorders	**174**	**(36.0)**	**107**	**(22.0)**

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**174**	**(36.0)**	**107**	**(22.0)**
Abdominal discomfort	0	(0.0)	1	(0.2)
Abdominal distension	3	(0.6)	1	(0.2)
Abdominal pain	12	(2.5)	12	(2.5)
Abdominal pain lower	1	(0.2)	0	(0.0)
Abdominal pain upper	9	(1.9)	8	(1.6)
Anal pruritus	0	(0.0)	1	(0.2)
Aphthous ulcer	1	(0.2)	1	(0.2)
Autoimmune colitis	2	(0.4)	0	(0.0)
Cheilitis	1	(0.2)	0	(0.0)
Chronic gastritis	1	(0.2)	0	(0.0)
Colitis	15	(3.1)	4	(0.8)
Colitis ulcerative	1	(0.2)	0	(0.0)
Constipation	9	(1.9)	12	(2.5)
Diarrhoea	90	(18.6)	56	(11.5)
Dry mouth	23	(4.8)	8	(1.6)
Dyspepsia	0	(0.0)	2	(0.4)
Dysphagia	1	(0.2)	1	(0.2)
Erosive oesophagitis	1	(0.2)	0	(0.0)
Faeces soft	2	(0.4)	2	(0.4)
Flatulence	3	(0.6)	2	(0.4)
Frequent bowel movements	3	(0.6)	2	(0.4)
Gastrooesophageal reflux disease	2	(0.4)	0	(0.0)
Glossodynia	2	(0.4)	1	(0.2)
Hypoaesthesia oral	0	(0.0)	1	(0.2)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Lip dry	2	(0.4)	1	(0.2)
Lip pain	0	(0.0)	1	(0.2)
Mouth ulceration	0	(0.0)	2	(0.4)
Nausea	37	(7.7)	33	(6.8)
Odynophagia	1	(0.2)	0	(0.0)
Oral lichen planus	1	(0.2)	0	(0.0)
Oral lichenoid reaction	1	(0.2)	0	(0.0)
Oral mucosa erosion	1	(0.2)	0	(0.0)
Oral pain	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Palatal swelling	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**174**	**(36.0)**	**107**	**(22.0)**
Pancreatitis	1	(0.2)	0	(0.0)
Proctitis	1	(0.2)	0	(0.0)
Stomatitis	10	(2.1)	3	(0.6)
Tongue blistering	1	(0.2)	0	(0.0)
Tongue discolouration	1	(0.2)	0	(0.0)
Vomiting	15	(3.1)	5	(1.0)
General disorders and administration site conditions	**161**	**(33.3)**	**141**	**(29.0)**
Asthenia	47	(9.7)	40	(8.2)
Axillary pain	0	(0.0)	1	(0.2)
Catheter site bruise	1	(0.2)	0	(0.0)
Chest pain	1	(0.2)	1	(0.2)
Chills	7	(1.4)	2	(0.4)
Fatigue	104	(21.5)	93	(19.1)
Feeling abnormal	1	(0.2)	0	(0.0)
Feeling cold	1	(0.2)	1	(0.2)
Influenza like illness	2	(0.4)	5	(1.0)
Infusion site urticaria	0	(0.0)	1	(0.2)
Injection site rash	0	(0.0)	1	(0.2)
Localised oedema	1	(0.2)	0	(0.0)
Malaise	0	(0.0)	2	(0.4)
Non-cardiac chest pain	1	(0.2)	0	(0.0)
Oedema peripheral	5	(1.0)	5	(1.0)
Pain	5	(1.0)	0	(0.0)
Peripheral swelling	1	(0.2)	1	(0.2)
Pyrexia	5	(1.0)	6	(1.2)
Thirst	1	(0.2)	0	(0.0)
Xerosis	0	(0.0)	1	(0.2)
Hepatobiliary disorders	**18**	**(3.7)**	**11**	**(2.3)**
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Cholestasis	1	(0.2)	0	(0.0)
Hepatic cytolysis	1	(0.2)	3	(0.6)
Hepatic pain	1	(0.2)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hepatobiliary disorders	**18**	**(3.7)**	**11**	**(2.3)**
Hepatitis	3	(0.6)	1	(0.2)
Hepatotoxicity	2	(0.4)	1	(0.2)
Hypertransaminasaemia	3	(0.6)	3	(0.6)
Immune system disorders	**3**	**(0.6)**	**0**	**(0.0)**
Sarcoidosis	3	(0.6)	0	(0.0)
Infections and infestations	**21**	**(4.3)**	**8**	**(1.6)**
Abscess soft tissue	1	(0.2)	0	(0.0)
Candida infection	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Conjunctivitis	1	(0.2)	0	(0.0)
Folliculitis	2	(0.4)	0	(0.0)
Gingivitis	1	(0.2)	1	(0.2)
Herpes virus infection	1	(0.2)	0	(0.0)
Hordeolum	0	(0.0)	1	(0.2)
Mucosal infection	1	(0.2)	0	(0.0)
Nasopharyngitis	1	(0.2)	2	(0.4)
Onychomycosis	0	(0.0)	1	(0.2)
Ophthalmic herpes zoster	0	(0.0)	1	(0.2)
Oral herpes	1	(0.2)	1	(0.2)
Otitis externa	1	(0.2)	0	(0.0)
Pharyngitis	1	(0.2)	0	(0.0)
Pneumonia	2	(0.4)	0	(0.0)
Pynria	1	(0.2)	0	(0.0)
Rash pustular	3	(0.6)	0	(0.0)
Rhinitis	2	(0.4)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Urinary tract infection	0	(0.0)	2	(0.4)
Viral infection	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**5**	**(1.0)**
Infusion related reaction	2	(0.4)	3	(0.6)
Limb injury	0	(0.0)	1	(0.2)
Neck injury	0	(0.0)	1	(0.2)
Skin abrasion	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**93**	**(19.3)**	**68**	**(14.0)**
Alanine aminotransferase increased	39	(8.1)	22	(4.5)
Amylase increased	10	(2.1)	9	(1.9)
Antinuclear antibody positive	0	(0.0)	1	(0.2)
Aspartate aminotransferase increased	31	(6.4)	11	(2.3)
Bilirubin conjugated increased	0	(0.0)	1	(0.2)
Blood alkaline phosphatase increased	7	(1.4)	3	(0.6)
Blood bilirubin increased	1	(0.2)	6	(1.2)
Blood bilirubin unconjugated increased	0	(0.0)	1	(0.2)
Blood cholesterol increased	0	(0.0)	2	(0.4)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	7	(1.4)	4	(0.8)
Blood creatinine increased	9	(1.9)	2	(0.4)
Blood glucose increased	0	(0.0)	1	(0.2)
Blood lactate dehydrogenase increased	1	(0.2)	2	(0.4)
Blood phosphorus decreased	0	(0.0)	2	(0.4)
Blood potassium decreased	1	(0.2)	0	(0.0)
Blood sodium decreased	2	(0.4)	1	(0.2)
Blood testosterone decreased	1	(0.2)	0	(0.0)
Blood thyroid stimulating hormone decreased	5	(1.0)	2	(0.4)
Blood thyroid stimulating hormone increased	9	(1.9)	9	(1.9)
Blood triglycerides increased	0	(0.0)	1	(0.2)
Body temperature increased	1	(0.2)	0	(0.0)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)
C-reactive protein increased	1	(0.2)	0	(0.0)
Eosinophil count increased	1	(0.2)	0	(0.0)
Faecal elastase concentration decreased	2	(0.4)	0	(0.0)
Gamma-glutamyltransferase increased	2	(0.4)	4	(0.8)
Glomerular filtration rate decreased	1	(0.2)	0	(0.0)
Heart rate increased	1	(0.2)	0	(0.0)
Lipase increased	15	(3.1)	12	(2.5)
Lymphocyte count decreased	4	(0.8)	2	(0.4)
Neutrophil count decreased	0	(0.0)	2	(0.4)
Platelet count decreased	4	(0.8)	2	(0.4)
Thyroxine free decreased	1	(0.2)	0	(0.0)
Thyroxine free increased	1	(0.2)	1	(0.2)
Transaminases increased	1	(0.2)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**93**	**(19.3)**	**68**	**(14.0)**
Tri-iodothyronine decreased	1	(0.2)	1	(0.2)
Tri-iodothyronine free decreased	0	(0.0)	3	(0.6)
Tri-iodothyronine free increased	0	(0.0)	1	(0.2)
Troponin I increased	1	(0.2)	0	(0.0)
Weight decreased	0	(0.0)	1	(0.2)
White blood cell count decreased	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**34**	**(7.0)**	**21**	**(4.3)**
Decreased appetite	17	(3.5)	4	(0.8)
Gout	1	(0.2)	0	(0.0)
Hyperamylasaemia	0	(0.0)	2	(0.4)
Hypercalcaemia	1	(0.2)	1	(0.2)
Hyperchloraemia	1	(0.2)	0	(0.0)
Hyperglycaemia	4	(0.8)	5	(1.0)
Hyperkalaemia	1	(0.2)	0	(0.0)
Hypernatraemia	1	(0.2)	0	(0.0)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)
Hypokalaemia	0	(0.0)	1	(0.2)
Hypomagnesaemia	2	(0.4)	1	(0.2)
Hypophosphataemia	3	(0.6)	7	(1.4)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Underweight	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**119**	**(24.6)**	**62**	**(12.8)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	79	(16.4)	39	(8.0)
Arthritis	6	(1.2)	3	(0.6)
Back pain	6	(1.2)	1	(0.2)
Bone pain	1	(0.2)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Joint effusion	0	(0.0)	1	(0.2)
Joint stiffness	3	(0.6)	1	(0.2)
Joint swelling	1	(0.2)	2	(0.4)
Limb discomfort	0	(0.0)	1	(0.2)
Muscle spasms	3	(0.6)	3	(0.6)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**119**	**(24.6)**	**62**	**(12.8)**
Muscular weakness	5	(1.0)	0	(0.0)
Musculoskeletal pain	2	(0.4)	3	(0.6)
Musculoskeletal stiffness	3	(0.6)	0	(0.0)
Myalgia	32	(6.6)	16	(3.3)
Myopathy	1	(0.2)	0	(0.0)
Myositis	4	(0.8)	0	(0.0)
Neck pain	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	1	(0.2)
Pain in extremity	5	(1.0)	2	(0.4)
Polyarthritis	2	(0.4)	0	(0.0)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Sjogren's syndrome	1	(0.2)	1	(0.2)
Spinal pain	1	(0.2)	1	(0.2)
Tendon pain	1	(0.2)	0	(0.0)
Tendonitis	1	(0.2)	0	(0.0)
Trigger finger	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.2)**	**0**	**(0.0)**
Lymphoma	1	(0.2)	0	(0.0)
Nervous system disorders	**60**	**(12.4)**	**41**	**(8.4)**
Balance disorder	0	(0.0)	1	(0.2)
Carpal tunnel syndrome	0	(0.0)	1	(0.2)
Cervicogenic headache	1	(0.2)	0	(0.0)
Cognitive disorder	0	(0.0)	1	(0.2)
Disturbance in attention	1	(0.2)	0	(0.0)
Dizziness	16	(3.3)	6	(1.2)
Dysgeusia	5	(1.0)	3	(0.6)
Facial paralysis	0	(0.0)	1	(0.2)
Headache	23	(4.8)	13	(2.7)
Hypoaesthesia	1	(0.2)	3	(0.6)
Lethargy	1	(0.2)	0	(0.0)
Memory impairment	0	(0.0)	2	(0.4)
Meningorrhagia	0	(0.0)	1	(0.2)
Migraine	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**60**	**(12.4)**	**41**	**(8.4)**
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Neuralgia	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Neuropathy peripheral	4	(0.8)	3	(0.6)
Paraesthesia	10	(2.1)	8	(1.6)
Peripheral motor neuropathy	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	2	(0.4)	1	(0.2)
Polyneuropathy	0	(0.0)	1	(0.2)
Presyncope	1	(0.2)	0	(0.0)
Radiculopathy	1	(0.2)	0	(0.0)
Somnolence	0	(0.0)	1	(0.2)
Syncope	0	(0.0)	1	(0.2)
Taste disorder	3	(0.6)	0	(0.0)
Tremor	2	(0.4)	1	(0.2)
Psychiatric disorders	**7**	**(1.4)**	**7**	**(1.4)**
Agitation	1	(0.2)	0	(0.0)
Delirium	1	(0.2)	0	(0.0)
Initial insomnia	0	(0.0)	1	(0.2)
Insomnia	3	(0.6)	5	(1.0)
Libido decreased	1	(0.2)	0	(0.0)
Mood altered	1	(0.2)	1	(0.2)
Sleep disorder	1	(0.2)	0	(0.0)
Renal and urinary disorders	**13**	**(2.7)**	**9**	**(1.9)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Glycosuria	2	(0.4)	1	(0.2)
Haematuria	0	(0.0)	1	(0.2)
Nephritis	3	(0.6)	0	(0.0)
Nocturia	1	(0.2)	0	(0.0)
Pollakiuria	0	(0.0)	1	(0.2)
Polyuria	0	(0.0)	1	(0.2)
Proteinuria	0	(0.0)	4	(0.8)
Renal impairment	1	(0.2)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Renal and urinary disorders	**13**	**(2.7)**	**9**	**(1.9)**
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Urge incontinence	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**6**	**(1.2)**	**4**	**(0.8)**
Erectile dysfunction	0	(0.0)	2	(0.4)
Genital erythema	1	(0.2)	0	(0.0)
Genital paraesthesia	1	(0.2)	0	(0.0)
Gynaecomastia	1	(0.2)	0	(0.0)
Menstruation delayed	0	(0.0)	1	(0.2)
Nipple pain	1	(0.2)	0	(0.0)
Pelvic pain	1	(0.2)	0	(0.0)
Prostatitis	1	(0.2)	0	(0.0)
Vulvovaginal inflammation	1	(0.2)	0	(0.0)
Vulvovaginal pruritus	0	(0.0)	1	(0.2)
Respiratory, tboracic and mediastinal disorders	**35**	**(7.2)**	**17**	**(3.5)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Asthma	1	(0.2)	0	(0.0)
Cough	12	(2.5)	10	(2.1)
Dyspnoea	5	(1.0)	3	(0.6)
Dyspnoea exertional	2	(0.4)	1	(0.2)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Nasal congestion	3	(0.6)	0	(0.0)
Oropharyngeal pain	1	(0.2)	0	(0.0)
Pleuritic pain	1	(0.2)	0	(0.0)
Pneumonitis	8	(1.7)	4	(0.8)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Rhinorrhoea	1	(0.2)	0	(0.0)
Sputum discoloured	1	(0.2)	0	(0.0)
Throat irritation	2	(0.4)	0	(0.0)
Wheezing	1	(0.2)	0	(0.0)
Skin and subcutaneous tissue disorders	**223**	**(46.2)**	**125**	**(25.7)**
Acne	1	(0.2)	0	(0.0)
Actinic keratosis	2	(0.4)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**223**	**(46.2)**	**125**	**(25.7)**
Alopecia	3	(0.6)	3	(0.6)
Angioedema	1	(0.2)	0	(0.0)
Chronic cutaneous lupus erythematosus	0	(0.0)	1	(0.2)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Dermal cyst	0	(0.0)	1	(0.2)
Dermatitis	4	(0.8)	6	(1.2)
Dermatitis acneiform	5	(1.0)	1	(0.2)
Dermatitis allergic	2	(0.4)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Dermatitis psoriasiform	2	(0.4)	0	(0.0)
Dry skin	8	(1.7)	17	(3.5)
Dyshidrotic eczema	1	(0.2)	0	(0.0)
Eczema	7	(1.4)	2	(0.4)
Eczema nummular	1	(0.2)	1	(0.2)
Erythema	8	(1.7)	4	(0.8)
Erythema multiforme	1	(0.2)	0	(0.0)
Hyperhidrosis	1	(0.2)	0	(0.0)
Hyperkeratosis	3	(0.6)	0	(0.0)
Lichen planus	4	(0.8)	0	(0.0)
Lichenification	1	(0.2)	0	(0.0)
Lichenoid keratosis	1	(0.2)	0	(0.0)
Macule	1	(0.2)	0	(0.0)
Nail dystrophy	1	(0.2)	0	(0.0)
Neurodermatitis	1	(0.2)	0	(0.0)
Night sweats	1	(0.2)	3	(0.6)
Pain of skin	1	(0.2)	0	(0.0)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)
Papule	0	(0.0)	1	(0.2)
Pemphigoid	1	(0.2)	0	(0.0)
Photosensitivity reaction	1	(0.2)	1	(0.2)
Prurigo	1	(0.2)	0	(0.0)
Pruritus	119	(24.6)	52	(10.7)
Psoriasis	3	(0.6)	2	(0.4)
Purpura	1	(0.2)	0	(0.0)
Rash	78	(16.1)	34	(7.0)
Rash erythematous	4	(0.8)	2	(0.4)

Participants With Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**223**	**(46.2)**	**125**	**(25.7)**
Rash follicular	1	(0.2)	0	(0.0)
Rash macular	4	(0.8)	1	(0.2)
Rash maculo-papular	36	(7.5)	9	(1.9)
Rash papular	3	(0.6)	1	(0.2)
Rash pruritic	7	(1.4)	3	(0.6)
Rosacea	1	(0.2)	0	(0.0)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)
Skin depigmentation	1	(0.2)	0	(0.0)
Skin exfoliation	2	(0.4)	0	(0.0)
Skin fissures	1	(0.2)	0	(0.0)
Skin hypopigmentation	1	(0.2)	0	(0.0)
Skin irritation	0	(0.0)	1	(0.2)
Skin lesion	5	(1.0)	0	(0.0)
Skin mass	1	(0.2)	2	(0.4)
Skin toxicity	1	(0.2)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)
Urticaria	2	(0.4)	2	(0.4)
Vitiligo	6	(1.2)	9	(1.9)
Xeroderma	2	(0.4)	0	(0.0)
Vascular disorders	**17**	**(3.5)**	**6**	**(1.2)**
Cyanosis	1	(0.2)	0	(0.0)
Flushing	2	(0.4)	1	(0.2)
Hot flush	4	(0.8)	4	(0.8)
Hypertension	7	(1.4)	1	(0.2)
Hypotension	1	(0.2)	0	(0.0)
Peripheral coldness	2	(0.4)	0	(0.0)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-27
Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	399	(82.6)	309	(63.6)
Grade 1	135	(28.0)	206	(42.4)
Grade 2	181	(37.5)	78	(16.0)
Grade 3	71	(14.7)	23	(4.7)
Grade 4	12	(2.5)	2	(0.4)
with no adverse events	84	(17.4)	177	(36.4)
Blood and lymphatic system disorders	**17**	**(3.5)**	**10**	**(2.1)**
Grade 1	15	(3.1)	9	(1.9)
Grade 2	2	(0.4)	1	(0.2)
Anaemia	6	(1.2)	2	(0.4)
Grade 1	6	(1.2)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Eosinophilia	4	(0.8)	1	(0.2)
Grade 1	4	(0.8)	1	(0.2)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Leukopenia	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Lymph node pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Lymphadenopathy	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Lymphocytosis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Lymphopenia	3	(0.6)	3	(0.6)
Grade 1	2	(0.4)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Neutropenia	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Thrombocytopenia	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Cardiac disorders	**4**	**(0.8)**	**4**	**(0.8)**

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cardiac disorders	**4**	**(0.8)**	**4**	**(0.8)**
Grade 1	4	(0.8)	2	(0.4)
Grade 3	0	(0.0)	2	(0.4)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Palpitations	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sinus bradycardia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Sinus tachycardia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tachycardia	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Congenital, familial and genetic disorders	**1**	**(0.2)**	**0**	**(0.0)**
Grade 1	1	(0.2)	0	(0.0)
Albinism	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ear and labyrintb disorders	**5**	**(1.0)**	**6**	**(1.2)**
Grade 1	5	(1.0)	2	(0.4)
Grade 2	0	(0.0)	4	(0.8)
Ear pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ear pruritus	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tinnitus	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vertigo	2	(0.4)	6	(1.2)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	0	(0.0)	4	(0.8)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Endocrine disorders	**118**	**(24.4)**	**17**	**(3.5)**
Grade 1	29	(6.0)	12	(2.5)
Grade 2	79	(16.4)	5	(1.0)
Grade 3	10	(2.1)	0	(0.0)
Adrenal insufficiency	13	(2.7)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	5	(1.0)	0	(0.0)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	3	(0.6)	1	(0.2)
Endocrine disorder	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Goitre	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperthyroidism	49	(10.1)	3	(0.6)
Grade 1	34	(7.0)	3	(0.6)
Grade 2	14	(2.9)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypophysitis	7	(1.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	5	(1.0)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Hypothyroidism	77	(15.9)	13	(2.7)
Grade 1	25	(5.2)	9	(1.9)
Grade 2	52	(10.8)	4	(0.8)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Thyroiditis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Thyroiditis subacute	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Eye disorders	**18**	**(3.7)**	**10**	**(2.1)**
Grade 1	12	(2.5)	8	(1.6)
Grade 2	6	(1.2)	2	(0.4)
Blepharitis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Conjunctival oedema	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Diplopia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Dry eye	7	(1.4)	5	(1.0)
Grade 1	7	(1.4)	3	(0.6)
Grade 2	0	(0.0)	2	(0.4)
Eczema eyelids	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Erythema of eyelid	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eye inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eye irritation	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Eyelid irritation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eyelid oedema	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Eyelid ptosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Iridocyclitis	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Iridocyclitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lacrimation increased	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Myopia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Ocular hyperaemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Periorbital oedema	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Scleritis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vision blurred	3	(0.6)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Xerophthalmia	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Gastrointestinal disorders	**174**	**(36.0)**	**107**	**(22.0)**
Grade 1	109	(22.6)	89	(18.3)
Grade 2	49	(10.1)	17	(3.5)
Grade 3	16	(3.3)	1	(0.2)
Abdominal discomfort	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Abdominal distension	3	(0.6)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Abdominal pain	12	(2.5)	12	(2.5)
Grade 1	10	(2.1)	11	(2.3)
Grade 2	2	(0.4)	1	(0.2)
Abdominal pain lower	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Abdominal pain upper	9	(1.9)	8	(1.6)
Grade 1	7	(1.4)	8	(1.6)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Abdominal pain upper	9	(1.9)	8	(1.6)
Grade 2	2	(0.4)	0	(0.0)
Anal pruritus	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Aphthous ulcer	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Autoimmune colitis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Cheilitis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Chronic gastritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Colitis	15	(3.1)	4	(0.8)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	6	(1.2)	2	(0.4)
Grade 3	5	(1.0)	0	(0.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Constipation	9	(1.9)	12	(2.5)
Grade 1	6	(1.2)	11	(2.3)
Grade 2	3	(0.6)	1	(0.2)
Diarrhoea	90	(18.6)	56	(11.5)
Grade 1	65	(13.5)	48	(9.9)
Grade 2	20	(4.1)	7	(1.4)
Grade 3	5	(1.0)	1	(0.2)
Dry mouth	23	(4.8)	8	(1.6)
Grade 1	20	(4.1)	8	(1.6)
Grade 2	3	(0.6)	0	(0.0)
Dyspepsia	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Dysphagia	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Erosive oesophagitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Faeces soft	2	(0.4)	2	(0.4)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Faeces soft	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Flatulence	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Frequent bowel movements	3	(0.6)	2	(0.4)
Grade 1	3	(0.6)	2	(0.4)
Gastrooesophageal reflux disease	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Glossodynia	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Hypoaesthesia oral	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Lip dry	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Lip pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Mouth ulceration	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Nausea	37	(7.7)	33	(6.8)
Grade 1	31	(6.4)	29	(6.0)
Grade 2	6	(1.2)	4	(0.8)
Odynophagia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Oral lichen planus	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral lichenoid reaction	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Oral mucosa erosion	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oral pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Palatal swelling	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pancreatitis	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Proctitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Stomatitis	10	(2.1)	3	(0.6)
Grade 1	5	(1.0)	2	(0.4)
Grade 2	5	(1.0)	1	(0.2)
Tongue blistering	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tongue discolouration	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vomiting	15	(3.1)	5	(1.0)
Grade 1	13	(2.7)	5	(1.0)
Grade 2	2	(0.4)	0	(0.0)
General disorders and administration site conditions	**161**	**(33.3)**	**141**	**(29.0)**
Grade 1	117	(24.2)	121	(24.9)
Grade 2	42	(8.7)	19	(3.9)
Grade 3	2	(0.4)	1	(0.2)
Asthenia	47	(9.7)	40	(8.2)
Grade 1	32	(6.6)	35	(7.2)
Grade 2	14	(2.9)	5	(1.0)
Grade 3	1	(0.2)	0	(0.0)
Axillary pain	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Catheter site bruise	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Chest pain	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Chills	7	(1.4)	2	(0.4)
Grade 1	7	(1.4)	2	(0.4)
Fatigue	104	(21.5)	93	(19.1)
Grade 1	79	(16.4)	81	(16.7)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Fatigue	104	(21.5)	93	(19.1)
Grade 2	24	(5.0)	11	(2.3)
Grade 3	1	(0.2)	1	(0.2)
Feeling abnormal	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Feeling cold	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Influenza like illness	2	(0.4)	5	(1.0)
Grade 1	1	(0.2)	4	(0.8)
Grade 2	1	(0.2)	1	(0.2)
Infusion site urticaria	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Injection site rash	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Localised oedema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Malaise	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Non-cardiac chest pain	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oedema peripheral	5	(1.0)	5	(1.0)
Grade 1	4	(0.8)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Pain	5	(1.0)	0	(0.0)
Grade 1	4	(0.8)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Peripheral swelling	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Pyrexia	5	(1.0)	6	(1.2)
Grade 1	3	(0.6)	5	(1.0)
Grade 2	2	(0.4)	1	(0.2)
Thirst	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Xerosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hepatobiliary disorders	**18**	**(3.7)**	**11**	**(2.3)**
Grade 1	4	(0.8)	5	(1.0)
Grade 2	3	(0.6)	4	(0.8)
Grade 3	11	(2.3)	2	(0.4)
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	7	(1.4)	2	(0.4)
Cholestasis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hepatic cytolysis	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Hepatic pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hepatitis	3	(0.6)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Hypertransaminasaemia	3	(0.6)	3	(0.6)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	2	(0.4)	2	(0.4)
Immune system disorders	**3**	**(0.6)**	**0**	**(0.0)**
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Sarcoidosis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**21**	**(4.3)**	**8**	**(1.6)**
Grade 1	9	(1.9)	6	(1.2)
Grade 2	10	(2.1)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Abscess soft tissue	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Candida infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Conjunctivitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Folliculitis	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Gingivitis	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Herpes virus infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hordeolum	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Mucosal infection	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Nasopharyngitis	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Onychomycosis	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Ophthalmic herpes zoster	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Oral herpes	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Otitis externa	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pharyngitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pneumonia	2	(0.4)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pneumonia	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pyuria	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Rash pustular	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Rhinitis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Urinary tract infection	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Viral infection	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**5**	**(1.0)**
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	3	(0.6)
Infusion related reaction	2	(0.4)	3	(0.6)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	3	(0.6)
Limb injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Neck injury	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Skin abrasion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Investigations	**93**	**(19.3)**	**68**	**(14.0)**
Grade 1	65	(13.5)	47	(9.7)
Grade 2	12	(2.5)	8	(1.6)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**93**	**(19.3)**	**68**	**(14.0)**
Grade 3	10	(2.1)	11	(2.3)
Grade 4	6	(1.2)	2	(0.4)
Alanine aminotransferase increased	39	(8.1)	22	(4.5)
Grade 1	31	(6.4)	21	(4.3)
Grade 2	4	(0.8)	0	(0.0)
Grade 3	4	(0.8)	1	(0.2)
Amylase increased	10	(2.1)	9	(1.9)
Grade 1	6	(1.2)	4	(0.8)
Grade 2	1	(0.2)	3	(0.6)
Grade 3	2	(0.4)	1	(0.2)
Grade 4	1	(0.2)	1	(0.2)
Antinuclear antibody positive	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Aspartate aminotransferase increased	31	(6.4)	11	(2.3)
Grade 1	23	(4.8)	10	(2.1)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	1	(0.2)	1	(0.2)
Bilirubin conjugated increased	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Blood alkaline phosphatase increased	7	(1.4)	3	(0.6)
Grade 1	6	(1.2)	3	(0.6)
Grade 3	1	(0.2)	0	(0.0)
Blood bilirubin increased	1	(0.2)	6	(1.2)
Grade 1	0	(0.0)	5	(1.0)
Grade 2	1	(0.2)	1	(0.2)
Blood bilirubin unconjugated increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood cholesterol increased	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	7	(1.4)	4	(0.8)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	2	(0.4)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Blood creatine phosphokinase increased	7	(1.4)	4	(0.8)
Grade 4	1	(0.2)	0	(0.0)
Blood creatinine increased	9	(1.9)	2	(0.4)
Grade 1	8	(1.7)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Blood glucose increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Blood lactate dehydrogenase increased	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Blood phosphorus decreased	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Blood potassium decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Blood sodium decreased	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Blood testosterone decreased	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Blood thyroid stimulating hormone decreased	5	(1.0)	2	(0.4)
Grade 1	5	(1.0)	2	(0.4)
Blood thyroid stimulating hormone increased	9	(1.9)	9	(1.9)
Grade 1	8	(1.7)	9	(1.9)
Grade 2	1	(0.2)	0	(0.0)
Blood triglycerides increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Body temperature increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
C-reactive protein increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eosinophil count increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Faecal elastase concentration decreased	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Gamma-glutamyltransferase increased	2	(0.4)	4	(0.8)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gamma-glutamyltransferase increased	2	(0.4)	4	(0.8)
Grade 1	0	(0.0)	4	(0.8)
Grade 2	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Glomerular filtration rate decreased	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Heart rate increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Lipase increased	15	(3.1)	12	(2.5)
Grade 1	9	(1.9)	3	(0.6)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	6	(1.2)
Grade 4	4	(0.8)	2	(0.4)
Lymphocyte count decreased	4	(0.8)	2	(0.4)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Neutrophil count decreased	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Platelet count decreased	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Thyroxine free decreased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Thyroxine free increased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Transaminases increased	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Tri-iodothyronine decreased	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tri-iodothyronine free decreased	0	(0.0)	3	(0.6)
Grade 1	0	(0.0)	3	(0.6)
Tri-iodothyronine free increased	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Troponin I increased	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Weight decreased	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
White blood cell count decreased	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**34**	**(7.0)**	**21**	**(4.3)**
Grade 1	21	(4.3)	18	(3.7)
Grade 2	8	(1.7)	1	(0.2)
Grade 3	4	(0.8)	2	(0.4)
Grade 4	1	(0.2)	0	(0.0)
Decreased appetite	17	(3.5)	4	(0.8)
Grade 1	13	(2.7)	3	(0.6)
Grade 2	3	(0.6)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Gout	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hyperamylasaemia	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Hypercalcaemia	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Hyperchloraemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperglycaemia	4	(0.8)	5	(1.0)
Grade 1	3	(0.6)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Hyperkalaemia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hypernatraemia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hypokalaemia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Hypomagnesaemia	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Hypophosphataemia	3	(0.6)	7	(1.4)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hypophosphataemia	3	(0.6)	7	(1.4)
Grade 1	1	(0.2)	5	(1.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	2	(0.4)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Underweight	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**119**	**(24.6)**	**62**	**(12.8)**
Grade 1	60	(12.4)	49	(10.1)
Grade 2	50	(10.4)	12	(2.5)
Grade 3	8	(1.7)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Arthralgia	79	(16.4)	39	(8.0)
Grade 1	45	(9.3)	33	(6.8)
Grade 2	33	(6.8)	6	(1.2)
Grade 3	1	(0.2)	0	(0.0)
Arthritis	6	(1.2)	3	(0.6)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	3	(0.6)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Back pain	6	(1.2)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	3	(0.6)	0	(0.0)
Bone pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Joint effusion	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Joint effusion	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Joint stiffness	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Joint swelling	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Limb discomfort	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Muscle spasms	3	(0.6)	3	(0.6)
Grade 1	3	(0.6)	3	(0.6)
Muscular weakness	5	(1.0)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Musculoskeletal pain	2	(0.4)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	1	(0.2)	1	(0.2)
Musculoskeletal stiffness	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Myalgia	32	(6.6)	16	(3.3)
Grade 1	25	(5.2)	14	(2.9)
Grade 2	5	(1.0)	2	(0.4)
Grade 3	2	(0.4)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Myositis	4	(0.8)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Neck pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Pain in extremity	5	(1.0)	2	(0.4)
Grade 1	4	(0.8)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Polyarthritis	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Sjogren's syndrome	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Spinal pain	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Tendon pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Tendonitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Trigger finger	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.2)**	**0**	**(0.0)**
Grade 3	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Nervous system disorders	**60**	**(12.4)**	**41**	**(8.4)**
Grade 1	44	(9.1)	30	(6.2)
Grade 2	12	(2.5)	9	(1.9)
Grade 3	4	(0.8)	2	(0.4)
Balance disorder	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Carpal tunnel syndrome	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Cervicogenic headache	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Cognitive disorder	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Disturbance in attention	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Disturbance in attention	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Dizziness	16	(3.3)	6	(1.2)
Grade 1	14	(2.9)	6	(1.2)
Grade 2	2	(0.4)	0	(0.0)
Dysgeusia	5	(1.0)	3	(0.6)
Grade 1	5	(1.0)	3	(0.6)
Facial paralysis	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Headache	23	(4.8)	13	(2.7)
Grade 1	17	(3.5)	10	(2.1)
Grade 2	6	(1.2)	3	(0.6)
Hypoaesthesia	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	3	(0.6)
Lethargy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Memory impairment	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	2	(0.4)
Meningorrhagia	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Migraine	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Neuralgia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Neuropathy peripheral	4	(0.8)	3	(0.6)
Grade 1	3	(0.6)	0	(0.0)
Grade 2	1	(0.2)	3	(0.6)
Paraesthesia	10	(2.1)	8	(1.6)
Grade 1	9	(1.9)	8	(1.6)
Grade 2	1	(0.2)	0	(0.0)
Peripheral motor neuropathy	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Peripheral motor neuropathy	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Polyneuropathy	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Presyncope	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Radiculopathy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Somnolence	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Syncope	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Taste disorder	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Tremor	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Psychiatric disorders	**7**	**(1.4)**	**7**	**(1.4)**
Grade 1	3	(0.6)	6	(1.2)
Grade 2	4	(0.8)	1	(0.2)
Agitation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Delirium	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Initial insomnia	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Insomnia	3	(0.6)	5	(1.0)
Grade 1	1	(0.2)	4	(0.8)
Grade 2	2	(0.4)	1	(0.2)
Libido decreased	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Mood altered	1	(0.2)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Mood altered	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Sleep disorder	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Renal and urinary disorders	**13**	**(2.7)**	**9**	**(1.9)**
Grade 1	5	(1.0)	7	(1.4)
Grade 2	3	(0.6)	2	(0.4)
Grade 3	4	(0.8)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Acute kidney injury	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Glycosuria	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Haematuria	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Nephritis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Nocturia	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pollakiuria	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Polyuria	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Proteinuria	0	(0.0)	4	(0.8)
Grade 1	0	(0.0)	3	(0.6)
Grade 2	0	(0.0)	1	(0.2)
Renal impairment	1	(0.2)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Renal impairment	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Urge incontinence	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**6**	**(1.2)**	**4**	**(0.8)**
Grade 1	3	(0.6)	2	(0.4)
Grade 2	3	(0.6)	2	(0.4)
Erectile dysfunction	0	(0.0)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Genital erythema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Genital paraesthesia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Gynaecomastia	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Menstruation delayed	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Nipple pain	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pelvic pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Prostatitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Vulvovaginal inflammation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Vulvovaginal pruritus	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Respiratory, tboracic and mediastinal disorders	**35**	**(7.2)**	**17**	**(3.5)**
Grade 1	19	(3.9)	16	(3.3)
Grade 2	13	(2.7)	1	(0.2)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**35**	**(7.2)**	**17**	**(3.5)**
Grade 3	2	(0.4)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Asthma	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Cough	12	(2.5)	10	(2.1)
Grade 1	8	(1.7)	10	(2.1)
Grade 2	4	(0.8)	0	(0.0)
Dyspnoea	5	(1.0)	3	(0.6)
Grade 1	4	(0.8)	3	(0.6)
Grade 2	1	(0.2)	0	(0.0)
Dyspnoea exertional	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Nasal congestion	3	(0.6)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Oropharyngeal pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pleuritic pain	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pneumonitis	8	(1.7)	4	(0.8)
Grade 1	4	(0.8)	3	(0.6)
Grade 2	3	(0.6)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Rhinorrhoea	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Sputum discoloured	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Sputum discoloured	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Throat irritation	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Wheezing	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin and subcutaneous tissue disorders	**223**	**(46.2)**	**125**	**(25.7)**
Grade 1	167	(34.6)	115	(23.7)
Grade 2	42	(8.7)	9	(1.9)
Grade 3	13	(2.7)	1	(0.2)
Grade 4	1	(0.2)	0	(0.0)
Acne	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Actinic keratosis	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Alopecia	3	(0.6)	3	(0.6)
Grade 1	3	(0.6)	3	(0.6)
Angioedema	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Chronic cutaneous lupus erythematosus	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dermal cyst	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Dermatitis	4	(0.8)	6	(1.2)
Grade 1	4	(0.8)	4	(0.8)
Grade 2	0	(0.0)	2	(0.4)
Dermatitis acneiform	5	(1.0)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Dermatitis allergic	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Dermatitis psoriasiform	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Dry skin	8	(1.7)	17	(3.5)
Grade 1	8	(1.7)	17	(3.5)
Dyshidrotic eczema	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Eczema	7	(1.4)	2	(0.4)
Grade 1	7	(1.4)	2	(0.4)
Eczema nummular	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Erythema	8	(1.7)	4	(0.8)
Grade 1	8	(1.7)	4	(0.8)
Erythema multiforme	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperhidrosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Hyperkeratosis	3	(0.6)	0	(0.0)
Grade 1	3	(0.6)	0	(0.0)
Lichen planus	4	(0.8)	0	(0.0)
Grade 2	4	(0.8)	0	(0.0)
Lichenification	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Lichenoid keratosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Macule	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Nail dystrophy	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Neurodermatitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Night sweats	1	(0.2)	3	(0.6)
Grade 1	1	(0.2)	2	(0.4)
Grade 2	0	(0.0)	1	(0.2)
Pain of skin	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Papule	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Pemphigoid	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Photosensitivity reaction	1	(0.2)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Prurigo	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pruritus	119	(24.6)	52	(10.7)
Grade 1	98	(20.3)	50	(10.3)
Grade 2	18	(3.7)	2	(0.4)
Grade 3	3	(0.6)	0	(0.0)
Psoriasis	3	(0.6)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Purpura	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Rash	78	(16.1)	34	(7.0)
Grade 1	58	(12.0)	31	(6.4)
Grade 2	13	(2.7)	2	(0.4)
Grade 3	7	(1.4)	1	(0.2)
Rash erythematous	4	(0.8)	2	(0.4)
Grade 1	4	(0.8)	2	(0.4)
Rash follicular	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Rash macular	4	(0.8)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Rash maculo-papular	36	(7.5)	9	(1.9)
Grade 1	26	(5.4)	8	(1.6)
Grade 2	8	(1.7)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Rash papular	3	(0.6)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Rash pruritic	7	(1.4)	3	(0.6)
Grade 1	3	(0.6)	2	(0.4)
Grade 2	2	(0.4)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Rosacea	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Skin depigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin exfoliation	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Skin fissures	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Skin hypopigmentation	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin irritation	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Skin lesion	5	(1.0)	0	(0.0)
Grade 1	4	(0.8)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Skin mass	1	(0.2)	2	(0.4)
Grade 1	1	(0.2)	2	(0.4)
Skin toxicity	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Urticaria	2	(0.4)	2	(0.4)
Grade 1	2	(0.4)	2	(0.4)
Vitiligo	6	(1.2)	9	(1.9)
Grade 1	6	(1.2)	9	(1.9)
Xeroderma	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)
Vascular disorders	**17**	**(3.5)**	**6**	**(1.2)**

Participants With Drug-Related Adverse Events by SOC and PT by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vascular disorders	**17**	**(3.5)**	**6**	**(1.2)**
Grade 1	12	(2.5)	6	(1.2)
Grade 2	3	(0.6)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Cyanosis	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Flushing	2	(0.4)	1	(0.2)
Grade 1	2	(0.4)	1	(0.2)
Hot flush	4	(0.8)	4	(0.8)
Grade 1	4	(0.8)	4	(0.8)
Hypertension	7	(1.4)	1	(0.2)
Grade 1	3	(0.6)	1	(0.2)
Grade 2	3	(0.6)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Peripheral coldness	2	(0.4)	0	(0.0)
Grade 1	2	(0.4)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a system organ class is counted a single time for that system organ class.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.2.3 Grade 3 to 5 Adverse Events

Table 14.3-28
Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	137	(28.4)	98	(20.2)
with no adverse events	346	(71.6)	388	(79.8)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(0.2)**
Lymphopenia	0	(0.0)	1	(0.2)
Cardiac disorders	**4**	**(0.8)**	**7**	**(1.4)**
Acute myocardial infarction	0	(0.0)	2	(0.4)
Atrial fibrillation	4	(0.8)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Cardiomyopathy	1	(0.2)	0	(0.0)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Mitral valve prolapse	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	5	(1.0)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	1	(0.2)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Eye disorders	**1**	**(0.2)**	**1**	**(0.2)**
Glaucoma	1	(0.2)	1	(0.2)
Gastrointestinal disorders	**23**	**(4.8)**	**1**	**(0.2)**
Anal fistula	1	(0.2)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Diarrhoea	8	(1.7)	1	(0.2)
Haematemesis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Inguinal hernia	1	(0.2)	0	(0.0)
Lip dry	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	2	(0.4)	0	(0.0)

Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**23**	**(4.8)**	**1**	**(0.2)**
Proctitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**4**	**(0.8)**	**2**	**(0.4)**
Asthenia	1	(0.2)	0	(0.0)
Chest pain	0	(0.0)	1	(0.2)
Fatigue	2	(0.4)	1	(0.2)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)
Hepatobiliary disorders	**11**	**(2.3)**	**2**	**(0.4)**
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Infections and infestations	**14**	**(2.9)**	**10**	**(2.1)**
Abdominal wall abscess	0	(0.0)	1	(0.2)
Anorectal infection	1	(0.2)	0	(0.0)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Cellulitis	3	(0.6)	1	(0.2)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Dermo-hypodermitis	0	(0.0)	1	(0.2)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Infected seroma	0	(0.0)	1	(0.2)
Lower respiratory tract infection	1	(0.2)	0	(0.0)
Pneumonia	1	(0.2)	1	(0.2)
Postoperative wound infection	1	(0.2)	0	(0.0)
Pyelonephritis	0	(0.0)	1	(0.2)
Rash pustular	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Urinary tract infection	0	(0.0)	1	(0.2)
Viral infection	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**5**	**(1.0)**	**6**	**(1.2)**
Anastomotic leak	0	(0.0)	1	(0.2)
Ankle fracture	1	(0.2)	0	(0.0)

Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**5**	**(1.0)**	**6**	**(1.2)**
Arthropod bite	0	(0.0)	1	(0.2)
Foreign body	1	(0.2)	0	(0.0)
Lower limb fracture	0	(0.0)	1	(0.2)
Procedural pain	1	(0.2)	0	(0.0)
Seroma	1	(0.2)	0	(0.0)
Soft tissue injury	0	(0.0)	1	(0.2)
Upper limb fracture	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)
Wrist fracture	1	(0.2)	0	(0.0)
Investigations	**20**	**(4.1)**	**19**	**(3.9)**
Alanine aminotransferase increased	5	(1.0)	1	(0.2)
Amylase increased	3	(0.6)	2	(0.4)
Aspartate aminotransferase increased	3	(0.6)	3	(0.6)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood creatine phosphokinase increased	4	(0.8)	4	(0.8)
Blood sodium decreased	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)
Glomerular filtration rate decreased	1	(0.2)	0	(0.0)
Lipase increased	5	(1.0)	8	(1.6)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Transaminases increased	1	(0.2)	0	(0.0)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**12**	**(2.5)**	**9**	**(1.9)**
Decreased appetite	2	(0.4)	0	(0.0)
Dehydration	1	(0.2)	0	(0.0)
Hyperglycaemia	2	(0.4)	1	(0.2)
Hyperkalaemia	1	(0.2)	0	(0.0)
Hyperlipasaemia	0	(0.0)	1	(0.2)
Hypoalbuminaemia	1	(0.2)	0	(0.0)
Hypokalaemia	1	(0.2)	0	(0.0)
Hypophosphataemia	3	(0.6)	3	(0.6)
Iron deficiency	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	2	(0.4)	4	(0.8)

Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**13**	**(2.7)**	**6**	**(1.2)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	1	(0.2)	2	(0.4)
Arthritis	1	(0.2)	0	(0.0)
Back pain	2	(0.4)	0	(0.0)
Compartment syndrome	1	(0.2)	0	(0.0)
Fibromyalgia	0	(0.0)	1	(0.2)
Flank pain	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)
Myalgia	2	(0.4)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Pain in extremity	0	(0.0)	1	(0.2)
Polyarthritis	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**5**	**(1.0)**	**10**	**(2.1)**
Basal cell carcinoma	0	(0.0)	2	(0.4)
Breast cancer	1	(0.2)	0	(0.0)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Lymphoma	1	(0.2)	0	(0.0)
Malignant melanoma	0	(0.0)	1	(0.2)
Meningioma	1	(0.2)	0	(0.0)
Prostate cancer	1	(0.2)	1	(0.2)
Recurrent cancer	1	(0.2)	2	(0.4)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)
Nervous system disorders	**8**	**(1.7)**	**6**	**(1.2)**
Carpal tunnel syndrome	1	(0.2)	0	(0.0)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Meningorrhagia	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)

Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**8**	**(1.7)**	**6**	**(1.2)**
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Presyncope	0	(0.0)	1	(0.2)
Seizure	0	(0.0)	1	(0.2)
Syncope	2	(0.4)	2	(0.4)
Psychiatric disorders	**1**	**(0.2)**	**4**	**(0.8)**
Anxiety	0	(0.0)	1	(0.2)
Completed suicide	0	(0.0)	1	(0.2)
Depression	1	(0.2)	0	(0.0)
Mania	0	(0.0)	1	(0.2)
Suicidal ideation	0	(0.0)	1	(0.2)
Renal and urinary disorders	**7**	**(1.4)**	**2**	**(0.4)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Haematuria	0	(0.0)	1	(0.2)
Nephritis	1	(0.2)	0	(0.0)
Nephrolithiasis	1	(0.2)	1	(0.2)
Renal failure	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**1**	**(0.2)**	**2**	**(0.4)**
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Vaginal prolapse	0	(0.0)	1	(0.2)
Respiratory, thoracic and mediastinal disorders	**4**	**(0.8)**	**5**	**(1.0)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Asthma	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	2	(0.4)
Hypoxia	0	(0.0)	1	(0.2)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pleural effusion	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Pulmonary embolism	0	(0.0)	2	(0.4)
Pulmonary oedema	0	(0.0)	1	(0.2)

Participants With Grade 3-5 Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**15**	**(3.1)**	**3**	**(0.6)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)
Vascular disorders	**17**	**(3.5)**	**19**	**(3.9)**
Embolism	0	(0.0)	1	(0.2)
Haematoma	0	(0.0)	1	(0.2)
Hypertension	16	(3.3)	17	(3.5)
Hypotension	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Recurrent Cancer: recurrence of disease under the study

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-29
Participants With Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	137	(28.4)	98	(20.2)
with no adverse events	346	(71.6)	388	(79.8)
Hypertension	16	(3.3)	17	(3.5)
Diarrhoea	8	(1.7)	1	(0.2)
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Rash	7	(1.4)	2	(0.4)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Alanine aminotransferase increased	5	(1.0)	1	(0.2)
Colitis	5	(1.0)	0	(0.0)
Lipase increased	5	(1.0)	8	(1.6)
Atrial fibrillation	4	(0.8)	1	(0.2)
Blood creatine phosphokinase increased	4	(0.8)	4	(0.8)
Amylase increased	3	(0.6)	2	(0.4)
Aspartate aminotransferase increased	3	(0.6)	3	(0.6)
Cellulitis	3	(0.6)	1	(0.2)
Hypophosphataemia	3	(0.6)	3	(0.6)
Pruritus	3	(0.6)	0	(0.0)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Back pain	2	(0.4)	0	(0.0)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Decreased appetite	2	(0.4)	0	(0.0)
Fatigue	2	(0.4)	1	(0.2)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Hyperglycaemia	2	(0.4)	1	(0.2)
Hypopituitarism	2	(0.4)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Pancreatitis	2	(0.4)	0	(0.0)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Syncope	2	(0.4)	2	(0.4)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)

Participants With Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Type 2 diabetes mellitus	2	(0.4)	4	(0.8)
Acute respiratory failure	1	(0.2)	0	(0.0)
Anal fistula	1	(0.2)	0	(0.0)
Ankle fracture	1	(0.2)	0	(0.0)
Anorectal infection	1	(0.2)	0	(0.0)
Arthralgia	1	(0.2)	2	(0.4)
Arthritis	1	(0.2)	0	(0.0)
Asthenia	1	(0.2)	0	(0.0)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood sodium decreased	1	(0.2)	0	(0.0)
Breast cancer	1	(0.2)	0	(0.0)
Cardiomyopathy	1	(0.2)	0	(0.0)
Carpal tunnel syndrome	1	(0.2)	0	(0.0)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Compartment syndrome	1	(0.2)	0	(0.0)
Dehydration	1	(0.2)	0	(0.0)
Depression	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Flank pain	1	(0.2)	0	(0.0)
Foreign body	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)
Glaucoma	1	(0.2)	1	(0.2)
Glomerular filtration rate decreased	1	(0.2)	0	(0.0)
Haematemesis	1	(0.2)	0	(0.0)
Hyperkalaemia	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypoalbuminaemia	1	(0.2)	0	(0.0)
Hypokalaemia	1	(0.2)	0	(0.0)
Hypophysitis	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Inguinal hernia	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Iron deficiency	1	(0.2)	0	(0.0)
Lip dry	1	(0.2)	0	(0.0)

Participants With Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lower respiratory tract infection	1	(0.2)	0	(0.0)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Meningioma	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Nephrolithiasis	1	(0.2)	1	(0.2)
Osteoarthritis	1	(0.2)	0	(0.0)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pleural effusion	1	(0.2)	0	(0.0)
Pneumonia	1	(0.2)	1	(0.2)
Pneumonitis	1	(0.2)	0	(0.0)
Polyarthritis	1	(0.2)	0	(0.0)
Postoperative wound infection	1	(0.2)	0	(0.0)
Procedural pain	1	(0.2)	0	(0.0)
Proctitis	1	(0.2)	0	(0.0)
Prostate cancer	1	(0.2)	1	(0.2)
Rash pustular	1	(0.2)	0	(0.0)
Recurrent cancer	1	(0.2)	2	(0.4)
Renal failure	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Seroma	1	(0.2)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)
Transaminases increased	1	(0.2)	0	(0.0)
Viral infection	1	(0.2)	0	(0.0)
Wrist fracture	1	(0.2)	0	(0.0)
Abdominal wall abscess	0	(0.0)	1	(0.2)
Acute myocardial infarction	0	(0.0)	2	(0.4)
Anastomotic leak	0	(0.0)	1	(0.2)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Anxiety	0	(0.0)	1	(0.2)
Arthropod bite	0	(0.0)	1	(0.2)

Participants With Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Asthma	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Basal cell carcinoma	0	(0.0)	2	(0.4)
Cardiac failure	0	(0.0)	1	(0.2)
Chest pain	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	2	(0.4)
Completed suicide	0	(0.0)	1	(0.2)
Dermo-hypodermitis	0	(0.0)	1	(0.2)
Embolism	0	(0.0)	1	(0.2)
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Fibromyalgia	0	(0.0)	1	(0.2)
Haematoma	0	(0.0)	1	(0.2)
Haematuria	0	(0.0)	1	(0.2)
Hyperlipasaemia	0	(0.0)	1	(0.2)
Hypoxia	0	(0.0)	1	(0.2)
Infected seroma	0	(0.0)	1	(0.2)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)
Lower limb fracture	0	(0.0)	1	(0.2)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Lymphopenia	0	(0.0)	1	(0.2)
Malignant melanoma	0	(0.0)	1	(0.2)
Mania	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Mitral valve prolapse	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Pain in extremity	0	(0.0)	1	(0.2)
Presyncope	0	(0.0)	1	(0.2)
Pulmonary embolism	0	(0.0)	2	(0.4)
Pulmonary oedema	0	(0.0)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.2)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Seizure	0	(0.0)	1	(0.2)
Soft tissue injury	0	(0.0)	1	(0.2)
Suicidal ideation	0	(0.0)	1	(0.2)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)

Participants With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Upper limb fracture	0	(0.0)	1	(0.2)
Urinary tract infection	0	(0.0)	1	(0.2)
Vaginal prolapse	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Recurrent Cancer: recurrence of disease under the study

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

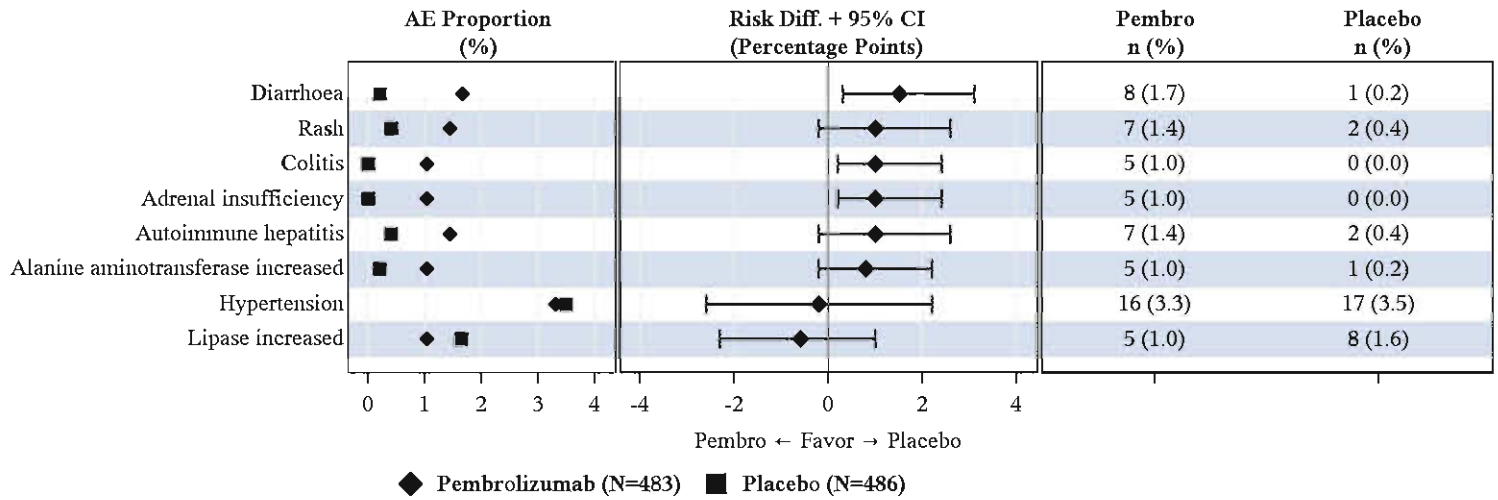
Table 14.3-30
Participants With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	1	(12.5)	15	(23.8)
with no adverse events	7	(87.5)	48	(76.2)
Dysphagia	1	(12.5)	0	(0.0)
Seizure	1	(12.5)	0	(0.0)
Alanine aminotransferase increased	0	(0.0)	1	(1.6)
Anaemia	0	(0.0)	1	(1.6)
Appendicitis	0	(0.0)	1	(1.6)
Aspartate aminotransferase increased	0	(0.0)	2	(3.2)
COVID-19	0	(0.0)	1	(1.6)
Cardiac failure	0	(0.0)	1	(1.6)
Death	0	(0.0)	1	(1.6)
Embolism	0	(0.0)	1	(1.6)
Hepatotoxicity	0	(0.0)	1	(1.6)
Hypophosphataemia	0	(0.0)	1	(1.6)
Lipase increased	0	(0.0)	1	(1.6)
Lung adenocarcinoma	0	(0.0)	1	(1.6)
Myasthenia gravis	0	(0.0)	1	(1.6)
Pancreatitis	0	(0.0)	1	(1.6)
Pneumonia	0	(0.0)	1	(1.6)
Pneumonitis	0	(0.0)	1	(1.6)
Pneumonitis aspiration	0	(0.0)	1	(1.6)
Tooth abscess	0	(0.0)	1	(1.6)
Transaminases increased	0	(0.0)	1	(1.6)
Urinary tract infection	0	(0.0)	1	(1.6)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Figure 14.3-2
Rainfall Plot for Grade 3-5 Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 1% in One or More Treatment Groups)
(APaT Population)



Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-31
Time to Onset of Grade 3-5 Adverse Events
(APaT Population)

	Pembrolizumab n [a] (%)	Placebo n [a] (%)
Participants in population	483	486
Participants with Grade 3-5 Adverse Event(%)	137 (28.4)	98 (20.2)
Time to Onset of First Grade 3-5 Adverse Event (days)[b]		
Mean	144.6	193.3
Median	125.0	168.5
SD	111.0	145.6
Range	1.0 to 452.0	1.0 to 945.0

[a] (%) = Number of participants with grades 3-5 adverse events/Number of participants in population.

[b] Time to onset statistics are based on number of participants with grade 3-5 adverse events.

Non-serious adverse events up to 30 days of last dose and serious adverse events up to 90 days of last dose are included.

MedDRA 25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Grades are based on NCI CTCAE version 4.03.

Adverse events occurred after the first dose of second course are excluded.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adttae]

Table 14.3-32
Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Number of participants exposed	483	486
Total exposure[b] in person-months	4945.05	5420.53
Blood and lymphatic system disorders	**0 (0.00)**	**1 (0.02)**
Lymphopenia	0 (0.00)	1 (0.02)
Cardiac disorders	**5 (0.10)**	**7 (0.13)**
Acute myocardial infarction	0 (0.00)	2 (0.04)
Atrial fibrillation	4 (0.08)	1 (0.02)
Autoimmune myocarditis	0 (0.00)	1 (0.02)
Cardiac failure	0 (0.00)	1 (0.02)
Cardiomyopathy	1 (0.02)	0 (0.00)
Mitral valve incompetence	0 (0.00)	1 (0.02)
Mitral valve prolapse	0 (0.00)	1 (0.02)
Endocrine disorders	**10 (0.20)**	**0 (0.00)**
Adrenal insufficiency	5 (0.10)	0 (0.00)
Endocrine disorder	1 (0.02)	0 (0.00)
Hyperthyroidism	1 (0.02)	0 (0.00)
Hypophysitis	1 (0.02)	0 (0.00)
Hypopituitarism	2 (0.04)	0 (0.00)
Eye disorders	**1 (0.02)**	**1 (0.02)**
Glaucoma	1 (0.02)	1 (0.02)
Gastrointestinal disorders	**24 (0.49)**	**1 (0.02)**
Anal fistula	1 (0.02)	0 (0.00)
Autoimmune colitis	2 (0.04)	0 (0.00)
Colitis	5 (0.10)	0 (0.00)
Diarrhoea	8 (0.16)	1 (0.02)
Haematemesis	1 (0.02)	0 (0.00)
Immune-mediated enterocolitis	1 (0.02)	0 (0.00)
Inguinal hernia	1 (0.02)	0 (0.00)
Lip dry	1 (0.02)	0 (0.00)
Palatal oedema	1 (0.02)	0 (0.00)
Pancreatitis	2 (0.04)	0 (0.00)
Proctitis	1 (0.02)	0 (0.00)
General disorders and administration site conditions	**4 (0.08)**	**2 (0.04)**
Asthenia	1 (0.02)	0 (0.00)

Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
General disorders and administration site conditions	**4 (0.08)**	**2 (0.04)**
Chest pain	0 (0.00)	1 (0.02)
Fatigue	2 (0.04)	1 (0.02)
Systemic inflammatory response syndrome	1 (0.02)	0 (0.00)
Hepatobiliary disorders	**11 (0.22)**	**2 (0.04)**
Autoimmune hepatitis	7 (0.14)	2 (0.04)
Hepatitis	2 (0.04)	0 (0.00)
Hepatotoxicity	2 (0.04)	0 (0.00)
Infections and infestations	**15 (0.30)**	**12 (0.22)**
Abdominal wall abscess	0 (0.00)	2 (0.04)
Anorectal infection	1 (0.02)	0 (0.00)
COVID-19 pneumonia	2 (0.04)	3 (0.06)
Cellulitis	3 (0.06)	1 (0.02)
Cellulitis streptococcal	1 (0.02)	0 (0.00)
Dermo-hypodermitis	0 (0.00)	1 (0.02)
Enterocolitis infectious	1 (0.02)	0 (0.00)
Infected seroma	0 (0.00)	1 (0.02)
Lower respiratory tract infection	1 (0.02)	0 (0.00)
Pneumonia	1 (0.02)	1 (0.02)
Postoperative wound infection	1 (0.02)	0 (0.00)
Pyelonephritis	0 (0.00)	1 (0.02)
Rash pustular	1 (0.02)	0 (0.00)
Sepsis	1 (0.02)	0 (0.00)
Septic shock	1 (0.02)	0 (0.00)
Urinary tract infection	0 (0.00)	2 (0.04)
Viral infection	1 (0.02)	0 (0.00)
Injury, poisoning and procedural complications	**5 (0.10)**	**6 (0.11)**
Anastomotic leak	0 (0.00)	1 (0.02)
Ankle fracture	1 (0.02)	0 (0.00)
Arthropod bite	0 (0.00)	1 (0.02)
Foreign body	1 (0.02)	0 (0.00)
Lower limb fracture	0 (0.00)	1 (0.02)
Procedural pain	1 (0.02)	0 (0.00)
Seroma	1 (0.02)	0 (0.00)

Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Injury, poisoning and procedural complications	**5 (0.10)**	**6 (0.11)**
Soft tissue injury	0 (0.00)	1 (0.02)
Upper limb fracture	0 (0.00)	1 (0.02)
Vascular pseudoaneurysm	0 (0.00)	1 (0.02)
Wrist fracture	1 (0.02)	0 (0.00)
Investigations	**29 (0.59)**	**25 (0.46)**
Alanine aminotransferase increased	5 (0.10)	1 (0.02)
Amylase increased	5 (0.10)	2 (0.04)
Aspartate aminotransferase increased	3 (0.06)	3 (0.06)
Blood alkaline phosphatase increased	1 (0.02)	0 (0.00)
Blood creatine phosphokinase increased	4 (0.08)	4 (0.07)
Blood sodium decreased	1 (0.02)	0 (0.00)
Gamma-glutamyltransferase increased	1 (0.02)	1 (0.02)
Glomerular filtration rate decreased	1 (0.02)	0 (0.00)
Lipase increased	7 (0.14)	12 (0.22)
Lymphocyte count decreased	0 (0.00)	1 (0.02)
Transaminases increased	1 (0.02)	0 (0.00)
Ultrasound bladder abnormal	0 (0.00)	1 (0.02)
Metabolism and nutrition disorders	**19 (0.38)**	**10 (0.18)**
Decreased appetite	3 (0.06)	0 (0.00)
Dehydration	1 (0.02)	0 (0.00)
Hyperglycaemia	2 (0.04)	1 (0.02)
Hyperkalaemia	1 (0.02)	0 (0.00)
Hyperlipasaemia	0 (0.00)	1 (0.02)
Hypoalbuminaemia	1 (0.02)	0 (0.00)
Hypokalaemia	1 (0.02)	0 (0.00)
Hypophosphataemia	5 (0.10)	4 (0.07)
Iron deficiency	1 (0.02)	0 (0.00)
Type 1 diabetes mellitus	2 (0.04)	0 (0.00)

Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Metabolism and nutrition disorders	**19 (0.38)**	**10 (0.18)**
Type 2 diabetes mellitus	2 (0.04)	4 (0.07)
Musculoskeletal and connective tissue disorders	**14 (0.28)**	**6 (0.11)**
Antisynthetase syndrome	0 (0.00)	1 (0.02)
Arthralgia	1 (0.02)	2 (0.04)
Arthritis	1 (0.02)	0 (0.00)
Back pain	2 (0.04)	0 (0.00)
Compartment syndrome	1 (0.02)	0 (0.00)
Fibromyalgia	0 (0.00)	1 (0.02)
Flank pain	1 (0.02)	0 (0.00)
Immune-mediated arthritis	1 (0.02)	0 (0.00)
Intervertebral disc protrusion	0 (0.00)	1 (0.02)
Myalgia	2 (0.04)	0 (0.00)
Myopathy	1 (0.02)	0 (0.00)
Myositis	2 (0.04)	0 (0.00)
Osteoarthritis	1 (0.02)	0 (0.00)
Pain in extremity	0 (0.00)	1 (0.02)
Polyarthritis	1 (0.02)	0 (0.00)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**5 (0.10)**	**11 (0.20)**
Basal cell carcinoma	0 (0.00)	3 (0.06)
Breast cancer	1 (0.02)	0 (0.00)
Lung neoplasm malignant	0 (0.00)	1 (0.02)
Lymphoma	1 (0.02)	0 (0.00)
Malignant melanoma	0 (0.00)	1 (0.02)
Meningioma	1 (0.02)	0 (0.00)
Prostate cancer	1 (0.02)	1 (0.02)
Recurrent cancer	1 (0.02)	2 (0.04)
Renal cell carcinoma	0 (0.00)	1 (0.02)
Transitional cell carcinoma	0 (0.00)	1 (0.02)
Transitional cell carcinoma recurrent	0 (0.00)	1 (0.02)
Nervous system disorders	**8 (0.16)**	**7 (0.13)**
Carpal tunnel syndrome	1 (0.02)	0 (0.00)

Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Nervous system disorders	**8 (0.16)**	**7 (0.13)**
Lumbar radiculopathy	1 (0.02)	0 (0.00)
Meningorrhagia	0 (0.00)	1 (0.02)
Myasthenia gravis	2 (0.04)	0 (0.00)
Myelitis transverse	1 (0.02)	0 (0.00)
Neuralgic amyotrophy	0 (0.00)	1 (0.02)
Peripheral sensory neuropathy	1 (0.02)	0 (0.00)
Presyncope	0 (0.00)	1 (0.02)
Seizure	0 (0.00)	1 (0.02)
Syncope	2 (0.04)	3 (0.06)
Psychiatric disorders	**1 (0.02)**	**4 (0.07)**
Anxiety	0 (0.00)	1 (0.02)
Completed suicide	0 (0.00)	1 (0.02)
Depression	1 (0.02)	0 (0.00)
Mania	0 (0.00)	1 (0.02)
Suicidal ideation	0 (0.00)	1 (0.02)
Renal and urinary disorders	**7 (0.14)**	**2 (0.04)**
Acute kidney injury	2 (0.04)	0 (0.00)
Autoimmune nephritis	2 (0.04)	0 (0.00)
Haematuria	0 (0.00)	1 (0.02)
Nephritis	1 (0.02)	0 (0.00)
Nephrolithiasis	1 (0.02)	1 (0.02)
Renal failure	1 (0.02)	0 (0.00)
Reproductive system and breast disorders	**1 (0.02)**	**2 (0.04)**
Endometrial hyperplasia	0 (0.00)	1 (0.02)
Ovarian cyst torsion	1 (0.02)	0 (0.00)
Vaginal prolapse	0 (0.00)	1 (0.02)
Respiratory, thoracic and mediastinal disorders	**4 (0.08)**	**7 (0.13)**
Acute respiratory failure	1 (0.02)	0 (0.00)
Asthma	0 (0.00)	1 (0.02)
Chronic obstructive pulmonary disease	0 (0.00)	2 (0.04)
Hypoxia	0 (0.00)	1 (0.02)
Interstitial lung disease	1 (0.02)	0 (0.00)
Pleural effusion	1 (0.02)	0 (0.00)

Exposure-Adjusted Grade 3-5 Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Respiratory, thoracic and mediastinal disorders	**4 (0.08)**	**7 (0.13)**
Pneumonitis	1 (0.02)	0 (0.00)
Pulmonary embolism	0 (0.00)	2 (0.04)
Pulmonary oedema	0 (0.00)	1 (0.02)
Skin and subcutaneous tissue disorders	**18 (0.36)**	**3 (0.06)**
Dermatitis bullous	1 (0.02)	0 (0.00)
Pemphigoid	1 (0.02)	0 (0.00)
Pruritus	3 (0.06)	0 (0.00)
Rash	7 (0.14)	2 (0.04)
Rash maculo-papular	3 (0.06)	1 (0.02)
Rash pruritic	2 (0.04)	0 (0.00)
Skin ulcer	1 (0.02)	0 (0.00)
Vascular disorders	**18 (0.36)**	**30 (0.55)**
Embolism	0 (0.00)	1 (0.02)
Haematoma	0 (0.00)	1 (0.02)
Hypertension	17 (0.34)	28 (0.52)
Hypotension	1 (0.02)	0 (0.00)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-33
Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	483	444	397	310
Total exposure[c] in person-months	1397.3	1262.2	2112.7	172.9
Blood and lymphatic system disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Lymphopenia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac disorders	**1(8.1)**	**3(28.8)**	**1(211.7)**	**0(0.0)**
Acute myocardial infarction	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Atrial fibrillation	1(10.8)	2(25.7)	1(211.7)	0(0.0)
Autoimmune myocarditis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiomyopathy	0(0.0)	1(37.7)	0(0.0)	0(0.0)
Mitral valve incompetence	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mitral valve prolapse	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Endocrine disorders	**2(8.1)**	**5(28.3)**	**2(20.6)**	**1(347.5)**
Adrenal insufficiency	0(0.0)	3(25.5)	1(13.5)	1(347.5)
Endocrine disorder	0(0.0)	1(284.7)	0(0.0)	0(0.0)
Hyperthyroidism	1(144.9)	0(0.0)	0(0.0)	0(0.0)
Hypophysitis	1(760.9)	0(0.0)	0(0.0)	0(0.0)
Hypopituitarism	0(0.0)	1(17.9)	1(43.2)	0(0.0)
Eye disorders	**0(0.0)**	**0(0.0)**	**1(36.1)**	**0(0.0)**
Glaucoma	0(0.0)	0(0.0)	1(36.1)	0(0.0)
Gastrointestinal disorders	**8(13.8)**	**11(34.7)**	**3(13.8)**	**2(450.3)**
Anal fistula	1(152.2)	0(0.0)	0(0.0)	0(0.0)
Autoimmune colitis	0(0.0)	2(69.7)	0(0.0)	0(0.0)
Colitis	3(24.8)	2(54.2)	0(0.0)	0(0.0)
Diarrhoea	3(16.7)	3(29.7)	1(10.0)	1(258.8)
Haematemesis	0(0.0)	1(109.9)	0(0.0)	0(0.0)
Immune-mediated enterocolitis	0(0.0)	0(0.0)	0(0.0)	1(1729.8)
Inguinal hernia	0(0.0)	0(0.0)	1(363.2)	0(0.0)
Lip dry	1(507.3)	0(0.0)	0(0.0)	0(0.0)
Palatal oedema	0(0.0)	1(39.7)	0(0.0)	0(0.0)
Pancreatitis	0(0.0)	1(18.0)	1(18.0)	0(0.0)
Proctitis	0(0.0)	1(4411.8)	0(0.0)	0(0.0)
General disorders and administration site conditions	**2(22.6)**	**0(0.0)**	**1(16.1)**	**1(154.0)**

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	486	471	443	350
Total exposure[c] in person-months	1435.9	1370.6	2437.4	176.7
Blood and lymphatic system disorders	**0(0.0)**	**1(39.2)**	**0(0.0)**	**0(0.0)**
Lymphopenia	0(0.0)	1(39.2)	0(0.0)	0(0.0)
Cardiac disorders	**1(5.2)**	**3(19.1)**	**3(30.3)**	**0(0.0)**
Acute myocardial infarction	0(0.0)	1(16.7)	1(32.2)	0(0.0)
Atrial fibrillation	0(0.0)	0(0.0)	1(42.6)	0(0.0)
Autoimmune myocarditis	1(95.1)	0(0.0)	0(0.0)	0(0.0)
Cardiac failure	0(0.0)	1(55.7)	0(0.0)	0(0.0)
Cardiomyopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mitral valve incompetence	0(0.0)	1(52.8)	0(0.0)	0(0.0)
Mitral valve prolapse	0(0.0)	0(0.0)	1(22.5)	0(0.0)
Endocrine disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Adrenal insufficiency	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Endocrine disorder	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hyperthyroidism	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypophysitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypopituitarism	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eye disorders	**1(202.9)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Glaucoma	1(202.9)	0(0.0)	0(0.0)	0(0.0)
Gastrointestinal disorders	**0(0.0)**	**0(0.0)**	**1(20.4)**	**0(0.0)**
Anal fistula	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Autoimmune colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Diarrhoea	0(0.0)	0(0.0)	1(20.4)	0(0.0)
Haematemesis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated enterocolitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Inguinal hernia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lip dry	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Palatal oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pancreatitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Proctitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
General disorders and administration site conditions	**1(22.7)**	**0(0.0)**	**1(18.0)**	**0(0.0)**

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
General disorders and administration site conditions	**2(22.6)**	**0(0.0)**	**1(16.1)**	**1(154.0)**
Asthenia	1(35.8)	0(0.0)	0(0.0)	0(0.0)
Chest pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Fatigue	1(32.6)	0(0.0)	1(477.1)	0(0.0)
Systemic inflammatory response syndrome	0(0.0)	0(0.0)	0(0.0)	1(154.0)
Hepatobiliary disorders	**7(35.4)**	**2(24.3)**	**2(38.3)**	**0(0.0)**
Autoimmune hepatitis	5(39.9)	1(21.0)	1(20.1)	0(0.0)
Hepatitis	1(26.9)	0(0.0)	1(412.4)	0(0.0)
Hepatotoxicity	1(28.6)	1(207.2)	0(0.0)	0(0.0)
Infections and infestations	**8(30.4)**	**2(11.2)**	**4(26.2)**	**1(146.6)**
Abdominal wall abscess	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Anorectal infection	1(160.2)	0(0.0)	0(0.0)	0(0.0)
COVID-19 pneumonia	1(31.6)	0(0.0)	1(18.3)	0(0.0)
Cellulitis	1(14.4)	0(0.0)	2(66.3)	0(0.0)
Cellulitis streptococcal	1(434.8)	0(0.0)	0(0.0)	0(0.0)
Dermo-hypodermitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Enterocolitis infectious	1(1014.6)	0(0.0)	0(0.0)	0(0.0)
Infected seroma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lower respiratory tract infection	1(1521.8)	0(0.0)	0(0.0)	0(0.0)
Pneumonia	1(34.2)	0(0.0)	0(0.0)	0(0.0)
Postoperative wound infection	1(380.5)	0(0.0)	0(0.0)	0(0.0)
Pyelonephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Rash pustular	0(0.0)	0(0.0)	1(124.8)	0(0.0)
Sepsis	0(0.0)	1(182.4)	0(0.0)	0(0.0)
Septic shock	0(0.0)	0(0.0)	0(0.0)	1(146.6)
Urinary tract infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Viral infection	0(0.0)	1(41.9)	0(0.0)	0(0.0)
Injury, poisoning and procedural complications	**1(8.1)**	**1(8.5)**	**2(18.0)**	**1(146.6)**
Anastomotic leak	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ankle fracture	0(0.0)	0(0.0)	0(0.0)	1(146.6)
Arthropod bite	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Foreign body	0(0.0)	1(35.5)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
General disorders and administration site conditions	**1(22.7)**	**0(0.0)**	**1(18.0)**	**0(0.0)**
Asthenia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Chest pain	0(0.0)	0(0.0)	1(18.0)	0(0.0)
Fatigue	1(70.8)	0(0.0)	0(0.0)	0(0.0)
Systemic inflammatory response syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hepatobiliary disorders	**1(27.8)**	**1(87.7)**	**0(0.0)**	**0(0.0)**
Autoimmune hepatitis	1(27.8)	1(87.7)	0(0.0)	0(0.0)
Hepatitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hepatotoxicity	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infections and infestations	**3(10.2)**	**3(12.8)**	**6(29.8)**	**0(0.0)**
Abdominal wall abscess	0(0.0)	1(22.7)	1(1279.0)	0(0.0)
Anorectal infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
COVID-19 pneumonia	0(0.0)	0(0.0)	3(29.0)	0(0.0)
Cellulitis	0(0.0)	1(38.2)	0(0.0)	0(0.0)
Cellulitis streptococcal	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dermo-hypodermitis	1(3043.7)	0(0.0)	0(0.0)	0(0.0)
Enterocolitis infectious	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infected seroma	1(338.2)	0(0.0)	0(0.0)	0(0.0)
Lower respiratory tract infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pneumonia	0(0.0)	0(0.0)	1(26.8)	0(0.0)
Postoperative wound infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pyelonephritis	0(0.0)	0(0.0)	1(16.7)	0(0.0)
Rash pustular	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Sepsis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Septic shock	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Urinary tract infection	1(19.3)	1(73.0)	0(0.0)	0(0.0)
Viral infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Injury, poisoning and procedural complications	**1(6.2)**	**1(8.3)**	**2(10.8)**	**2(187.2)**
Anastomotic leak	1(95.1)	0(0.0)	0(0.0)	0(0.0)
Ankle fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Arthropod bite	0(0.0)	0(0.0)	1(20.8)	0(0.0)
Foreign body	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Injury, poisoning and procedural complications	**1(8.1)**	**1(8.5)**	**2(18.0)**	**1(146.6)**
Lower limb fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Procedural pain	0(0.0)	0(0.0)	1(19.8)	0(0.0)
Seroma	1(304.4)	0(0.0)	0(0.0)	0(0.0)
Soft tissue injury	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Upper limb fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vascular pseudoaneurysm	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Wrist fracture	0(0.0)	0(0.0)	1(2205.9)	0(0.0)
Investigations	**15(25.0)**	**2(4.9)**	**11(30.1)**	**1(40.2)**
Alanine aminotransferase increased	3(35.4)	1(17.2)	1(22.8)	0(0.0)
Amylase increased	2(17.0)	0(0.0)	3(42.2)	0(0.0)
Aspartate aminotransferase increased	3(125.1)	0(0.0)	0(0.0)	0(0.0)
Blood alkaline phosphatase increased	1(47.6)	0(0.0)	0(0.0)	0(0.0)
Blood creatine phosphokinase increased	2(24.7)	0(0.0)	2(27.2)	0(0.0)
Blood sodium decreased	0(0.0)	0(0.0)	1(27.3)	0(0.0)
Gamma-glutamyltransferase increased	1(47.6)	0(0.0)	0(0.0)	0(0.0)
Glomerular filtration rate decreased	0(0.0)	1(52.8)	0(0.0)	0(0.0)
Lipase increased	2(10.8)	0(0.0)	4(28.4)	1(40.2)
Lymphocyte count decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Transaminases increased	1(202.9)	0(0.0)	0(0.0)	0(0.0)
Ultrasound bladder abnormal	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Metabolism and nutrition disorders	**4(7.6)**	**9(26.3)**	**6(72.1)**	**0(0.0)**
Decreased appetite	0(0.0)	3(54.0)	0(0.0)	0(0.0)
Dehydration	1(49.9)	0(0.0)	0(0.0)	0(0.0)
Hyperglycaemia	1(17.4)	0(0.0)	1(17.6)	0(0.0)
Hyperkalaemia	0(0.0)	0(0.0)	1(8013.9)	0(0.0)
Hyperlipasaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypoalbuminaemia	0(0.0)	1(35.9)	0(0.0)	0(0.0)
Hypokalaemia	0(0.0)	0(0.0)	1(412.4)	0(0.0)
Hypophosphataemia	0(0.0)	3(25.2)	2(94.0)	0(0.0)
Iron deficiency	0(0.0)	1(53.7)	0(0.0)	0(0.0)
Type 1 diabetes mellitus	0(0.0)	1(32.7)	1(412.4)	0(0.0)
Type 2 diabetes mellitus	2(70.8)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Injury, poisoning and procedural complications	**1(6.2)**	**1(8.3)**	**2(10.8)**	**2(187.2)**
Lower limb fracture	0(0.0)	0(0.0)	1(59.2)	0(0.0)
Procedural pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seroma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Soft tissue injury	0(0.0)	0(0.0)	0(0.0)	1(221.2)
Upper limb fracture	0(0.0)	1(1801.1)	0(0.0)	0(0.0)
Vascular pseudoaneurysm	0(0.0)	0(0.0)	0(0.0)	1(162.2)
Wrist fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Investigations	**6(9.4)**	**5(10.3)**	**13(29.7)**	**1(48.5)**
Alanine aminotransferase increased	1(144.9)	0(0.0)	0(0.0)	0(0.0)
Amylase increased	1(27.1)	0(0.0)	1(27.1)	0(0.0)
Aspartate aminotransferase increased	1(14.9)	0(0.0)	1(11.0)	1(48.5)
Blood alkaline phosphatase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Blood creatine phosphokinase increased	0(0.0)	1(8.7)	3(25.6)	0(0.0)
Blood sodium decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Gamma-glutamyltransferase increased	1(36.2)	0(0.0)	0(0.0)	0(0.0)
Glomerular filtration rate decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lipase increased	2(6.2)	3(12.3)	7(36.8)	0(0.0)
Lymphocyte count decreased	0(0.0)	0(0.0)	1(477.1)	0(0.0)
Transaminases increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ultrasound bladder abnormal	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Metabolism and nutrition disorders	**0(0.0)**	**2(7.6)**	**8(27.5)**	**0(0.0)**
Decreased appetite	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dehydration	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hyperglycaemia	0(0.0)	0(0.0)	1(25.5)	0(0.0)
Hyperkalaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hyperlipasaemia	0(0.0)	1(85.3)	0(0.0)	0(0.0)
Hypoalbuminaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypokalaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypophosphataemia	0(0.0)	0(0.0)	4(28.8)	0(0.0)
Iron deficiency	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Type 1 diabetes mellitus	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Type 2 diabetes mellitus	0(0.0)	1(9.8)	3(26.5)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Musculoskeletal and connective tissue disorders	**7(23.9)**	**3(16.4)**	**3(31.7)**	**1(4006.9)**
Antisynthetase syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Arthralgia	1(82.3)	0(0.0)	0(0.0)	0(0.0)
Arthritis	0(0.0)	1(90.3)	0(0.0)	0(0.0)
Back pain	0(0.0)	0(0.0)	1(13.6)	1(4006.9)
Compartment syndrome	0(0.0)	1(37.7)	0(0.0)	0(0.0)
Fibromyalgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Flank pain	1(105.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated arthritis	0(0.0)	0(0.0)	1(900.5)	0(0.0)
Intervertebral disc protrusion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myalgia	1(19.6)	1(39.2)	0(0.0)	0(0.0)
Myopathy	1(87.0)	0(0.0)	0(0.0)	0(0.0)
Myositis	2(70.0)	0(0.0)	0(0.0)	0(0.0)
Osteoarthritis	1(3043.7)	0(0.0)	0(0.0)	0(0.0)
Pain in extremity	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Polyarthritis	0(0.0)	0(0.0)	1(49.6)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1(7.1)**	**2(18.8)**	**2(25.4)**	**0(0.0)**
Basal cell carcinoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Breast cancer	0(0.0)	0(0.0)	1(33.3)	0(0.0)
Lung neoplasm malignant	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lymphoma	0(0.0)	0(0.0)	1(20.5)	0(0.0)
Malignant melanoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Meningioma	1(49.1)	0(0.0)	0(0.0)	0(0.0)
Prostate cancer	0(0.0)	1(47.8)	0(0.0)	0(0.0)
Recurrent cancer	0(0.0)	1(39.2)	0(0.0)	0(0.0)
Renal cell carcinoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Transitional cell carcinoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Transitional cell carcinoma recurrent	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nervous system disorders	**3(16.4)**	**4(37.3)**	**1(2205.9)**	**0(0.0)**
Carpal tunnel syndrome	0(0.0)	1(83.0)	0(0.0)	0(0.0)
Lumbar radiculopathy	0(0.0)	1(83.0)	0(0.0)	0(0.0)
Meningorrhagia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myasthenia gravis	2(76.1)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Musculoskeletal and connective tissue disorders	**1(6.0)**	**2(14.2)**	**2(16.3)**	**1(54.6)**
Antisynthetase syndrome	0(0.0)	0(0.0)	0(0.0)	1(54.6)
Arthralgia	1(21.5)	1(44.3)	0(0.0)	0(0.0)
Arthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Back pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Compartment syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Fibromyalgia	0(0.0)	0(0.0)	1(107.2)	0(0.0)
Flank pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated arthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Intervertebral disc protrusion	0(0.0)	0(0.0)	1(18.9)	0(0.0)
Myalgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myositis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Osteoarthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pain in extremity	0(0.0)	1(35.1)	0(0.0)	0(0.0)
Polyarthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1(3.0)**	**3(12.0)**	**4(12.9)**	**3(129.9)**
Basal cell carcinoma	0(0.0)	0(0.0)	1(6.5)	2(392.2)
Breast cancer	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lung neoplasm malignant	0(0.0)	0(0.0)	1(19.7)	0(0.0)
Lymphoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Malignant melanoma	1(35.4)	0(0.0)	0(0.0)	0(0.0)
Meningioma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Prostate cancer	0(0.0)	0(0.0)	1(293.2)	0(0.0)
Recurrent cancer	0(0.0)	1(27.2)	0(0.0)	1(55.6)
Renal cell carcinoma	0(0.0)	1(39.2)	0(0.0)	0(0.0)
Transitional cell carcinoma	0(0.0)	1(147.1)	0(0.0)	0(0.0)
Transitional cell carcinoma recurrent	0(0.0)	0(0.0)	1(24.3)	0(0.0)
Nervous system disorders	**2(11.0)**	**3(28.9)**	**1(12.1)**	**1(51.8)**
Carpal tunnel syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lumbar radiculopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Meningorrhagia	0(0.0)	0(0.0)	0(0.0)	1(51.8)
Myasthenia gravis	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Nervous system disorders	**3(16.4)**	**4(37.3)**	**1(2205.9)**	**0(0.0)**
Myelitis transverse	0(0.0)	1(34.7)	0(0.0)	0(0.0)
Neuralgic amyotrophy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Peripheral sensory neuropathy	0(0.0)	1(41.3)	0(0.0)	0(0.0)
Presyncope	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seizure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Syncope	1(27.1)	0(0.0)	1(2205.9)	0(0.0)
Psychiatric disorders	**0(0.0)**	**1(350.3)**	**0(0.0)**	**0(0.0)**
Anxiety	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Completed suicide	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Depression	0(0.0)	1(350.3)	0(0.0)	0(0.0)
Mania	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Suicidal ideation	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Renal and urinary disorders	**1(4.9)**	**2(14.1)**	**4(39.8)**	**0(0.0)**
Acute kidney injury	0(0.0)	0(0.0)	2(115.4)	0(0.0)
Autoimmune nephritis	0(0.0)	2(91.7)	0(0.0)	0(0.0)
Haematuria	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nephritis	0(0.0)	0(0.0)	1(30.3)	0(0.0)
Nephrolithiasis	1(38.5)	0(0.0)	0(0.0)	0(0.0)
Renal failure	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Reproductive system and breast disorders	**0(0.0)**	**1(824.9)**	**0(0.0)**	**0(0.0)**
Endometrial hyperplasia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ovarian cyst torsion	0(0.0)	1(824.9)	0(0.0)	0(0.0)
Vaginal prolapse	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Respiratory, thoracic and mediastinal disorders	**1(9.5)**	**0(0.0)**	**2(18.9)**	**1(193.1)**
Acute respiratory failure	0(0.0)	0(0.0)	0(0.0)	1(193.1)
Asthma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Chronic obstructive pulmonary disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypoxia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Interstitial lung disease	0(0.0)	0(0.0)	1(32.9)	0(0.0)
Pleural effusion	0(0.0)	0(0.0)	1(65.6)	0(0.0)
Pneumonitis	1(66.2)	0(0.0)	0(0.0)	0(0.0)
Pulmonary embolism	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Nervous system disorders	**2(11.0)**	**3(28.9)**	**1(12.1)**	**1(51.8)**
Myelitis transverse	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neuralgic amyotrophy	0(0.0)	0(0.0)	1(44.5)	0(0.0)
Peripheral sensory neuropathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Presyncope	0(0.0)	1(47.8)	0(0.0)	0(0.0)
Seizure	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Syncope	2(32.3)	1(53.7)	0(0.0)	0(0.0)
Psychiatric disorders	**2(28.4)**	**0(0.0)**	**1(9.5)**	**1(38.2)**
Anxiety	1(3043.7)	0(0.0)	0(0.0)	0(0.0)
Completed suicide	0(0.0)	0(0.0)	1(22.2)	0(0.0)
Depression	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mania	1(98.2)	0(0.0)	0(0.0)	0(0.0)
Suicidal ideation	0(0.0)	0(0.0)	0(0.0)	1(38.2)
Renal and urinary disorders	**1(23.7)**	**0(0.0)**	**1(33.3)**	**0(0.0)**
Acute kidney injury	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Autoimmune nephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Haematuria	0(0.0)	0(0.0)	1(33.3)	0(0.0)
Nephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nephrolithiasis	1(82.3)	0(0.0)	0(0.0)	0(0.0)
Renal failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Reproductive system and breast disorders	**0(0.0)**	**2(94.6)**	**0(0.0)**	**0(0.0)**
Endometrial hyperplasia	0(0.0)	1(123.3)	0(0.0)	0(0.0)
Ovarian cyst torsion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vaginal prolapse	0(0.0)	1(76.7)	0(0.0)	0(0.0)
Respiratory, thoracic and mediastinal disorders	**0(0.0)**	**6(48.0)**	**1(19.0)**	**0(0.0)**
Acute respiratory failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Asthma	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Chronic obstructive pulmonary disease	0(0.0)	1(26.9)	1(19.0)	0(0.0)
Hypoxia	0(0.0)	1(52.8)	0(0.0)	0(0.0)
Interstitial lung disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pleural effusion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pneumonitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pulmonary embolism	0(0.0)	2(44.3)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Respiratory, thoracic and mediastinal disorders	**1(9.5)**	**0(0.0)**	**2(18.9)**	**1(193.1)**
Pulmonary oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Skin and subcutaneous tissue disorders	**12(38.9)**	**4(34.0)**	**1(14.4)**	**1(238.5)**
Dermatitis bullous	1(144.9)	0(0.0)	0(0.0)	0(0.0)
Pemphigoid	0(0.0)	0(0.0)	0(0.0)	1(238.5)
Pruritus	3(68.7)	0(0.0)	0(0.0)	0(0.0)
Rash	5(37.6)	2(55.1)	0(0.0)	0(0.0)
Rash maculo-papular	2(60.7)	1(284.7)	0(0.0)	0(0.0)
Rash pruritic	1(31.0)	1(55.7)	0(0.0)	0(0.0)
Skin ulcer	0(0.0)	0(0.0)	1(107.2)	0(0.0)
Vascular disorders	**10(25.1)**	**5(32.4)**	**3(50.7)**	**0(0.0)**
Embolism	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Haematoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypertension	10(27.2)	4(31.2)	3(50.7)	0(0.0)
Hypotension	0(0.0)	1(38.7)	0(0.0)	0(0.0)

Exposure-Adjusted Grade 3-5 Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Respiratory, thoracic and mediastinal disorders	**0(0.0)**	**6(48.0)**	**1(19.0)**	**0(0.0)**
Pulmonary oedema	0(0.0)	1(51.0)	0(0.0)	0(0.0)
Skin and subcutaneous tissue disorders	**1(15.9)**	**1(32.7)**	**0(0.0)**	**1(139.9)**
Dermatitis bullous	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pemphigoid	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pruritus	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Rash	1(30.3)	0(0.0)	0(0.0)	1(139.9)
Rash maculo-papular	0(0.0)	1(1801.1)	0(0.0)	0(0.0)
Rash pruritic	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Skin ulcer	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vascular disorders	**10(13.4)**	**11(25.7)**	**9(37.6)**	**0(0.0)**
Embolism	0(0.0)	0(0.0)	1(412.4)	0(0.0)
Haematoma	0(0.0)	0(0.0)	1(28.3)	0(0.0)
Hypertension	10(14.5)	11(29.8)	7(34.7)	0(0.0)
Hypotension	0(0.0)	0(0.0)	0(0.0)	0(0.0)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Number of subjects exposed to drug at the start of indicated time interval.

[c] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.2.4 Grade 3 to 5 Adverse Events Related to Study Intervention

Table 14.3-34
Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	83	(17.2)	25	(5.1)
with no adverse events	400	(82.8)	461	(94.9)
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Rash	7	(1.4)	1	(0.2)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Diarrhoea	5	(1.0)	1	(0.2)
Lipase increased	5	(1.0)	8	(1.6)
Alanine aminotransferase increased	4	(0.8)	1	(0.2)
Amylase increased	3	(0.6)	2	(0.4)
Blood creatine phosphokinase increased	3	(0.6)	2	(0.4)
Pruritus	3	(0.6)	0	(0.0)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Rash maculo-papular	2	(0.4)	0	(0.0)
Rash pruritic	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Arthralgia	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Asthenia	1	(0.2)	0	(0.0)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood sodium decreased	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Decreased appetite	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Fatigue	1	(0.2)	1	(0.2)

Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)
Hypertension	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophosphataemia	1	(0.2)	2	(0.4)
Hypophysitis	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lip dry	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Polyarthritis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Transaminases increased	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)

Participants With Drug-Related Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-35
Participants With Drug-Related Grade 3-5 Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	83	(17.2)	25	(5.1)
with no adverse events	400	(82.8)	461	(94.9)
Cardiac disorders	**0**	**(0.0)**	**2**	**(0.4)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	5	(1.0)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	1	(0.2)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Gastrointestinal disorders	**16**	**(3.3)**	**1**	**(0.2)**
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Diarrhoea	5	(1.0)	1	(0.2)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Lip dry	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**2**	**(0.4)**	**1**	**(0.2)**
Asthenia	1	(0.2)	0	(0.0)
Fatigue	1	(0.2)	1	(0.2)
Hepatobiliary disorders	**11**	**(2.3)**	**2**	**(0.4)**
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Infections and infestations	**2**	**(0.4)**	**0**	**(0.0)**
Cellulitis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)

Participants With Drug-Related Grade 3-5 Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**16**	**(3.3)**	**13**	**(2.7)**
Alanine aminotransferase increased	4	(0.8)	1	(0.2)
Amylase increased	3	(0.6)	2	(0.4)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood creatine phosphokinase increased	3	(0.6)	2	(0.4)
Blood sodium decreased	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)
Lipase increased	5	(1.0)	8	(1.6)
Lymphocyte count decreased	0	(0.0)	1	(0.2)
Transaminases increased	1	(0.2)	0	(0.0)
Metabolism and nutrition disorders	**5**	**(1.0)**	**2**	**(0.4)**
Decreased appetite	1	(0.2)	0	(0.0)
Hypophosphataemia	1	(0.2)	2	(0.4)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**9**	**(1.9)**	**1**	**(0.2)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Polyarthritis	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.2)**	**0**	**(0.0)**
Lymphoma	1	(0.2)	0	(0.0)
Nervous system disorders	**4**	**(0.8)**	**2**	**(0.4)**
Meningorrhagia	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)

Participants With Drug-Related Grade 3-5 Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**4**	**(0.8)**	**2**	**(0.4)**
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Renal and urinary disorders	**5**	**(1.0)**	**0**	**(0.0)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**3**	**(0.6)**	**0**	**(0.0)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Skin and subcutaneous tissue disorders	**14**	**(2.9)**	**1**	**(0.2)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Rash	7	(1.4)	1	(0.2)
Rash maculo-papular	2	(0.4)	0	(0.0)
Rash pruritic	2	(0.4)	0	(0.0)
Vascular disorders	**2**	**(0.4)**	**0**	**(0.0)**
Hypertension	1	(0.2)	0	(0.0)
Hypotension	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.3 Serious Adverse Events, Including Deaths

14.3.1.3.1 Deaths Due to Adverse Events

Table 14.3-36
Participants With Adverse Events Resulting in Death
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	1	(0.2)	5	(1.0)
with no adverse events	482	(99.8)	481	(99.0)
Infections and infestations	**1**	**(0.2)**	**2**	**(0.4)**
COVID-19 pneumonia	1	(0.2)	1	(0.2)
Pneumonia	0	(0.0)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**2**	**(0.4)**
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Recurrent cancer	0	(0.0)	1	(0.2)
Psycbiatric disorders	**0**	**(0.0)**	**1**	**(0.2)**
Completed suicide	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Recurrent Cancer: recurrence of disease under the study
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.3.2 Other Serious Adverse Events

Table 14.3-37
Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	103	(21.3)	96	(19.8)
with no adverse events	380	(78.7)	390	(80.2)
Blood and lymphatic system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Lymphadenopathy	1	(0.2)	0	(0.0)
Cardiac disorders	**6**	**(1.2)**	**8**	**(1.6)**
Acute myocardial infarction	0	(0.0)	2	(0.4)
Atrial fibrillation	4	(0.8)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Cardiomyopathy	1	(0.2)	0	(0.0)
Coronary artery disease	0	(0.0)	2	(0.4)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Ear and lahyrinth disorders	**0**	**(0.0)**	**1**	**(0.2)**
Vertigo	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	5	(1.0)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Eye disorders	**1**	**(0.2)**	**1**	**(0.2)**
Glaucoma	0	(0.0)	1	(0.2)
Macular detachment	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**13**	**(2.7)**	**1**	**(0.2)**
Anal fistula	1	(0.2)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	4	(0.8)	0	(0.0)
Diarrhoea	2	(0.4)	1	(0.2)
Haematemesis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Gastrointestinal disorders	**13**	**(2.7)**	**1**	**(0.2)**
Inguinal hernia	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**1**	**(0.2)**	**3**	**(0.6)**
Chest pain	0	(0.0)	1	(0.2)
Cyst	1	(0.2)	0	(0.0)
Infusion site urticaria	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)
Hepatobiliary disorders	**3**	**(0.6)**	**1**	**(0.2)**
Autoimmune hepatitis	3	(0.6)	1	(0.2)
Immune system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Sarcoidosis	1	(0.2)	0	(0.0)
Infections and infestations	**14**	**(2.9)**	**10**	**(2.1)**
Abdominal wall abscess	0	(0.0)	1	(0.2)
Abscess soft tissue	1	(0.2)	0	(0.0)
Anorectal infection	1	(0.2)	0	(0.0)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Cellulitis	3	(0.6)	1	(0.2)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Cystitis	0	(0.0)	1	(0.2)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Infected seroma	0	(0.0)	1	(0.2)
Lower respiratory tract infection	1	(0.2)	0	(0.0)
Pneumonia	2	(0.4)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.2)
Sepsis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Urinary tract infection	0	(0.0)	1	(0.2)
Viral infection	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**7**	**(1.4)**	**6**	**(1.2)**
Anastomotic leak	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**7**	**(1.4)**	**6**	**(1.2)**
Ankle fracture	1	(0.2)	0	(0.0)
Foot fracture	1	(0.2)	0	(0.0)
Foreign body	1	(0.2)	0	(0.0)
Humerus fracture	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	1	(0.2)
Lower limb fracture	0	(0.0)	1	(0.2)
Procedural pain	1	(0.2)	0	(0.0)
Seroma	1	(0.2)	0	(0.0)
Soft tissue injury	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)
Wound dehiscence	1	(0.2)	0	(0.0)
Wrist fracture	1	(0.2)	0	(0.0)
Investigations	**2**	**(0.4)**	**2**	**(0.4)**
Aspartate aminotransferase increased	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**4**	**(0.8)**	**0**	**(0.0)**
Decreased appetite	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**7**	**(1.4)**	**4**	**(0.8)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	0	(0.0)	1	(0.2)
Arthritis	1	(0.2)	0	(0.0)
Compartment syndrome	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)
Muscular weakness	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Pseudarthrosis	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**33**	**(6.8)**	**55**	**(11.3)**
Basal cell carcinoma	17	(3.5)	27	(5.6)
Bladder cancer	1	(0.2)	0	(0.0)
Bowen's disease	1	(0.2)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)
Chronic lymphocytic leukaemia	1	(0.2)	0	(0.0)
Lentigo maligna	0	(0.0)	1	(0.2)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Lymphoma	1	(0.2)	0	(0.0)
Malignant melanoma	4	(0.8)	5	(1.0)
Malignant melanoma in situ	5	(1.0)	6	(1.2)
Meningioma	1	(0.2)	0	(0.0)
Prostate cancer	2	(0.4)	1	(0.2)
Recurrent cancer	1	(0.2)	2	(0.4)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)
Second primary malignancy	0	(0.0)	1	(0.2)
Squamous cell carcinoma of skin	5	(1.0)	14	(2.9)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)
Nervous system disorders	**6**	**(1.2)**	**5**	**(1.0)**
Carpal tunnel syndrome	1	(0.2)	0	(0.0)
Facial paralysis	0	(0.0)	1	(0.2)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Meningorrhagia	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Paraesthesia	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Seizure	0	(0.0)	1	(0.2)
Psychiatric disorders	**1**	**(0.2)**	**3**	**(0.6)**
Completed suicide	0	(0.0)	1	(0.2)
Depression	1	(0.2)	0	(0.0)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Psychiatric disorders	**1**	**(0.2)**	**3**	**(0.6)**
Mania	0	(0.0)	1	(0.2)
Suicidal ideation	0	(0.0)	2	(0.4)
Renal and urinary disorders	**7**	**(1.4)**	**2**	**(0.4)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Haematuria	0	(0.0)	1	(0.2)
Nephritis	1	(0.2)	0	(0.0)
Nephrolithiasis	0	(0.0)	1	(0.2)
Renal failure	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**2**	**(0.4)**	**1**	**(0.2)**
Benign prostatic hyperplasia	1	(0.2)	0	(0.0)
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**9**	**(1.9)**	**4**	**(0.8)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Asthma	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)
Cough	1	(0.2)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pleural effusion	1	(0.2)	0	(0.0)
Pneumonitis	2	(0.4)	0	(0.0)
Pulmonary embolism	1	(0.2)	2	(0.4)
Skin and subcutaneous tissue disorders	**2**	**(0.4)**	**1**	**(0.2)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Rash	0	(0.0)	1	(0.2)
Skin ulcer	1	(0.2)	0	(0.0)
Vascular disorders	**2**	**(0.4)**	**1**	**(0.2)**
Haematoma	1	(0.2)	1	(0.2)

Participants With Serious Adverse Events
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Vascular disorders	**2**	**(0.4)**	**1**	**(0.2)**
Hypertension	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Recurrent Cancer: recurrence of disease under the study

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-38
Participants With Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	103	(21.3)	96	(19.8)
with no adverse events	380	(78.7)	390	(80.2)
Basal cell carcinoma	17	(3.5)	27	(5.6)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Malignant melanoma in situ	5	(1.0)	6	(1.2)
Squamous cell carcinoma of skin	5	(1.0)	14	(2.9)
Atrial fibrillation	4	(0.8)	1	(0.2)
Colitis	4	(0.8)	0	(0.0)
Malignant melanoma	4	(0.8)	5	(1.0)
Autoimmune hepatitis	3	(0.6)	1	(0.2)
Cellulitis	3	(0.6)	1	(0.2)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
COVID-19 pneumonia	2	(0.4)	3	(0.6)
Diarrhoea	2	(0.4)	1	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Pneumonia	2	(0.4)	1	(0.2)
Pneumonitis	2	(0.4)	0	(0.0)
Prostate cancer	2	(0.4)	1	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Abscess soft tissue	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Anal fistula	1	(0.2)	0	(0.0)
Ankle fracture	1	(0.2)	0	(0.0)
Anorectal infection	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Benign prostatic hyperplasia	1	(0.2)	0	(0.0)
Bladder cancer	1	(0.2)	0	(0.0)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)
Bowen's disease	1	(0.2)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)

Participants With Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Cardiomyopathy	1	(0.2)	0	(0.0)
Carpal tunnel syndrome	1	(0.2)	0	(0.0)
Cellulitis streptococcal	1	(0.2)	0	(0.0)
Chronic lymphocytic leukaemia	1	(0.2)	0	(0.0)
Compartment syndrome	1	(0.2)	0	(0.0)
Cough	1	(0.2)	0	(0.0)
Cyst	1	(0.2)	0	(0.0)
Decreased appetite	1	(0.2)	0	(0.0)
Depression	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Enterocolitis infectious	1	(0.2)	0	(0.0)
Foot fracture	1	(0.2)	0	(0.0)
Foreign body	1	(0.2)	0	(0.0)
Haematemesis	1	(0.2)	0	(0.0)
Haematoma	1	(0.2)	1	(0.2)
Hypertension	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Inguinal hernia	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Lower respiratory tract infection	1	(0.2)	0	(0.0)
Lumbar radiculopathy	1	(0.2)	0	(0.0)
Lymphadenopathy	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Meningioma	1	(0.2)	0	(0.0)
Muscular weakness	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myocarditis	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Ovarian cyst torsion	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pleural effusion	1	(0.2)	0	(0.0)
Procedural pain	1	(0.2)	0	(0.0)

Participants With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pulmonary embolism	1	(0.2)	2	(0.4)
Recurrent cancer	1	(0.2)	2	(0.4)
Renal failure	1	(0.2)	0	(0.0)
Sarcoidosis	1	(0.2)	0	(0.0)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Seroma	1	(0.2)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Viral infection	1	(0.2)	0	(0.0)
Wound dehiscence	1	(0.2)	0	(0.0)
Wrist fracture	1	(0.2)	0	(0.0)
Abdominal wall abscess	0	(0.0)	1	(0.2)
Acute myocardial infarction	0	(0.0)	2	(0.4)
Anastomotic leak	0	(0.0)	1	(0.2)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthralgia	0	(0.0)	1	(0.2)
Aspartate aminotransferase increased	0	(0.0)	1	(0.2)
Asthma	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Chest pain	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)
Completed suicide	0	(0.0)	1	(0.2)
Coronary artery disease	0	(0.0)	2	(0.4)
Cystitis	0	(0.0)	1	(0.2)
Endometrial hyperplasia	0	(0.0)	1	(0.2)
Facial paralysis	0	(0.0)	1	(0.2)
Glaucoma	0	(0.0)	1	(0.2)
Haematuria	0	(0.0)	1	(0.2)
Humerus fracture	0	(0.0)	1	(0.2)
Infected seroma	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	1	(0.2)
Infusion site urticaria	0	(0.0)	1	(0.2)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)
Lentigo maligna	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Lower limb fracture	0	(0.0)	1	(0.2)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Mania	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Nephrolithiasis	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Paraesthesia	0	(0.0)	1	(0.2)
Pseudarthrosis	0	(0.0)	1	(0.2)
Pyelonephritis	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)
Rash	0	(0.0)	1	(0.2)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Second primary malignancy	0	(0.0)	1	(0.2)
Seizure	0	(0.0)	1	(0.2)
Soft tissue injury	0	(0.0)	1	(0.2)
Suicidal ideation	0	(0.0)	2	(0.4)
Transitional cell carcinoma	0	(0.0)	1	(0.2)
Transitional cell carcinoma recurrent	0	(0.0)	1	(0.2)
Ultrasound bladder abnormal	0	(0.0)	1	(0.2)
Urinary tract infection	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	1	(0.2)
Vertigo	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Recurrent Cancer: recurrence of disease under the study
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

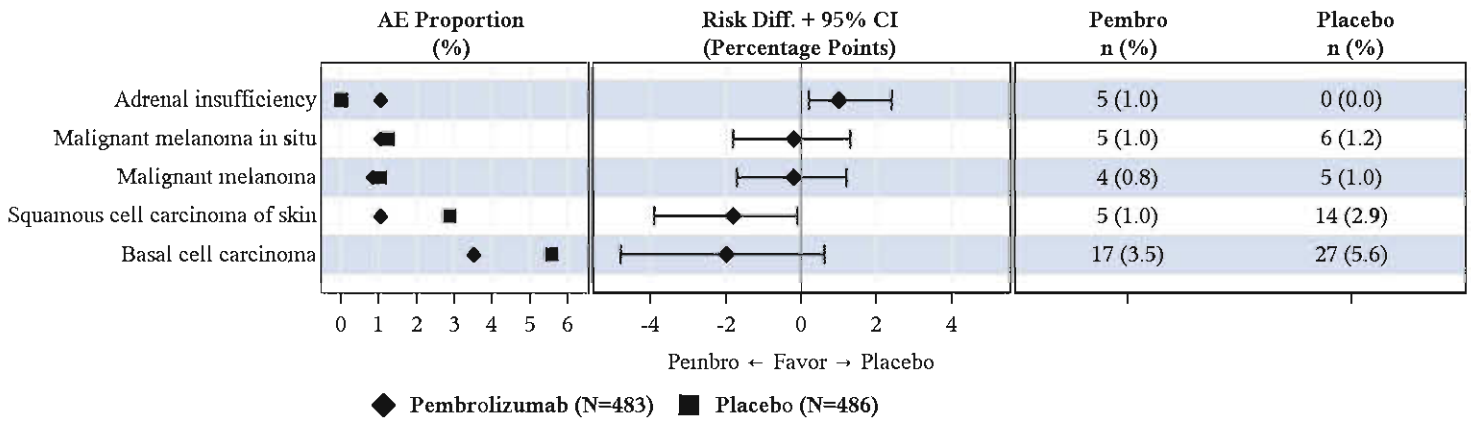
Table 14.3-39
Participants With Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	1	(12.5)	10	(15.9)
with no adverse events	7	(87.5)	53	(84.1)
Seizure	1	(12.5)	0	(0.0)
Appendicitis	0	(0.0)	1	(1.6)
Basal cell carcinoma	0	(0.0)	1	(1.6)
COVID-19	0	(0.0)	1	(1.6)
Cardiac failure	0	(0.0)	1	(1.6)
Death	0	(0.0)	1	(1.6)
Embolism	0	(0.0)	1	(1.6)
Hepatotoxicity	0	(0.0)	1	(1.6)
Lung adenocarcinoma	0	(0.0)	1	(1.6)
Mucinous adenocarcinoma of appendix	0	(0.0)	1	(1.6)
Myasthenia gravis	0	(0.0)	1	(1.6)
Pneumonia	0	(0.0)	1	(1.6)
Pneumonitis	0	(0.0)	1	(1.6)
Pneumonitis aspiration	0	(0.0)	1	(1.6)
Rib fracture	0	(0.0)	1	(1.6)
Seminoma	0	(0.0)	1	(1.6)
Skin lesion	0	(0.0)	1	(1.6)
Squamous cell carcinoma	0	(0.0)	1	(1.6)
Urinary tract infection	0	(0.0)	1	(1.6)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
SAEs were followed 90 days after last dose of study treatment in Part 2.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Figure 14.3-3
Rainfall Plot for Serious Adverse Event Preferred Terms Sorted by Risk Difference
(Incidence ≥ 1% in One or More Treatment Groups)
(APaT Population)



Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-40
Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Number of participants exposed	483	486
Total exposure[b] in person-months	4945.05	5420.53
Blood and lymphatic system disorders	**1 (0.02)**	**0 (0.00)**
Lymphadenopathy	1 (0.02)	0 (0.00)
Cardiac disorders	**7 (0.14)**	**8 (0.15)**
Acute myocardial infarction	0 (0.00)	2 (0.04)
Atrial fibrillation	5 (0.10)	1 (0.02)
Autoimmune myocarditis	0 (0.00)	1 (0.02)
Cardiac failure	0 (0.00)	1 (0.02)
Cardiomyopathy	1 (0.02)	0 (0.00)
Coronary artery disease	0 (0.00)	2 (0.04)
Mitral valve incompetence	0 (0.00)	1 (0.02)
Myocarditis	1 (0.02)	0 (0.00)
Ear and lahyrinth disorders	**0 (0.00)**	**1 (0.02)**
Vertigo	0 (0.00)	1 (0.02)
Endocrine disorders	**10 (0.20)**	**0 (0.00)**
Adrenal insufficiency	5 (0.10)	0 (0.00)
Endocrine disorder	1 (0.02)	0 (0.00)
Hypophysitis	2 (0.04)	0 (0.00)
Hypopituitarism	2 (0.04)	0 (0.00)
Eye disorders	**1 (0.02)**	**1 (0.02)**
Glaucoma	0 (0.00)	1 (0.02)
Macular detachment	1 (0.02)	0 (0.00)
Gastrointestinal disorders	**13 (0.26)**	**1 (0.02)**
Anal fistula	1 (0.02)	0 (0.00)
Autoimmune colitis	2 (0.04)	0 (0.00)
Colitis	4 (0.08)	0 (0.00)
Diarrhoea	2 (0.04)	1 (0.02)
Haematemesis	1 (0.02)	0 (0.00)
Immune-mediated enterocolitis	1 (0.02)	0 (0.00)
Inguinal hernia	1 (0.02)	0 (0.00)
Pancreatitis	1 (0.02)	0 (0.00)
General disorders and administration site conditions	**1 (0.02)**	**3 (0.06)**
Chest pain	0 (0.00)	1 (0.02)

Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
General disorders and administration site conditions	**1 (0.02)**	**3 (0.06)**
Cyst	1 (0.02)	0 (0.00)
Infusion site urticaria	0 (0.00)	1 (0.02)
Pyrexia	0 (0.00)	1 (0.02)
Hepatobiliary disorders	**3 (0.06)**	**1 (0.02)**
Autoimmune hepatitis	3 (0.06)	1 (0.02)
Immune system disorders	**1 (0.02)**	**0 (0.00)**
Sarcoidosis	1 (0.02)	0 (0.00)
Infections and infestations	**15 (0.30)**	**12 (0.22)**
Abdominal wall abscess	0 (0.00)	2 (0.04)
Abscess soft tissue	1 (0.02)	0 (0.00)
Anorectal infection	1 (0.02)	0 (0.00)
COVID-19 pneumonia	2 (0.04)	3 (0.06)
Cellulitis	3 (0.06)	1 (0.02)
Cellulitis streptococcal	1 (0.02)	0 (0.00)
Cystitis	0 (0.00)	1 (0.02)
Enterocolitis infectious	1 (0.02)	0 (0.00)
Infected seroma	0 (0.00)	1 (0.02)
Lower respiratory tract infection	1 (0.02)	0 (0.00)
Pneumonia	2 (0.04)	1 (0.02)
Pyelonephritis	0 (0.00)	1 (0.02)
Sepsis	1 (0.02)	0 (0.00)
Septic shock	1 (0.02)	0 (0.00)
Urinary tract infection	0 (0.00)	2 (0.04)
Viral infection	1 (0.02)	0 (0.00)
Injury, poisoning and procedural complications	**7 (0.14)**	**6 (0.11)**
Anastomotic leak	0 (0.00)	1 (0.02)
Ankle fracture	1 (0.02)	0 (0.00)
Foot fracture	1 (0.02)	0 (0.00)
Foreign body	1 (0.02)	0 (0.00)
Humerus fracture	0 (0.00)	1 (0.02)
Infusion related reaction	0 (0.00)	1 (0.02)
Lower limb fracture	0 (0.00)	1 (0.02)
Procedural pain	1 (0.02)	0 (0.00)
Seroma	1 (0.02)	0 (0.00)

Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Injury, poisoning and procedural complications	**7 (0.14)**	**6 (0.11)**
Soft tissue injury	0 (0.00)	1 (0.02)
Vascular pseudoaneurysm	0 (0.00)	1 (0.02)
Wound dehiscence	1 (0.02)	0 (0.00)
Wrist fracture	1 (0.02)	0 (0.00)
Investigations	**2 (0.04)**	**2 (0.04)**
Aspartate aminotransferase increased	0 (0.00)	1 (0.02)
Blood creatine phosphokinase increased	1 (0.02)	0 (0.00)
Lipase increased	1 (0.02)	0 (0.00)
Ultrasound bladder abnormal	0 (0.00)	1 (0.02)
Metabolism and nutrition disorders	**5 (0.10)**	**0 (0.00)**
Decreased appetite	2 (0.04)	0 (0.00)
Type 1 diabetes mellitus	2 (0.04)	0 (0.00)
Type 2 diabetes mellitus	1 (0.02)	0 (0.00)
Musculoskeletal and connective tissue disorders	**7 (0.14)**	**4 (0.07)**
Antisynthetase syndrome	0 (0.00)	1 (0.02)
Arthralgia	0 (0.00)	1 (0.02)
Arthritis	1 (0.02)	0 (0.00)
Compartment syndrome	1 (0.02)	0 (0.00)
Immune-mediated arthritis	1 (0.02)	0 (0.00)
Intervertebral disc protrusion	0 (0.00)	1 (0.02)
Muscular weakness	1 (0.02)	0 (0.00)
Myopathy	1 (0.02)	0 (0.00)
Myositis	2 (0.04)	0 (0.00)
Pseudarthrosis	0 (0.00)	1 (0.02)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**52 (1.05)**	**97 (1.79)**
Basal cell carcinoma	23 (0.47)	57 (1.05)
Bladder cancer	1 (0.02)	0 (0.00)
Bowen's disease	1 (0.02)	1 (0.02)
Breast cancer	1 (0.02)	0 (0.00)

Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**52 (1.05)**	**97 (1.79)**
Chronic lymphocytic leukaemia	1 (0.02)	0 (0.00)
Lentigo maligna	0 (0.00)	1 (0.02)
Lung neoplasm malignant	0 (0.00)	1 (0.02)
Lymphoma	1 (0.02)	0 (0.00)
Malignant melanoma	5 (0.10)	6 (0.11)
Malignant melanoma in situ	5 (0.10)	6 (0.11)
Meningioma	1 (0.02)	0 (0.00)
Prostate cancer	2 (0.04)	1 (0.02)
Recurrent cancer	1 (0.02)	2 (0.04)
Renal cell carcinoma	0 (0.00)	1 (0.02)
Seborrhoeic keratosis	1 (0.02)	0 (0.00)
Second primary malignancy	0 (0.00)	1 (0.02)
Squamous cell carcinoma of skin	9 (0.18)	18 (0.33)
Transitional cell carcinoma	0 (0.00)	1 (0.02)
Transitional cell carcinoma recurrent	0 (0.00)	1 (0.02)
Nervous system disorders	**6 (0.12)**	**5 (0.09)**
Carpal tunnel syndrome	1 (0.02)	0 (0.00)
Facial paralysis	0 (0.00)	1 (0.02)
Lumbar radiculopathy	1 (0.02)	0 (0.00)
Meningorrhagia	0 (0.00)	1 (0.02)
Myasthenia gravis	2 (0.04)	0 (0.00)
Myelitis transverse	1 (0.02)	0 (0.00)
Neuralgic amyotrophy	0 (0.00)	1 (0.02)
Paraesthesia	0 (0.00)	1 (0.02)
Peripheral sensory neuropathy	1 (0.02)	0 (0.00)
Seizure	0 (0.00)	1 (0.02)
Psycbiatric disorders	**1 (0.02)**	**4 (0.07)**
Completed suicide	0 (0.00)	1 (0.02)
Depression	1 (0.02)	0 (0.00)
Mania	0 (0.00)	1 (0.02)
Suicidal ideation	0 (0.00)	2 (0.04)
Renal and urinary disorders	**7 (0.14)**	**2 (0.04)**
Acute kidney injury	2 (0.04)	0 (0.00)

Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Renal and urinary disorders	**7 (0.14)**	**2 (0.04)**
Autoimmune nephritis	2 (0.04)	0 (0.00)
Haematuria	0 (0.00)	1 (0.02)
Nephritis	1 (0.02)	0 (0.00)
Nephrolithiasis	0 (0.00)	1 (0.02)
Renal failure	1 (0.02)	0 (0.00)
Tubulointerstitial nephritis	1 (0.02)	0 (0.00)
Reproductive system and breast disorders	**2 (0.04)**	**1 (0.02)**
Benign prostatic hyperplasia	1 (0.02)	0 (0.00)
Endometrial hyperplasia	0 (0.00)	1 (0.02)
Ovarian cyst torsion	1 (0.02)	0 (0.00)
Respiratory, tboracic and mediastinal disorders	**9 (0.18)**	**4 (0.07)**
Acute respiratory failure	1 (0.02)	0 (0.00)
Asthma	0 (0.00)	1 (0.02)
Chronic obstructive pulmonary disease	0 (0.00)	1 (0.02)
Cough	1 (0.02)	0 (0.00)
Immune-mediated lung disease	2 (0.04)	0 (0.00)
Interstitial lung disease	1 (0.02)	0 (0.00)
Pleural effusion	1 (0.02)	0 (0.00)
Pneumonitis	2 (0.04)	0 (0.00)
Pulmonary embolism	1 (0.02)	2 (0.04)
Skin and subcutaneous tissue disorders	**2 (0.04)**	**1 (0.02)**
Dermatitis bullous	1 (0.02)	0 (0.00)
Rash	0 (0.00)	1 (0.02)
Skin ulcer	1 (0.02)	0 (0.00)
Vascular disorders	**2 (0.04)**	**1 (0.02)**
Haematoma	1 (0.02)	1 (0.02)

Exposure-Adjusted Serious Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Vascular disorders	**2 (0.04)**	**1 (0.02)**
Hypertension	1 (0.02)	0 (0.00)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-41
Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	483	444	397	310
Total exposure[c] in person-months	1397.3	1262.2	2112.7	172.9
Blood and lymphatic system disorders	**0(0.0)**	**0(0.0)**	**1(18.7)**	**0(0.0)**
Lymphadenopathy	0(0.0)	0(0.0)	1(18.7)	0(0.0)
Cardiac disorders	**1(5.5)**	**2(12.0)**	**3(24.3)**	**1(95.8)**
Acute myocardial infarction	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Atrial fibrillation	1(8.1)	1(9.1)	3(47.3)	0(0.0)
Autoimmune myocarditis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiomyopathy	0(0.0)	1(37.7)	0(0.0)	0(0.0)
Coronary artery disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mitral valve incompetence	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myocarditis	0(0.0)	0(0.0)	0(0.0)	1(95.8)
Ear and lahyrinth disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Vertigo	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Endocrine disorders	**1(3.7)**	**6(30.9)**	**2(20.6)**	**1(347.5)**
Adrenal insufficiency	0(0.0)	3(25.5)	1(13.5)	1(347.5)
Endocrine disorder	0(0.0)	1(284.7)	0(0.0)	0(0.0)
Hypophysitis	1(31.9)	1(58.9)	0(0.0)	0(0.0)
Hypopituitarism	0(0.0)	1(17.9)	1(43.2)	0(0.0)
Eye disorders	**0(0.0)**	**1(63.8)**	**0(0.0)**	**0(0.0)**
Glaucoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Macular detachment	0(0.0)	1(63.8)	0(0.0)	0(0.0)
Gastrointestinal disorders	**3(8.4)**	**5(23.0)**	**3(15.1)**	**2(450.3)**
Anal fistula	1(152.2)	0(0.0)	0(0.0)	0(0.0)
Autoimmune colitis	0(0.0)	2(69.7)	0(0.0)	0(0.0)
Colitis	2(18.2)	1(16.9)	1(50.4)	0(0.0)
Diarrhoea	0(0.0)	1(32.7)	0(0.0)	1(258.8)
Haematemesis	0(0.0)	1(109.9)	0(0.0)	0(0.0)
Immune-mediated enterocolitis	0(0.0)	0(0.0)	0(0.0)	1(1729.8)
Inguinal hernia	0(0.0)	0(0.0)	1(363.2)	0(0.0)
Pancreatitis	0(0.0)	0(0.0)	1(18.0)	0(0.0)
General disorders and administration site conditions	**0(0.0)**	**0(0.0)**	**1(17.5)**	**0(0.0)**

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Number of Subjects exposed[b]	486	471	443	350
Total exposure[c] in person-months	1435.9	1370.6	2437.4	176.7
Blood and lymphatic system disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Lymphadenopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac disorders	**1(4.5)**	**4(21.7)**	**3(35.1)**	**0(0.0)**
Acute myocardial infarction	0(0.0)	1(16.7)	1(32.2)	0(0.0)
Atrial fibrillation	0(0.0)	0(0.0)	1(42.6)	0(0.0)
Autoimmune myocarditis	1(95.1)	0(0.0)	0(0.0)	0(0.0)
Cardiac failure	0(0.0)	1(55.7)	0(0.0)	0(0.0)
Cardiomyopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Coronary artery disease	0(0.0)	1(17.4)	1(32.2)	0(0.0)
Mitral valve incompetence	0(0.0)	1(52.8)	0(0.0)	0(0.0)
Myocarditis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ear and lahyrinth disorders	**1(434.8)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Vertigo	1(434.8)	0(0.0)	0(0.0)	0(0.0)
Endocrine disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Adrenal insufficiency	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Endocrine disorder	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypophysitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypopituitarism	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eye disorders	**1(202.9)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Glaucoma	1(202.9)	0(0.0)	0(0.0)	0(0.0)
Macular detachment	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Gastrointestinal disorders	**0(0.0)**	**0(0.0)**	**1(20.4)**	**0(0.0)**
Anal fistula	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Autoimmune colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Diarrhoea	0(0.0)	0(0.0)	1(20.4)	0(0.0)
Haematemesis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated enterocolitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Inguinal hernia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pancreatitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
General disorders and administration site conditions	**2(25.2)**	**0(0.0)**	**1(18.0)**	**0(0.0)**

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
General disorders and administration site conditions	**0(0.0)**	**0(0.0)**	**1(17.5)**	**0(0.0)**
Chest pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cyst	0(0.0)	0(0.0)	1(17.5)	0(0.0)
Infusion site urticaria	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pyrexia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hepatobiliary disorders	**2(38.5)**	**0(0.0)**	**1(20.1)**	**0(0.0)**
Autoimmune hepatitis	2(38.5)	0(0.0)	1(20.1)	0(0.0)
Immune system disorders	**0(0.0)**	**1(35.9)**	**0(0.0)**	**0(0.0)**
Sarcoidosis	0(0.0)	1(35.9)	0(0.0)	0(0.0)
Infections and infestations	**9(33.9)**	**2(13.4)**	**3(20.7)**	**1(146.6)**
Abdominal wall abscess	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Abscess soft tissue	1(34.6)	0(0.0)	0(0.0)	0(0.0)
Anorectal infection	1(160.2)	0(0.0)	0(0.0)	0(0.0)
COVID-19 pneumonia	1(31.6)	0(0.0)	1(18.3)	0(0.0)
Cellulitis	1(14.4)	0(0.0)	2(66.3)	0(0.0)
Cellulitis streptococcal	1(434.8)	0(0.0)	0(0.0)	0(0.0)
Cystitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Enterocolitis infectious	1(1014.6)	0(0.0)	0(0.0)	0(0.0)
Infected seroma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lower respiratory tract infection	1(1521.8)	0(0.0)	0(0.0)	0(0.0)
Pneumonia	2(56.9)	0(0.0)	0(0.0)	0(0.0)
Pyelonephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Sepsis	0(0.0)	1(182.4)	0(0.0)	0(0.0)
Septic shock	0(0.0)	0(0.0)	0(0.0)	1(146.6)
Urinary tract infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Viral infection	0(0.0)	1(41.9)	0(0.0)	0(0.0)
Injury, poisoning and procedural complications	**1(5.5)**	**2(13.2)**	**2(11.7)**	**2(109.6)**
Anastomotic leak	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ankle fracture	0(0.0)	0(0.0)	0(0.0)	1(146.6)
Foot fracture	0(0.0)	1(350.3)	0(0.0)	0(0.0)
Foreign body	0(0.0)	1(35.5)	0(0.0)	0(0.0)
Humerus fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infusion related reaction	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
General disorders and administration site conditions	**2(25.2)**	**0(0.0)**	**1(18.0)**	**0(0.0)**
Chest pain	0(0.0)	0(0.0)	1(18.0)	0(0.0)
Cyst	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infusion site urticaria	1(34.6)	0(0.0)	0(0.0)	0(0.0)
Pyrexia	1(49.1)	0(0.0)	0(0.0)	0(0.0)
Hepatobiliary disorders	**0(0.0)**	**1(87.7)**	**0(0.0)**	**0(0.0)**
Autoimmune hepatitis	0(0.0)	1(87.7)	0(0.0)	0(0.0)
Immune system disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Sarcoidosis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infections and infestations	**2(6.2)**	**3(11.4)**	**7(32.2)**	**0(0.0)**
Abdominal wall abscess	0(0.0)	1(22.7)	1(1279.0)	0(0.0)
Abscess soft tissue	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Anorectal infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
COVID-19 pneumonia	0(0.0)	0(0.0)	3(29.0)	0(0.0)
Cellulitis	0(0.0)	1(38.2)	0(0.0)	0(0.0)
Cellulitis streptococcal	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cystitis	0(0.0)	0(0.0)	1(62.9)	0(0.0)
Enterocolitis infectious	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infected seroma	1(338.2)	0(0.0)	0(0.0)	0(0.0)
Lower respiratory tract infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pneumonia	0(0.0)	0(0.0)	1(26.8)	0(0.0)
Pyelonephritis	0(0.0)	0(0.0)	1(16.7)	0(0.0)
Sepsis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Septic shock	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Urinary tract infection	1(19.3)	1(73.0)	0(0.0)	0(0.0)
Viral infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Injury, poisoning and procedural complications	**2(15.3)**	**0(0.0)**	**1(5.1)**	**3(68.0)**
Anastomotic leak	1(95.1)	0(0.0)	0(0.0)	0(0.0)
Ankle fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Foot fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Foreign body	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Humerus fracture	0(0.0)	0(0.0)	0(0.0)	1(29.9)
Infusion related reaction	1(3043.7)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Injury, poisoning and procedural complications	**1(5.5)**	**2(13.2)**	**2(11.7)**	**2(109.6)**
Lower limb fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Procedural pain	0(0.0)	0(0.0)	1(19.8)	0(0.0)
Seroma	1(304.4)	0(0.0)	0(0.0)	0(0.0)
Soft tissue injury	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vascular pseudoaneurysm	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Wound dehiscence	0(0.0)	0(0.0)	0(0.0)	1(87.6)
Wrist fracture	0(0.0)	0(0.0)	1(2205.9)	0(0.0)
Investigations	**1(22.7)**	**0(0.0)**	**1(21.5)**	**0(0.0)**
Aspartate aminotransferase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Blood creatine phosphokinase increased	1(70.8)	0(0.0)	0(0.0)	0(0.0)
Lipase increased	0(0.0)	0(0.0)	1(21.5)	0(0.0)
Ultrasound bladder abnormal	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Metabolism and nutrition disorders	**1(7.9)**	**3(50.6)**	**1(412.4)**	**0(0.0)**
Decreased appetite	0(0.0)	2(69.7)	0(0.0)	0(0.0)
Type 1 diabetes mellitus	0(0.0)	1(32.7)	1(412.4)	0(0.0)
Type 2 diabetes mellitus	1(138.3)	0(0.0)	0(0.0)	0(0.0)
Musculoskeletal and connective tissue disorders	**4(25.7)**	**2(29.6)**	**1(900.5)**	**0(0.0)**
Antisynthetase syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Arthralgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Arthritis	0(0.0)	1(90.3)	0(0.0)	0(0.0)
Compartment syndrome	0(0.0)	1(37.7)	0(0.0)	0(0.0)
Immune-mediated arthritis	0(0.0)	0(0.0)	1(900.5)	0(0.0)
Intervertebral disc protrusion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Muscular weakness	1(39.0)	0(0.0)	0(0.0)	0(0.0)
Myopathy	1(87.0)	0(0.0)	0(0.0)	0(0.0)
Myositis	2(70.0)	0(0.0)	0(0.0)	0(0.0)
Pseudarthrosis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**16(12.0)**	**20(23.5)**	**16(39.5)**	**0(0.0)**
Basal cell carcinoma	8(14.3)	8(25.7)	7(49.2)	0(0.0)
Bladder cancer	0(0.0)	0(0.0)	1(19.0)	0(0.0)
Bowen's disease	1(138.3)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Injury, poisoning and procedural complications	**2(15.3)**	**0(0.0)**	**1(5.1)**	**3(68.0)**
Lower limb fracture	0(0.0)	0(0.0)	1(59.2)	0(0.0)
Procedural pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seroma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Soft tissue injury	0(0.0)	0(0.0)	0(0.0)	1(221.2)
Vascular pseudoaneurysm	0(0.0)	0(0.0)	0(0.0)	1(162.2)
Wound dehiscence	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Wrist fracture	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Investigations	**0(0.0)**	**1(29.3)**	**1(32.6)**	**0(0.0)**
Aspartate aminotransferase increased	0(0.0)	0(0.0)	1(32.6)	0(0.0)
Blood creatine phosphokinase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lipase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ultrasound bladder abnormal	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Metabolism and nutrition disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**0(0.0)**
Decreased appetite	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Type 1 diabetes mellitus	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Type 2 diabetes mellitus	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Musculoskeletal and connective tissue disorders	**1(8.9)**	**1(12.1)**	**1(8.8)**	**1(54.6)**
Antisynthetase syndrome	0(0.0)	0(0.0)	0(0.0)	1(54.6)
Arthralgia	0(0.0)	1(44.3)	0(0.0)	0(0.0)
Arthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Compartment syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated arthritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Intervertebral disc protrusion	0(0.0)	0(0.0)	1(18.9)	0(0.0)
Muscular weakness	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myositis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pseudarthrosis	1(45.4)	0(0.0)	0(0.0)	0(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**27(11.0)**	**24(13.1)**	**37(23.3)**	**9(79.9)**
Basal cell carcinoma	20(14.3)	11(10.9)	20(22.5)	6(113.7)
Bladder cancer	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Bowen's disease	0(0.0)	1(71.3)	0(0.0)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**16(12.0)**	**20(23.5)**	**16(39.5)**	**0(0.0)**
Breast cancer	0(0.0)	0(0.0)	1(33.3)	0(0.0)
Chronic lymphocytic leukaemia	0(0.0)	0(0.0)	1(22.8)	0(0.0)
Lentigo maligna	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lung neoplasm malignant	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lymphoma	0(0.0)	0(0.0)	1(20.5)	0(0.0)
Malignant melanoma	2(14.5)	1(11.6)	2(36.9)	0(0.0)
Malignant melanoma in situ	2(16.0)	2(24.8)	1(73.6)	0(0.0)
Meningioma	1(49.1)	0(0.0)	0(0.0)	0(0.0)
Prostate cancer	0(0.0)	1(19.6)	1(149.3)	0(0.0)
Recurrent cancer	0(0.0)	1(39.2)	0(0.0)	0(0.0)
Renal cell carcinoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seborrhoeic keratosis	1(138.3)	0(0.0)	0(0.0)	0(0.0)
Second primary malignancy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Squamous cell carcinoma of skin	1(3.8)	7(39.4)	1(73.6)	0(0.0)
Transitional cell carcinoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Transitional cell carcinoma recurrent	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nervous system disorders	**2(13.7)**	**4(51.9)**	**0(0.0)**	**0(0.0)**
Carpal tunnel syndrome	0(0.0)	1(83.0)	0(0.0)	0(0.0)
Facial paralysis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lumbar radiculopathy	0(0.0)	1(83.0)	0(0.0)	0(0.0)
Meningorrhagia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myasthenia gravis	2(76.1)	0(0.0)	0(0.0)	0(0.0)
Myelitis transverse	0(0.0)	1(34.7)	0(0.0)	0(0.0)
Neuralgic amyotrophy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Paraesthesia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Peripheral sensory neuropathy	0(0.0)	1(41.3)	0(0.0)	0(0.0)
Seizure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Psycbiatric disorders	**0(0.0)**	**1(350.3)**	**0(0.0)**	**0(0.0)**
Completed suicide	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Depression	0(0.0)	1(350.3)	0(0.0)	0(0.0)
Mania	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Suicidal ideation	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Renal and urinary disorders	**0(0.0)**	**2(11.6)**	**5(37.6)**	**0(0.0)**

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**27(11.0)**	**24(13.1)**	**37(23.3)**	**9(79.9)**
Breast cancer	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Chronic lymphocytic leukaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lentigo maligna	0(0.0)	0(0.0)	0(0.0)	1(24.2)
Lung neoplasm malignant	0(0.0)	0(0.0)	1(19.7)	0(0.0)
Lymphoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Malignant melanoma	1(5.6)	1(7.2)	4(37.3)	0(0.0)
Malignant melanoma in situ	0(0.0)	2(11.8)	4(60.1)	0(0.0)
Meningioma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Prostate cancer	0(0.0)	0(0.0)	1(293.2)	0(0.0)
Recurrent cancer	0(0.0)	1(27.2)	0(0.0)	1(55.6)
Renal cell carcinoma	0(0.0)	1(39.2)	0(0.0)	0(0.0)
Seborrhoeic keratosis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Second primary malignancy	1(70.8)	0(0.0)	0(0.0)	0(0.0)
Squamous cell carcinoma of skin	5(11.7)	6(19.3)	6(19.2)	1(1729.8)
Transitional cell carcinoma	0(0.0)	1(147.1)	0(0.0)	0(0.0)
Transitional cell carcinoma recurrent	0(0.0)	0(0.0)	1(24.3)	0(0.0)
Nervous system disorders	**2(20.0)**	**1(15.6)**	**1(12.1)**	**1(51.8)**
Carpal tunnel syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Facial paralysis	1(138.3)	0(0.0)	0(0.0)	0(0.0)
Lumbar radiculopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Meningorrhagia	0(0.0)	0(0.0)	0(0.0)	1(51.8)
Myasthenia gravis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Myelitis transverse	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neuralgic amyotrophy	0(0.0)	0(0.0)	1(44.5)	0(0.0)
Paraesthesia	1(380.5)	0(0.0)	0(0.0)	0(0.0)
Peripheral sensory neuropathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seizure	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Psycbiatric disorders	**1(10.0)**	**0(0.0)**	**2(15.2)**	**1(38.2)**
Completed suicide	0(0.0)	0(0.0)	1(22.2)	0(0.0)
Depression	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mania	1(98.2)	0(0.0)	0(0.0)	0(0.0)
Suicidal ideation	0(0.0)	0(0.0)	1(11.5)	1(38.2)
Renal and urinary disorders	**1(23.7)**	**0(0.0)**	**1(33.3)**	**0(0.0)**

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Renal and urinary disorders	**0(0.0)**	**2(11.6)**	**5(37.6)**	**0(0.0)**
Acute kidney injury	0(0.0)	0(0.0)	2(115.4)	0(0.0)
Autoimmune nephritis	0(0.0)	2(91.7)	0(0.0)	0(0.0)
Haematuria	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nephritis	0(0.0)	0(0.0)	1(30.3)	0(0.0)
Nephrolithiasis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Renal failure	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Tubulointerstitial nephritis	0(0.0)	0(0.0)	1(30.6)	0(0.0)
Reproductive system and breast disorders	**1(19.1)**	**1(824.9)**	**0(0.0)**	**0(0.0)**
Benign prostatic hyperplasia	1(44.8)	0(0.0)	0(0.0)	0(0.0)
Endometrial hyperplasia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ovarian cyst torsion	0(0.0)	1(824.9)	0(0.0)	0(0.0)
Respiratory, tboracic and mediastinal disorders	**2(8.9)**	**2(10.3)**	**3(16.7)**	**2(128.1)**
Acute respiratory failure	0(0.0)	0(0.0)	0(0.0)	1(193.1)
Asthma	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Chronic obstructive pulmonary disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cough	1(3043.7)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated lung disease	0(0.0)	1(18.0)	1(71.8)	0(0.0)
Interstitial lung disease	0(0.0)	0(0.0)	1(32.9)	0(0.0)
Pleural effusion	0(0.0)	0(0.0)	1(65.6)	0(0.0)
Pneumonitis	1(22.2)	0(0.0)	0(0.0)	1(95.8)
Pulmonary embolism	0(0.0)	1(54.7)	0(0.0)	0(0.0)
Skin and subcutaneous tissue disorders	**1(27.1)**	**0(0.0)**	**1(107.2)**	**0(0.0)**
Dermatitis bullous	1(144.9)	0(0.0)	0(0.0)	0(0.0)
Rash	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Skin ulcer	0(0.0)	0(0.0)	1(107.2)	0(0.0)
Vascular disorders	**1(19.7)**	**0(0.0)**	**1(47.3)**	**0(0.0)**
Haematoma	1(48.3)	0(0.0)	0(0.0)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Renal and urinary disorders	**1(23.7)**	**0(0.0)**	**1(33.3)**	**0(0.0)**
Acute kidney injury	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Autoimmune nephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Haematuria	0(0.0)	0(0.0)	1(33.3)	0(0.0)
Nephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nephrolithiasis	1(82.3)	0(0.0)	0(0.0)	0(0.0)
Renal failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Tubulointerstitial nephritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Reproductive system and breast disorders	**0(0.0)**	**1(123.3)**	**0(0.0)**	**0(0.0)**
Benign prostatic hyperplasia	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Endometrial hyperplasia	0(0.0)	1(123.3)	0(0.0)	0(0.0)
Ovarian cyst torsion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Respiratory, tboracic and mediastinal disorders	**0(0.0)**	**3(37.8)**	**1(19.0)**	**0(0.0)**
Acute respiratory failure	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Asthma	0(0.0)	1(239.8)	0(0.0)	0(0.0)
Chronic obstructive pulmonary disease	0(0.0)	0(0.0)	1(19.0)	0(0.0)
Cough	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Immune-mediated lung disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Interstitial lung disease	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pleural effusion	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pneumonitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pulmonary embolism	0(0.0)	2(44.3)	0(0.0)	0(0.0)
Skin and subcutaneous tissue disorders	**0(0.0)**	**0(0.0)**	**0(0.0)**	**1(139.9)**
Dermatitis bullous	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Rash	0(0.0)	0(0.0)	0(0.0)	1(139.9)
Skin ulcer	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vascular disorders	**0(0.0)**	**0(0.0)**	**1(28.3)**	**0(0.0)**
Haematoma	0(0.0)	0(0.0)	1(28.3)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a] Pembrolizumab			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Vascular disorders	**1(19.7)**	**0(0.0)**	**1(47.3)**	**0(0.0)**
Hypertension	0(0.0)	0(0.0)	1(47.3)	0(0.0)

Exposure-Adjusted Serious Adverse Events by Observation Period
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months) [a]			
	Placebo			
Observation period of drug exposure	0-3 months	3-6 months	6-12 months	Beyond 12 months
Vascular disorders	**0(0.0)**	**0(0.0)**	**1(28.3)**	**0(0.0)**
Hypertension	0(0.0)	0(0.0)	0(0.0)	0(0.0)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Number of subjects exposed to drug at the start of indicated time interval.

[c] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-42
Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	483		415		348		486		464		430	
with one or more adverse events	47	(9.7)	47	(11.3)	27	(7.8)	37	(7.6)	34	(7.3)	44	(10.2)
with no adverse events	436	(90.3)	372	(89.6)	322	(92.5)	449	(92.4)	430	(92.7)	386	(89.8)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Lymphadenopathy	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Cardiac disorders	**1**	**(0.2)**	**4**	**(1.0)**	**2**	**(0.6)**	**1**	**(0.2)**	**4**	**(0.9)**	**3**	**(0.7)**
Acute myocardial infarction	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Atrial fibrillation	1	(0.2)	3	(0.7)	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Cardiac failure	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cardiomyopathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Coronary artery disease	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Mitral valve incompetence	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Myocarditis	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Ear and labyrinth disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**
Vertigo	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Endocrine disorders	**2**	**(0.4)**	**6**	**(1.4)**	**2**	**(0.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Adrenal insufficiency	0	(0.0)	4	(1.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Endocrine disorders	**2**	**(0.4)**	**6**	**(1.4)**	**2**	**(0.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Endocrine disorder	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypophysitis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypopituitarism	0	(0.0)	1	(0.2)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Eye disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**
Glaucoma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Macular detachment	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**6**	**(1.2)**	**4**	**(1.0)**	**3**	**(0.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**
Anal fistula	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Autoimmune colitis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Colitis	2	(0.4)	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Diarrhoea	1	(0.2)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)
Haematemesis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Immune-mediated enterocolitis	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Inguinal hernia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pancreatitis	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**	**2**	**(0.4)**	**0**	**(0.0)**	**1**	**(0.2)**
Chest pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**	**2**	**(0.4)**	**0**	**(0.0)**	**1**	**(0.2)**
Cyst	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Infusion site urticaria	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Pyrexia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Hepatobiliary disorders	**2**	**(0.4)**	**0**	**(0.0)**	**1**	**(0.3)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**
Autoimmune hepatitis	2	(0.4)	0	(0.0)	1	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)
Immune system disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Sarcoidosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infections and infestations	**10**	**(2.1)**	**2**	**(0.5)**	**3**	**(0.9)**	**2**	**(0.4)**	**5**	**(1.1)**	**4**	**(0.9)**
Abdominal wall abscess	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Abscess soft tissue	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anorectal infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
COVID-19 pneumonia	1	(0.2)	0	(0.0)	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.5)
Cellulitis	1	(0.2)	1	(0.2)	1	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)
Cellulitis streptococcal	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Cystitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Enterocolitis infectious	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infected seroma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**10**	**(2.1)**	**2**	**(0.5)**	**3**	**(0.9)**	**2**	**(0.4)**	**5**	**(1.1)**	**4**	**(0.9)**
Lower respiratory tract infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pneumonia	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Pyelonephritis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Sepsis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Septic shock	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Urinary tract infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)
Viral infection	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**2**	**(0.5)**	**3**	**(0.9)**	**2**	**(0.4)**	**1**	**(0.2)**	**3**	**(0.7)**
Anastomotic leak	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Ankle fracture	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Foot fracture	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Foreign body	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Humerus fracture	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Lower limb fracture	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Procedural pain	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Seroma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Soft tissue injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Vascular pseudoaneurysm	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Wound dehiscence	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**2**	**(0.5)**	**3**	**(0.9)**	**2**	**(0.4)**	**1**	**(0.2)**	**3**	**(0.7)**
Wrist fracture	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.3)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.2)**
Aspartate aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Lipase increased	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Ultrasound bladder abnormal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders	**2**	**(0.4)**	**2**	**(0.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Decreased appetite	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Type 1 diabetes mellitus	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Musculoskeletal and connective tissue disorders	**4**	**(0.8)**	**3**	**(0.7)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.5)**
Antisynthetase syndrome	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Arthralgia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Arthritis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Compartment syndrome	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Immune-mediated arthritis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Intervertebral disc protrusion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Muscular weakness	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**4**	**(0.8)**	**3**	**(0.7)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.5)**
Myopathy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pseudarthrosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**15**	**(3.1)**	**16**	**(3.9)**	**6**	**(1.7)**	**20**	**(4.1)**	**21**	**(4.5)**	**23**	**(5.3)**
Basal cell carcinoma	8	(1.7)	8	(1.9)	2	(0.6)	11	(2.3)	9	(1.9)	10	(2.3)
Bladder cancer	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Bowen's disease	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Breast cancer	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Chronic lymphocytic leukaemia	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Lentigo maligna	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Lung neoplasm malignant	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Lymphoma	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Malignant melanoma	2	(0.4)	2	(0.5)	1	(0.3)	1	(0.2)	2	(0.4)	2	(0.5)
Malignant melanoma in situ	2	(0.4)	3	(0.7)	0	(0.0)	0	(0.0)	5	(1.1)	1	(0.2)
Meningioma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Prostate cancer	0	(0.0)	2	(0.5)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Recurrent cancer	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Renal cell carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**15**	**(3.1)**	**16**	**(3.9)**	**6**	**(1.7)**	**20**	**(4.1)**	**21**	**(4.5)**	**23**	**(5.3)**
Second primary malignancy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Squamous cell carcinoma of skin	2	(0.4)	4	(1.0)	0	(0.0)	6	(1.2)	3	(0.6)	6	(1.4)
Transitional cell carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Transitional cell carcinoma recurrent	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nervous system disorders	**2**	**(0.4)**	**4**	**(1.0)**	**0**	**(0.0)**	**3**	**(0.6)**	**0**	**(0.0)**	**2**	**(0.5)**
Carpal tunnel syndrome	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Facial paralysis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Lumbar radiculopathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Meningorrhagia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Myelitis transverse	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Neuralgic amyotrophy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Peripheral sensory neuropathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Psychiatric disorders	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**2**	**(0.5)**
Completed suicide	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Depression	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**2**	**(0.5)**
Mania	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Suicidal ideation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.5)
Renal and urinary disorders	**1**	**(0.2)**	**3**	**(0.7)**	**3**	**(0.9)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.2)**
Acute kidney injury	0	(0.0)	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Autoimmune nephritis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Haematuria	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nephritis	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Nephrolithiasis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Renal failure	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Tubulointerstitial nephritis	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Reproductive system and breast disorders	**2**	**(0.4)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**
Benign prostatic hyperplasia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Endometrial hyperplasia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Ovarian cyst torsion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**2**	**(0.4)**	**4**	**(1.0)**	**3**	**(0.9)**	**1**	**(0.2)**	**2**	**(0.4)**	**1**	**(0.2)**
Acute respiratory failure	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Asthma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)
Chronic obstructive pulmonary disease	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**2**	**(0.4)**	**4**	**(1.0)**	**3**	**(0.9)**	**1**	**(0.2)**	**2**	**(0.4)**	**1**	**(0.2)**
Cough	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Immune-mediated lung disease	0	(0.0)	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Interstitial lung disease	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Pleural effusion	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Pulmonary embolism	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.4)	0	(0.0)
Skin and subcutaneous tissue disorders	**1**	**(0.2)**	**1**	**(0.2)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**
Dermatitis bullous	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rash	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Skin ulcer	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**
Haematoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Participants With Serious Adverse Events by Time Period (Incidence >0% in Any Column)
(APaT Population)

	Pembrolizumab						Placebo					
	Month 0 - <4		Month 4 - <8		Month ≥8		Month 0 - <4		Month 4 - <8		Month ≥8	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**
Hypertension	0	(0.0)	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.3.3 Intervention-related Serious Adverse Events

Table 14.3-43
Participants With Serious Drug-Related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	49	(10.1)	11	(2.3)
with no adverse events	434	(89.9)	475	(97.7)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Colitis	4	(0.8)	0	(0.0)
Autoimmune hepatitis	3	(0.6)	1	(0.2)
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Diarrhoea	2	(0.4)	1	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Abscess soft tissue	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Arthritis	1	(0.2)	0	(0.0)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)
Cough	1	(0.2)	0	(0.0)
Decreased appetite	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Lymphoma	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Muscular weakness	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Pneumonia	1	(0.2)	0	(0.0)

Participants With Serious Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pneumonitis	1	(0.2)	0	(0.0)
Sarcoidosis	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Facial paralysis	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	1	(0.2)
Infusion site urticaria	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-44
Participants With Serious Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	49	(10.1)	11	(2.3)
with no adverse events	434	(89.9)	475	(97.7)
Cardiac disorders	**0**	**(0.0)**	**2**	**(0.4)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	5	(1.0)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Eye disorders	**1**	**(0.2)**	**0**	**(0.0)**
Macular detachment	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**9**	**(1.9)**	**1**	**(0.2)**
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	4	(0.8)	0	(0.0)
Diarrhoea	2	(0.4)	1	(0.2)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**0**	**(0.0)**	**2**	**(0.4)**
Infusion site urticaria	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	1	(0.2)
Hepatobiliary disorders	**3**	**(0.6)**	**1**	**(0.2)**
Autoimmune hepatitis	3	(0.6)	1	(0.2)
Immune system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Sarcoidosis	1	(0.2)	0	(0.0)
Infections and infestations	**4**	**(0.8)**	**0**	**(0.0)**
Abscess soft tissue	1	(0.2)	0	(0.0)
Cellulitis	1	(0.2)	0	(0.0)

Participants With Serious Drug-Related Adverse Events by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**4**	**(0.8)**	**0**	**(0.0)**
Pneumonia	1	(0.2)	0	(0.0)
Septic shock	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**1**	**(0.2)**
Infusion related reaction	0	(0.0)	1	(0.2)
Investigations	**2**	**(0.4)**	**0**	**(0.0)**
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Metabolism and nutrition disorders	**4**	**(0.8)**	**0**	**(0.0)**
Decreased appetite	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**6**	**(1.2)**	**1**	**(0.2)**
Antisynthetase syndrome	0	(0.0)	1	(0.2)
Arthritis	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Muscular weakness	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.2)**	**0**	**(0.0)**
Lymphoma	1	(0.2)	0	(0.0)
Nervous system disorders	**4**	**(0.8)**	**3**	**(0.6)**
Facial paralysis	0	(0.0)	1	(0.2)
Meningorrhagia	0	(0.0)	1	(0.2)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)
Renal and urinary disorders	**6**	**(1.2)**	**0**	**(0.0)**

Participants With Serious Drug-Related Adverse Events by SOC and PT (Incidence > 0% in One or More Treatment Groups) (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Renal and urinary disorders	**6**	**(1.2)**	**0**	**(0.0)**
Acute kidney injury	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**6**	**(1.2)**	**0**	**(0.0)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Cough	1	(0.2)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Skin and subcutaneous tissue disorders	**1**	**(0.2)**	**0**	**(0.0)**
Dermatitis bullous	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.4 Other Clinically Meaningful Adverse Events

14.3.1.4.1 Adverse Events Leading to Study Intervention Discontinuation

Table 14.3-45
Participants With Adverse Events Resulting in Treatment Discontinuation by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	83	(17.2)	23	(4.7)
with no adverse events	400	(82.8)	463	(95.3)
Blood and lymphatic system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Cardiac disorders	**1**	**(0.2)**	**3**	**(0.6)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Cardiomyopathy	1	(0.2)	0	(0.0)
Mitral valve incompetence	0	(0.0)	1	(0.2)
Tachycardia	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	3	(0.6)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Hypothyroidism	2	(0.4)	0	(0.0)
Eye disorders	**1**	**(0.2)**	**0**	**(0.0)**
Macular detachment	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**13**	**(2.7)**	**2**	**(0.4)**
Autoimmune colitis	1	(0.2)	0	(0.0)
Chronic gastritis	1	(0.2)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Diarrhoea	2	(0.4)	2	(0.4)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**1**	**(0.2)**	**2**	**(0.4)**
Asthenia	0	(0.0)	1	(0.2)

Participants With Adverse Events Resulting in Treatment Discontinuation by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**1**	**(0.2)**	**2**	**(0.4)**
Malaise	0	(0.0)	1	(0.2)
Oedema peripheral	1	(0.2)	0	(0.0)
Hepatobiliary disorders	**10**	**(2.1)**	**2**	**(0.4)**
Autoimmune hepatitis	6	(1.2)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Infections and infestations	**1**	**(0.2)**	**2**	**(0.4)**
COVID-19 pneumonia	0	(0.0)	1	(0.2)
Pneumonia	0	(0.0)	1	(0.2)
Rhinitis	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**1**	**(0.2)**	**0**	**(0.0)**
Infusion related reaction	1	(0.2)	0	(0.0)
Investigations	**6**	**(1.2)**	**3**	**(0.6)**
Alanine aminotransferase increased	3	(0.6)	1	(0.2)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Blood creatinine increased	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)
Grip strength decreased	0	(0.0)	1	(0.2)
Lipase increased	1	(0.2)	0	(0.0)
Weight decreased	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**1**	**(0.2)**	**0**	**(0.0)**
Type 1 diabetes mellitus	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**15**	**(3.1)**	**1**	**(0.2)**
Arthralgia	3	(0.6)	0	(0.0)
Arthritis	2	(0.4)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	1	(0.2)
Myalgia	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)

Participants With Adverse Events Resulting in Treatment Discontinuation by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**15**	**(3.1)**	**1**	**(0.2)**
Myositis	2	(0.4)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Polyarthritis	2	(0.4)	0	(0.0)
Tendonitis	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(0.8)**	**4**	**(0.8)**
Breast cancer	1	(0.2)	0	(0.0)
Lung neoplasm malignant	0	(0.0)	1	(0.2)
Malignant melanoma	1	(0.2)	0	(0.0)
Prostate cancer	1	(0.2)	1	(0.2)
Recurrent cancer	1	(0.2)	1	(0.2)
Renal cell carcinoma	0	(0.0)	1	(0.2)
Nervous system disorders	**2**	**(0.4)**	**4**	**(0.8)**
Myasthenia gravis	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Neuropathy peripheral	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	0	(0.0)	1	(0.2)
Polyneuropathy	0	(0.0)	1	(0.2)
Psycbiatric disorders	**0**	**(0.0)**	**2**	**(0.4)**
Completed suicide	0	(0.0)	1	(0.2)
Mania	0	(0.0)	1	(0.2)
Renal and urinary disorders	**6**	**(1.2)**	**0**	**(0.0)**
Acute kidney injury	1	(0.2)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Renal impairment	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**1**	**(0.2)**	**0**	**(0.0)**
Genital erythema	1	(0.2)	0	(0.0)

Participants With Adverse Events Resulting in Treatment Discontinuation by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**7**	**(1.4)**	**0**	**(0.0)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Dyspnoea	1	(0.2)	0	(0.0)
Immune-mediated lung disease	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Skin and subcutaneous tissue disorders	**6**	**(1.2)**	**0**	**(0.0)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Lichen planus	1	(0.2)	0	(0.0)
Pruritus	1	(0.2)	0	(0.0)
Rash	3	(0.6)	0	(0.0)
Skin fissures	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Recurrent Cancer: recurrence of disease under the study
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-46
Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	77	(15.9)	12	(2.5)
with no adverse events	406	(84.1)	474	(97.5)
Autoimmune hepatitis	6	(1.2)	2	(0.4)
Colitis	5	(1.0)	0	(0.0)
Adrenal insufficiency	3	(0.6)	0	(0.0)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)
Arthralgia	3	(0.6)	0	(0.0)
Rash	3	(0.6)	0	(0.0)
Arthritis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Diarrhoea	2	(0.4)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Hypothyroidism	2	(0.4)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	1	(0.2)
Myositis	2	(0.4)	0	(0.0)
Polyarthritis	2	(0.4)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Acute kidney injury	1	(0.2)	0	(0.0)
Acute respiratory failure	1	(0.2)	0	(0.0)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Autoimmune colitis	1	(0.2)	0	(0.0)
Blood creatinine increased	1	(0.2)	0	(0.0)
Chronic gastritis	1	(0.2)	0	(0.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)
Genital erythema	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Immune-mediated lung disease	1	(0.2)	0	(0.0)
Infusion related reaction	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Interstitial lung disease	1	(0.2)	0	(0.0)
Lichen planus	1	(0.2)	0	(0.0)
Lipase increased	1	(0.2)	0	(0.0)
Macular detachment	1	(0.2)	0	(0.0)
Myalgia	1	(0.2)	0	(0.0)
Myasthenia gravis	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Oedema peripheral	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Pruritus	1	(0.2)	0	(0.0)
Renal impairment	1	(0.2)	0	(0.0)
Rhinitis	1	(0.2)	0	(0.0)
Skin fissures	1	(0.2)	0	(0.0)
Tendonitis	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	1	(0.2)	0	(0.0)
Asthenia	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Malaise	0	(0.0)	1	(0.2)
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	0	(0.0)	1	(0.2)
Polyneuropathy	0	(0.0)	1	(0.2)
Weight decreased	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-47
Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	77	(15.9)	12	(2.5)
with no adverse events	406	(84.1)	474	(97.5)
Blood and lymphatic system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Immune thrombocytopenia	1	(0.2)	0	(0.0)
Cardiac disorders	**0**	**(0.0)**	**1**	**(0.2)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Endocrine disorders	**10**	**(2.1)**	**0**	**(0.0)**
Adrenal insufficiency	3	(0.6)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Hypothyroidism	2	(0.4)	0	(0.0)
Eye disorders	**1**	**(0.2)**	**0**	**(0.0)**
Macular detachment	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**13**	**(2.7)**	**2**	**(0.4)**
Autoimmune colitis	1	(0.2)	0	(0.0)
Chronic gastritis	1	(0.2)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Colitis ulcerative	1	(0.2)	0	(0.0)
Diarrhoea	2	(0.4)	2	(0.4)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Palatal oedema	1	(0.2)	0	(0.0)
Pancreatitis	1	(0.2)	0	(0.0)
General disorders and administration site conditions	**1**	**(0.2)**	**2**	**(0.4)**
Asthenia	0	(0.0)	1	(0.2)
Malaise	0	(0.0)	1	(0.2)
Oedema peripheral	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hepatobiliary disorders	**10**	**(2.1)**	**2**	**(0.4)**
Autoimmune hepatitis	6	(1.2)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hepatotoxicity	2	(0.4)	0	(0.0)
Infections and infestations	**1**	**(0.2)**	**0**	**(0.0)**
Rhinitis	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**1**	**(0.2)**	**0**	**(0.0)**
Infusion related reaction	1	(0.2)	0	(0.0)
Investigations	**6**	**(1.2)**	**2**	**(0.4)**
Alanine aminotransferase increased	3	(0.6)	1	(0.2)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)
Blood creatinine increased	1	(0.2)	0	(0.0)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)
Lipase increased	1	(0.2)	0	(0.0)
Weight decreased	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**1**	**(0.2)**	**0**	**(0.0)**
Type 1 diabetes mellitus	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**15**	**(3.1)**	**1**	**(0.2)**
Arthralgia	3	(0.6)	0	(0.0)
Arthritis	2	(0.4)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	1	(0.2)
Myalgia	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Polyarthritis	2	(0.4)	0	(0.0)
Tendonitis	1	(0.2)	0	(0.0)
Nervous system disorders	**2**	**(0.4)**	**3**	**(0.6)**
Myasthenia gravis	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**2**	**(0.4)**	**3**	**(0.6)**
Neuralgic amyotrophy	0	(0.0)	1	(0.2)
Peripheral sensory neuropathy	0	(0.0)	1	(0.2)
Polyneuropathy	0	(0.0)	1	(0.2)
Renal and urinary disorders	**6**	**(1.2)**	**0**	**(0.0)**
Acute kidney injury	1	(0.2)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Renal impairment	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**1**	**(0.2)**	**0**	**(0.0)**
Genital erythema	1	(0.2)	0	(0.0)
Respiratory, tboracic and mediastinal disorders	**6**	**(1.2)**	**0**	**(0.0)**
Acute respiratory failure	1	(0.2)	0	(0.0)
Immune-mediated lung disease	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Skin and subcutaneous tissue disorders	**6**	**(1.2)**	**0**	**(0.0)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Lichen planus	1	(0.2)	0	(0.0)
Pruritus	1	(0.2)	0	(0.0)
Rash	3	(0.6)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Discontinuation
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**6**	**(1.2)**	**0**	**(0.0)**
Skin fissures	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.4.2 Adverse Events Leading to Study Intervention Interruption

Table 14.3-48
Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	106	(21.9)	81	(16.7)
with no adverse events	377	(78.1)	405	(83.3)
Blood and lymphatic system disorders	**1**	**(0.2)**	**1**	**(0.2)**
Lymphadenopathy	1	(0.2)	0	(0.0)
Neutropenia	0	(0.0)	1	(0.2)
Cardiac disorders	**2**	**(0.4)**	**5**	**(1.0)**
Acute myocardial infarction	0	(0.0)	1	(0.2)
Atrial fibrillation	1	(0.2)	1	(0.2)
Cardiac failure	0	(0.0)	1	(0.2)
Coronary artery disease	0	(0.0)	1	(0.2)
Sinus bradycardia	0	(0.0)	1	(0.2)
Ventricular extrasystoles	1	(0.2)	0	(0.0)
Ear and labyrinth disorders	**1**	**(0.2)**	**1**	**(0.2)**
Tinnitus	0	(0.0)	1	(0.2)
Vertigo	1	(0.2)	0	(0.0)
Endocrine disorders	**14**	**(2.9)**	**1**	**(0.2)**
Adrenal insufficiency	3	(0.6)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hyperthyroidism	6	(1.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypothyroidism	1	(0.2)	1	(0.2)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Eye disorders	**3**	**(0.6)**	**1**	**(0.2)**
Blepharitis	0	(0.0)	1	(0.2)
Dry eye	0	(0.0)	1	(0.2)
Eye irritation	1	(0.2)	0	(0.0)
Eyelid irritation	1	(0.2)	0	(0.0)
Myopia	1	(0.2)	0	(0.0)
Ocular hyperaemia	1	(0.2)	0	(0.0)
Periorbital oedema	1	(0.2)	0	(0.0)

Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Eye disorders	**3**	**(0.6)**	**1**	**(0.2)**
Vitreous floaters	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**24**	**(5.0)**	**11**	**(2.3)**
Abdominal pain	1	(0.2)	0	(0.0)
Abdominal pain upper	1	(0.2)	2	(0.4)
Anal fistula	1	(0.2)	0	(0.0)
Autoimmune colitis	1	(0.2)	0	(0.0)
Colitis	5	(1.0)	1	(0.2)
Diarrhoea	13	(2.7)	6	(1.2)
Haematemesis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Nausea	0	(0.0)	1	(0.2)
Proctitis	1	(0.2)	0	(0.0)
Stomatitis	1	(0.2)	0	(0.0)
Terminal ileitis	0	(0.0)	1	(0.2)
General disorders and administration site conditions	**13**	**(2.7)**	**10**	**(2.1)**
Asthenia	2	(0.4)	2	(0.4)
Fatigue	3	(0.6)	0	(0.0)
Influenza like illness	1	(0.2)	0	(0.0)
Malaise	0	(0.0)	1	(0.2)
Pyrexia	7	(1.4)	7	(1.4)
Hepatobiliary disorders	**3**	**(0.6)**	**3**	**(0.6)**
Autoimmune hepatitis	1	(0.2)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.2)
Hypertransaminasaemia	2	(0.4)	2	(0.4)
Immune system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Sarcoidosis	1	(0.2)	0	(0.0)
Infections and infestations	**15**	**(3.1)**	**13**	**(2.7)**
Abdominal wall abscess	0	(0.0)	1	(0.2)
Anorectal infection	1	(0.2)	0	(0.0)

Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Infections and infestations	**15**	**(3.1)**	**13**	**(2.7)**
Bronchitis	0	(0.0)	2	(0.4)
COVID-19	2	(0.4)	4	(0.8)
COVID-19 pneumonia	1	(0.2)	1	(0.2)
Cellulitis	1	(0.2)	0	(0.0)
Chronic hepatitis B	0	(0.0)	1	(0.2)
Erysipelas	1	(0.2)	0	(0.0)
Gastroenteritis viral	1	(0.2)	0	(0.0)
Herpes zoster	1	(0.2)	0	(0.0)
Infected dermal cyst	0	(0.0)	1	(0.2)
Influenza	0	(0.0)	1	(0.2)
Pneumonia	2	(0.4)	0	(0.0)
Rash pustular	2	(0.4)	0	(0.0)
Rhinitis	1	(0.2)	0	(0.0)
Sepsis	1	(0.2)	0	(0.0)
Upper respiratory tract infection	1	(0.2)	1	(0.2)
Upper respiratory tract infection bacterial	1	(0.2)	0	(0.0)
Urinary tract infection	1	(0.2)	1	(0.2)
Viral upper respiratory tract infection	0	(0.0)	1	(0.2)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**6**	**(1.2)**
Anastomotic leak	0	(0.0)	1	(0.2)
Infusion related reaction	0	(0.0)	3	(0.6)
Lumbar vertebral fracture	0	(0.0)	1	(0.2)
Upper limb fracture	0	(0.0)	1	(0.2)
Investigations	**14**	**(2.9)**	**16**	**(3.3)**
Alanine aminotransferase increased	4	(0.8)	0	(0.0)
Amylase increased	2	(0.4)	2	(0.4)
Aspartate aminotransferase increased	4	(0.8)	1	(0.2)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	2	(0.4)	2	(0.4)
Blood creatinine increased	1	(0.2)	4	(0.8)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)
Lipase increased	3	(0.6)	5	(1.0)

Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Investigations	**14**	**(2.9)**	**16**	**(3.3)**
Neutrophil count decreased	0	(0.0)	1	(0.2)
Platelet count decreased	1	(0.2)	1	(0.2)
SARS-CoV-2 test positive	1	(0.2)	2	(0.4)
Metabolism and nutrition disorders	**6**	**(1.2)**	**0**	**(0.0)**
Decreased appetite	1	(0.2)	0	(0.0)
Gout	1	(0.2)	0	(0.0)
Hypercalcaemia	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	2	(0.4)	0	(0.0)
Underweight	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**19**	**(3.9)**	**4**	**(0.8)**
Arthralgia	10	(2.1)	1	(0.2)
Arthritis	2	(0.4)	0	(0.0)
Back pain	1	(0.2)	1	(0.2)
Compartment syndrome	1	(0.2)	0	(0.0)
Fibromyalgia	0	(0.0)	1	(0.2)
Flank pain	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	1	(0.2)
Joint swelling	1	(0.2)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myositis	1	(0.2)	0	(0.0)
Neck pain	1	(0.2)	0	(0.0)
Osteoarthritis	1	(0.2)	0	(0.0)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Spinal stenosis	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.4)**	**0**	**(0.0)**
Malignant melanoma	1	(0.2)	0	(0.0)
Meningioma	1	(0.2)	0	(0.0)
Nervous system disorders	**4**	**(0.8)**	**4**	**(0.8)**
Carpal tunnel syndrome	1	(0.2)	0	(0.0)
Dizziness	1	(0.2)	1	(0.2)

Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Nervous system disorders	**4**	**(0.8)**	**4**	**(0.8)**
Facial paralysis	0	(0.0)	1	(0.2)
Headache	2	(0.4)	0	(0.0)
Hypoaesthesia	0	(0.0)	1	(0.2)
Neuropathy peripheral	0	(0.0)	2	(0.4)
Syncope	1	(0.2)	0	(0.0)
Psychiatric disorders	**0**	**(0.0)**	**1**	**(0.2)**
Insomnia	0	(0.0)	1	(0.2)
Renal and urinary disorders	**2**	**(0.4)**	**1**	**(0.2)**
Haematuria	0	(0.0)	1	(0.2)
Nephritis	2	(0.4)	0	(0.0)
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(0.2)**
Breast cyst	0	(0.0)	1	(0.2)
Respiratory, thoracic and mediastinal disorders	**13**	**(2.7)**	**11**	**(2.3)**
Asthma	0	(0.0)	2	(0.4)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)
Cough	6	(1.2)	2	(0.4)
Dyspnoea	1	(0.2)	3	(0.6)
Dyspnoea exertional	1	(0.2)	0	(0.0)
Lung infiltration	1	(0.2)	0	(0.0)
Nasal congestion	0	(0.0)	1	(0.2)
Pickwickian syndrome	1	(0.2)	0	(0.0)
Pneumonitis	3	(0.6)	1	(0.2)
Pulmonary embolism	1	(0.2)	1	(0.2)
Rhinorrhoea	0	(0.0)	1	(0.2)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**2**	**(0.4)**
Dermatitis	0	(0.0)	1	(0.2)
Pruritus	2	(0.4)	0	(0.0)
Rash	3	(0.6)	1	(0.2)
Rash maculo-papular	2	(0.4)	0	(0.0)
Rash pruritic	1	(0.2)	0	(0.0)

Participants With Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**2**	**(0.4)**
Skin ulcer	1	(0.2)	0	(0.0)
Vascular disorders	**3**	**(0.6)**	**2**	**(0.4)**
Haematoma	1	(0.2)	1	(0.2)
Hypertension	1	(0.2)	1	(0.2)
Hypotension	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-49
Participants With Drug-Related Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	73	(15.1)	32	(6.6)
with no adverse events	410	(84.9)	454	(93.4)
Cardiac disorders	**0**	**(0.0)**	**2**	**(0.4)**
Cardiac failure	0	(0.0)	1	(0.2)
Sinus bradycardia	0	(0.0)	1	(0.2)
Endocrine disorders	**14**	**(2.9)**	**1**	**(0.2)**
Adrenal insufficiency	3	(0.6)	0	(0.0)
Endocrine disorder	1	(0.2)	0	(0.0)
Hyperthyroidism	6	(1.2)	0	(0.0)
Hypophysitis	2	(0.4)	0	(0.0)
Hypothyroidism	1	(0.2)	1	(0.2)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Eye disorders	**2**	**(0.4)**	**1**	**(0.2)**
Blepharitis	0	(0.0)	1	(0.2)
Dry eye	0	(0.0)	1	(0.2)
Eye irritation	1	(0.2)	0	(0.0)
Eyelid irritation	1	(0.2)	0	(0.0)
Myopia	1	(0.2)	0	(0.0)
Ocular hyperaemia	1	(0.2)	0	(0.0)
Periorbital oedema	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**19**	**(3.9)**	**8**	**(1.6)**
Abdominal pain	1	(0.2)	0	(0.0)
Abdominal pain upper	1	(0.2)	1	(0.2)
Autoimmune colitis	1	(0.2)	0	(0.0)
Colitis	4	(0.8)	1	(0.2)
Diarrhoea	10	(2.1)	5	(1.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Nausea	0	(0.0)	1	(0.2)
Stomatitis	1	(0.2)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
General disorders and administration site conditions	**4**	**(0.8)**	**4**	**(0.8)**
Asthenia	2	(0.4)	0	(0.0)
Fatigue	1	(0.2)	0	(0.0)
Influenza like illness	1	(0.2)	0	(0.0)
Malaise	0	(0.0)	1	(0.2)
Pyrexia	0	(0.0)	3	(0.6)
Hepatobiliary disorders	**2**	**(0.4)**	**3**	**(0.6)**
Autoimmune hepatitis	1	(0.2)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.2)
Hypertransaminasaemia	1	(0.2)	2	(0.4)
Immune system disorders	**1**	**(0.2)**	**0**	**(0.0)**
Sarcoidosis	1	(0.2)	0	(0.0)
Infections and infestations	**2**	**(0.4)**	**0**	**(0.0)**
Pneumonia	1	(0.2)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**3**	**(0.6)**
Infusion related reaction	0	(0.0)	3	(0.6)
Investigations	**11**	**(2.3)**	**6**	**(1.2)**
Alanine aminotransferase increased	3	(0.6)	0	(0.0)
Amylase increased	2	(0.4)	2	(0.4)
Aspartate aminotransferase increased	4	(0.8)	0	(0.0)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)
Blood creatine phosphokinase MB increased	0	(0.0)	1	(0.2)
Blood creatine phosphokinase increased	2	(0.4)	0	(0.0)
Blood creatinine increased	1	(0.2)	1	(0.2)
Brain natriuretic peptide increased	0	(0.0)	1	(0.2)
Lipase increased	3	(0.6)	3	(0.6)
Neutrophil count decreased	0	(0.0)	1	(0.2)
Platelet count decreased	0	(0.0)	1	(0.2)

Participants With Drug-Related Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Metabolism and nutrition disorders	**5**	**(1.0)**	**0**	**(0.0)**
Decreased appetite	1	(0.2)	0	(0.0)
Gout	1	(0.2)	0	(0.0)
Hypercalcaemia	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	1	(0.2)	0	(0.0)
Underweight	1	(0.2)	0	(0.0)
Musculoskeletal and connective tissue disorders	**16**	**(3.3)**	**2**	**(0.4)**
Arthralgia	10	(2.1)	0	(0.0)
Arthritis	2	(0.4)	0	(0.0)
Back pain	1	(0.2)	1	(0.2)
Immune-mediated arthritis	1	(0.2)	1	(0.2)
Joint swelling	1	(0.2)	0	(0.0)
Myalgia	2	(0.4)	0	(0.0)
Myositis	1	(0.2)	0	(0.0)
Neck pain	1	(0.2)	0	(0.0)
Rheumatoid arthritis	1	(0.2)	0	(0.0)
Nervous system disorders	**0**	**(0.0)**	**3**	**(0.6)**
Facial paralysis	0	(0.0)	1	(0.2)
Neuropathy peripheral	0	(0.0)	2	(0.4)
Psycbiatric disorders	**0**	**(0.0)**	**1**	**(0.2)**
Insomnia	0	(0.0)	1	(0.2)
Renal and urinary disorders	**2**	**(0.4)**	**0**	**(0.0)**
Nephritis	2	(0.4)	0	(0.0)
Respiratory, tboracic and mediastinal disorders	**5**	**(1.0)**	**2**	**(0.4)**
Cough	2	(0.4)	0	(0.0)
Dyspnoea	0	(0.0)	1	(0.2)
Pneumonitis	3	(0.6)	1	(0.2)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**2**	**(0.4)**
Dermatitis	0	(0.0)	1	(0.2)
Pruritus	2	(0.4)	0	(0.0)

Participants With Drug-Related Adverse Events Resulting in Treatment Interruption by SOC and PT
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**2**	**(0.4)**
Rash	3	(0.6)	1	(0.2)
Rash maculo-papular	2	(0.4)	0	(0.0)
Rash pruritic	1	(0.2)	0	(0.0)
Skin ulcer	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
MedDRA V25.1 preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.3.1.5 Adverse Events of Special Interest

Table 14.3-50
Adverse Event Summary
AEOSI Overall
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
with no adverse event	300	(62.1)	440	(90.5)
with drug-related[a] adverse events	176	(36.4)	33	(6.8)
with toxicity grade 3-5 adverse events	53	(11.0)	6	(1.2)
with toxicity grade 3-5 drug-related adverse events	52	(10.8)	4	(0.8)
with serious adverse events	38	(7.9)	4	(0.8)
with serious drug-related adverse events	36	(7.5)	3	(0.6)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	47	(9.7)	4	(0.8)
discontinued drug due to a drug-related adverse event	47	(9.7)	4	(0.8)
discontinued drug due to a serious adverse event	27	(5.6)	2	(0.4)
discontinued drug due to a serious drug-related adverse event	27	(5.6)	2	(0.4)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-51
Adverse Event Summary
AEOSI Overall
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	0	(0.0)	19	(30.2)
with no adverse event	8	(100.0)	44	(69.8)
with drug-related[a] adverse events	0	(0.0)	14	(22.2)
with toxicity grade 3-5 adverse events	0	(0.0)	3	(4.8)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	3	(4.8)
with serious adverse events	0	(0.0)	2	(3.2)
with serious drug-related adverse events	0	(0.0)	2	(3.2)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	3	(4.8)
discontinued drug due to a drug-related adverse event	0	(0.0)	3	(4.8)
discontinued drug due to a serious adverse event	0	(0.0)	2	(3.2)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	2	(3.2)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-52
Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
with no adverse events	300	(62.1)	440	(90.5)
Adrenal Insufficiency	**13**	**(2.7)**	**0**	**(0.0)**
Adrenal insufficiency	13	(2.7)	0	(0.0)
Arthritis	**2**	**(0.4)**	**2**	**(0.4)**
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Colitis	**20**	**(4.1)**	**5**	**(1.0)**
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	16	(3.3)	5	(1.0)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Hepatitis	**11**	**(2.3)**	**3**	**(0.6)**
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Hepatitis	3	(0.6)	1	(0.2)
Hyperthyroidism	**51**	**(10.6)**	**3**	**(0.6)**
Hyperthyroidism	51	(10.6)	3	(0.6)
Hypophysitis	**12**	**(2.5)**	**0**	**(0.0)**
Hypophysitis	7	(1.4)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Hypothyroidism	**83**	**(17.2)**	**18**	**(3.7)**
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Hypothyroidism	82	(17.0)	17	(3.5)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)
Infusion Reactions	**3**	**(0.6)**	**7**	**(1.4)**
Drug hypersensitivity	1	(0.2)	2	(0.4)
Hypersensitivity	0	(0.0)	1	(0.2)
Infusion related reaction	2	(0.4)	4	(0.8)

Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Myasthenic Syndrome	**2**	**(0.4)**	**0**	**(0.0)**
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis	**1**	**(0.2)**	**0**	**(0.0)**
Myelitis transverse	1	(0.2)	0	(0.0)
Myocarditis	**1**	**(0.2)**	**1**	**(0.2)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Myositis	**6**	**(1.2)**	**1**	**(0.2)**
Myopathy	2	(0.4)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Nephritis	**7**	**(1.4)**	**0**	**(0.0)**
Autoimmune nephritis	2	(0.4)	0	(0.0)
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Nephritis	3	(0.6)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Pancreatitis	**2**	**(0.4)**	**0**	**(0.0)**
Pancreatitis	2	(0.4)	0	(0.0)
Pneumonitis	**13**	**(2.7)**	**4**	**(0.8)**
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Sarcoidosis	**5**	**(1.0)**	**0**	**(0.0)**
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Sarcoidosis	3	(0.6)	0	(0.0)
Severe Skin Reactions	**15**	**(3.1)**	**3**	**(0.6)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Erythema multiforme	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Severe Skin Reactions	**15**	**(3.1)**	**3**	**(0.6)**
Pruritus	3	(0.6)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Thyroiditis	**8**	**(1.7)**	**2**	**(0.4)**
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Thyroiditis	2	(0.4)	1	(0.2)
Type 1 Diabetes Mellitus	**2**	**(0.4)**	**0**	**(0.0)**
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Uveitis	**1**	**(0.2)**	**0**	**(0.0)**
Iridocyclitis	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-53
Exposure-Adjusted Adverse Event Summary
(Including Multiple Occurrences of Events)
AEOSI
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]			
	Pembrolizumab		Placebo	
Number of participants exposed	483		486	
Total exposure[b] in person-months	4945.05		5420.53	
Total events (rate)				
adverse events	283	(5.72)	56	(1.03)
drug-related[c] adverse events	266	(5.38)	42	(0.77)
toxicity grade 3-5 adverse events	60	(1.21)	6	(0.11)
toxicity grade 3-5 drug-related adverse events	58	(1.17)	4	(0.07)
serious adverse events	41	(0.83)	4	(0.07)
serious drug-related adverse events	38	(0.77)	3	(0.06)
adverse events leading to death	0	(0.00)	0	(0.00)
drug-related adverse events leading to death	0	(0.00)	0	(0.00)
adverse events resulting in drug discontinuation	47	(0.95)	4	(0.07)
drug-related adverse events resulting in drug discontinuation	47	(0.95)	4	(0.07)
serious adverse events resulting in drug discontinuation	27	(0.55)	2	(0.04)
serious drug-related adverse events resulting in drug discontinuation	27	(0.55)	2	(0.04)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.
[b] Drug exposure is defined as the between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.
[c] Determined by the investigator to be related to the drug.
Adverse events occurred after the first dose of second course are excluded.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-54
Exposure-Adjusted AEOSI Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Number of participants exposed	483	486
Total exposure[b] in person-months	4945.05	5420.53
Adrenal Insufficiency	**14 (0.28)**	**0 (0.00)**
Adrenal insufficiency	14 (0.28)	0 (0.00)
Arthritis	**3 (0.06)**	**5 (0.09)**
Immune-mediated arthritis	3 (0.06)	5 (0.09)
Colitis	**22 (0.44)**	**6 (0.11)**
Autoimmune colitis	2 (0.04)	0 (0.00)
Colitis	17 (0.34)	6 (0.11)
Immune-mediated enterocolitis	3 (0.06)	0 (0.00)
Hepatitis	**12 (0.24)**	**3 (0.06)**
Autoimmune hepatitis	8 (0.16)	2 (0.04)
Hepatitis	4 (0.08)	1 (0.02)
Hyperthyroidism	**51 (1.03)**	**4 (0.07)**
Hyperthyroidism	51 (1.03)	4 (0.07)
Hypophysitis	**13 (0.26)**	**0 (0.00)**
Hypophysitis	7 (0.14)	0 (0.00)
Hypopituitarism	5 (0.10)	0 (0.00)
Lymphocytic hypophysitis	1 (0.02)	0 (0.00)
Hypothyroidism	**85 (1.72)**	**20 (0.37)**
Autoimmune hypothyroidism	1 (0.02)	0 (0.00)
Hypothyroidism	84 (1.70)	19 (0.35)
Immune-mediated hypothyroidism	0 (0.00)	1 (0.02)
Infusion Reactions	**4 (0.08)**	**7 (0.13)**
Drug hypersensitivity	1 (0.02)	2 (0.04)
Hypersensitivity	0 (0.00)	1 (0.02)
Infusion related reaction	3 (0.06)	4 (0.07)
Myasthenic Syndrome	**2 (0.04)**	**0 (0.00)**
Myasthenia gravis	2 (0.04)	0 (0.00)
Myelitis	**1 (0.02)**	**0 (0.00)**
Myelitis transverse	1 (0.02)	0 (0.00)
Myocarditis	**1 (0.02)**	**1 (0.02)**
Autoimmune myocarditis	0 (0.00)	1 (0.02)
Myocarditis	1 (0.02)	0 (0.00)
Myositis	**6 (0.12)**	**1 (0.02)**
Myopathy	2 (0.04)	0 (0.00)

Exposure-Adjusted AEOSI Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Myositis	**6 (0.12)**	**1 (0.02)**
Myositis	4 (0.08)	1 (0.02)
Nephritis	**7 (0.14)**	**0 (0.00)**
Autoimmune nephritis	2 (0.04)	0 (0.00)
Glomerulonephritis acute	1 (0.02)	0 (0.00)
Nephritis	3 (0.06)	0 (0.00)
Tubulointerstitial nephritis	1 (0.02)	0 (0.00)
Pancreatitis	**2 (0.04)**	**0 (0.00)**
Pancreatitis	2 (0.04)	0 (0.00)
Pneumonitis	**16 (0.32)**	**4 (0.07)**
Immune-mediated lung disease	3 (0.06)	0 (0.00)
Interstitial lung disease	1 (0.02)	0 (0.00)
Pneumonitis	12 (0.24)	4 (0.07)
Sarcoidosis	**6 (0.12)**	**0 (0.00)**
Cutaneous sarcoidosis	1 (0.02)	0 (0.00)
Pulmonary sarcoidosis	2 (0.04)	0 (0.00)
Sarcoidosis	3 (0.06)	0 (0.00)
Severe Skin Reactions	**24 (0.49)**	**3 (0.06)**
Dermatitis bullous	1 (0.02)	0 (0.00)
Erythema multiforme	6 (0.12)	0 (0.00)
Pemphigoid	1 (0.02)	0 (0.00)
Pruritus	3 (0.06)	0 (0.00)
Rash	7 (0.14)	2 (0.04)
Rash maculo-papular	3 (0.06)	1 (0.02)
Rash pruritic	2 (0.04)	0 (0.00)
Rash pustular	1 (0.02)	0 (0.00)
Thyroiditis	**8 (0.16)**	**2 (0.04)**
Autoimmune thyroiditis	5 (0.10)	1 (0.02)
Immune-mediated thyroiditis	1 (0.02)	0 (0.00)
Thyroiditis	2 (0.04)	1 (0.02)
Type 1 Diabetes Mellitus	**2 (0.04)**	**0 (0.00)**
Type 1 diabetes mellitus	2 (0.04)	0 (0.00)
Uveitis	**4 (0.08)**	**0 (0.00)**
Iridocyclitis	2 (0.04)	0 (0.00)

Exposure-Adjusted AEOSI Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Uveitis	**4 (0.08)**	**0 (0.00)**
Iritis	2 (0.04)	0 (0.00)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-55
Adverse Event Summary
AEOSI - Adrenal Insufficiency
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	13	(2.7)	0	(0.0)
with no adverse event	470	(97.3)	486	(100.0)
with drug-related[a] adverse events	13	(2.7)	0	(0.0)
with toxicity grade 3-5 adverse events	5	(1.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	5	(1.0)	0	(0.0)
with serious adverse events	5	(1.0)	0	(0.0)
with serious drug-related adverse events	5	(1.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a drug-related adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	3	(0.6)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-56
Adverse Event Summary
AEOSI - Arthritis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	2	(0.4)	2	(0.4)
with no adverse event	481	(99.6)	484	(99.6)
with drug-related[a] adverse events	2	(0.4)	2	(0.4)
with toxicity grade 3-5 adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	1	(0.2)	0	(0.0)
with serious adverse events	1	(0.2)	0	(0.0)
with serious drug-related adverse events	1	(0.2)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	2	(0.4)	1	(0.2)
discontinued drug due to a drug-related adverse event	2	(0.4)	1	(0.2)
discontinued drug due to a serious adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	1	(0.2)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-57
Adverse Event Summary
AEOSI - Cholangitis Sclerosing
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	0	(0.0)	0	(0.0)
with no adverse event	483	(100.0)	486	(100.0)
with drug-related[a] adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-58
Adverse Event Summary
AEOSI - Colitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	20	(4.1)	5	(1.0)
with no adverse event	463	(95.9)	481	(99.0)
with drug-related[a] adverse events	19	(3.9)	4	(0.8)
with toxicity grade 3-5 adverse events	8	(1.7)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	8	(1.7)	0	(0.0)
with serious adverse events	7	(1.4)	0	(0.0)
with serious drug-related adverse events	7	(1.4)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	7	(1.4)	0	(0.0)
discontinued drug due to a drug-related adverse event	7	(1.4)	0	(0.0)
discontinued drug due to a serious adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	3	(0.6)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-59
Adverse Event Summary
AEOSI - Encephalitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	0	(0.0)	0	(0.0)
with no adverse event	483	(100.0)	486	(100.0)
with drug-related[a] adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-60
Adverse Event Summary
AEOSI - Guillain-Barre Syndrome
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	0	(0.0)	0	(0.0)
with no adverse event	483	(100.0)	486	(100.0)
with drug-related[a] adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-61
Adverse Event Summary
AEOSI - Hepatitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	11	(2.3)	3	(0.6)
with no adverse event	472	(97.7)	483	(99.4)
with drug-related[a] adverse events	11	(2.3)	3	(0.6)
with toxicity grade 3-5 adverse events	9	(1.9)	2	(0.4)
with toxicity grade 3-5 drug-related adverse events	9	(1.9)	2	(0.4)
with serious adverse events	3	(0.6)	1	(0.2)
with serious drug-related adverse events	3	(0.6)	1	(0.2)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	8	(1.7)	2	(0.4)
discontinued drug due to a drug-related adverse event	8	(1.7)	2	(0.4)
discontinued drug due to a serious adverse event	3	(0.6)	1	(0.2)
discontinued drug due to a serious drug-related adverse event	3	(0.6)	1	(0.2)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-62
Adverse Event Summary
AEOSI - Hyperthyroidism
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	51	(10.6)	3	(0.6)
with no adverse event	432	(89.4)	483	(99.4)
with drug-related[a] adverse events	49	(10.1)	3	(0.6)
with toxicity grade 3-5 adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	1	(0.2)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-63
Adverse Event Summary
AEOSI - Hypophysitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	12	(2.5)	0	(0.0)
with no adverse event	471	(97.5)	486	(100.0)
with drug-related[a] adverse events	12	(2.5)	0	(0.0)
with toxicity grade 3-5 adverse events	3	(0.6)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	3	(0.6)	0	(0.0)
with serious adverse events	4	(0.8)	0	(0.0)
with serious drug-related adverse events	4	(0.8)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a drug-related adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a serious adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	4	(0.8)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-64
Adverse Event Summary
AEOSI - Hypothyroidism
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	83	(17.2)	18	(3.7)
with no adverse event	400	(82.8)	468	(96.3)
with drug-related[a] adverse events	78	(16.1)	13	(2.7)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	2	(0.4)	0	(0.0)
discontinued drug due to a drug-related adverse event	2	(0.4)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-65
Adverse Event Summary
AEOSI - Infusion Reactions
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	3	(0.6)	7	(1.4)
with no adverse event	480	(99.4)	479	(98.6)
with drug-related[a] adverse events	2	(0.4)	3	(0.6)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	1	(0.2)
with serious drug-related adverse events	0	(0.0)	1	(0.2)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-66
Adverse Event Summary
AEOSI - Myasthenic Syndrome
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	2	(0.4)	0	(0.0)
with no adverse event	481	(99.6)	486	(100.0)
with drug-related[a] adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	2	(0.4)	0	(0.0)
with serious adverse events	2	(0.4)	0	(0.0)
with serious drug-related adverse events	2	(0.4)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	1	(0.2)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-67
Adverse Event Summary
AEOSI - Myelitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	1	(0.2)	0	(0.0)
with no adverse event	482	(99.8)	486	(100.0)
with drug-related[a] adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	1	(0.2)	0	(0.0)
with serious adverse events	1	(0.2)	0	(0.0)
with serious drug-related adverse events	1	(0.2)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	1	(0.2)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-68
Adverse Event Summary
AEOSI - Myocarditis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	1	(0.2)	1	(0.2)
with no adverse event	482	(99.8)	485	(99.8)
with drug-related[a] adverse events	0	(0.0)	1	(0.2)
with toxicity grade 3-5 adverse events	0	(0.0)	1	(0.2)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	1	(0.2)
with serious adverse events	1	(0.2)	1	(0.2)
with serious drug-related adverse events	0	(0.0)	1	(0.2)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	1	(0.2)
discontinued drug due to a drug-related adverse event	0	(0.0)	1	(0.2)
discontinued drug due to a serious adverse event	0	(0.0)	1	(0.2)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	1	(0.2)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-69
Adverse Event Summary
AEOSI - Myositis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	6	(1.2)	1	(0.2)
with no adverse event	477	(98.8)	485	(99.8)
with drug-related[a] adverse events	5	(1.0)	0	(0.0)
with toxicity grade 3-5 adverse events	3	(0.6)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	3	(0.6)	0	(0.0)
with serious adverse events	3	(0.6)	0	(0.0)
with serious drug-related adverse events	3	(0.6)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a drug-related adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	3	(0.6)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-70
Adverse Event Summary
AEOSI - Nephritis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	7	(1.4)	0	(0.0)
with no adverse event	476	(98.6)	486	(100.0)
with drug-related[a] adverse events	6	(1.2)	0	(0.0)
with toxicity grade 3-5 adverse events	3	(0.6)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	3	(0.6)	0	(0.0)
with serious adverse events	4	(0.8)	0	(0.0)
with serious drug-related adverse events	4	(0.8)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a drug-related adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a serious adverse event	4	(0.8)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	4	(0.8)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-71
Adverse Event Summary
AEOSI - Pancreatitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	2	(0.4)	0	(0.0)
with no adverse event	481	(99.6)	486	(100.0)
with drug-related[a] adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	1	(0.2)	0	(0.0)
with serious adverse events	1	(0.2)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-72
Adverse Event Summary
AEOSI - Pneumonitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	13	(2.7)	4	(0.8)
with no adverse event	470	(97.3)	482	(99.2)
with drug-related[a] adverse events	11	(2.3)	4	(0.8)
with toxicity grade 3-5 adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	2	(0.4)	0	(0.0)
with serious adverse events	5	(1.0)	0	(0.0)
with serious drug-related adverse events	4	(0.8)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a drug-related adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious adverse event	2	(0.4)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	2	(0.4)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-73
Adverse Event Summary
AEOSI - Sarcoidosis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	5	(1.0)	0	(0.0)
with no adverse event	478	(99.0)	486	(100.0)
with drug-related[a] adverse events	5	(1.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	1	(0.2)	0	(0.0)
with serious drug-related adverse events	1	(0.2)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	2	(0.4)	0	(0.0)
discontinued drug due to a drug-related adverse event	2	(0.4)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-74
Adverse Event Summary
AEOSI - Severe Skin Reactions
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	15	(3.1)	3	(0.6)
with no adverse event	468	(96.9)	483	(99.4)
with drug-related[a] adverse events	15	(3.1)	1	(0.2)
with toxicity grade 3-5 adverse events	14	(2.9)	3	(0.6)
with toxicity grade 3-5 drug-related adverse events	14	(2.9)	1	(0.2)
with serious adverse events	1	(0.2)	1	(0.2)
with serious drug-related adverse events	1	(0.2)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a drug-related adverse event	3	(0.6)	0	(0.0)
discontinued drug due to a serious adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	1	(0.2)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-75
Adverse Event Summary
AEOSI - Thyroiditis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	8	(1.7)	2	(0.4)
with no adverse event	475	(98.3)	484	(99.6)
with drug-related[a] adverse events	8	(1.7)	1	(0.2)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-76
Adverse Event Summary
AEOSI - Type 1 Diabetes Mellitus
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	2	(0.4)	0	(0.0)
with no adverse event	481	(99.6)	486	(100.0)
with drug-related[a] adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 adverse events	2	(0.4)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	2	(0.4)	0	(0.0)
with serious adverse events	2	(0.4)	0	(0.0)
with serious drug-related adverse events	2	(0.4)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a drug-related adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious adverse event	1	(0.2)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	1	(0.2)	0	(0.0)

[a] Determined by the investigator to be related to the drug.
Grades are based on NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-77
Adverse Event Summary
AEOSI - Uveitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	1	(0.2)	0	(0.0)
with no adverse event	482	(99.8)	486	(100.0)
with drug-related[a] adverse events	1	(0.2)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-78
Adverse Event Summary
AEOSI - Vasculitis
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	0	(0.0)	0	(0.0)
with no adverse event	483	(100.0)	486	(100.0)
with drug-related[a] adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 adverse events	0	(0.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious adverse event	0	(0.0)	0	(0.0)
discontinued drug due to a serious drug-related adverse event	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the drug.

Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-79
Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
Grade 1	38	(7.9)	22	(4.5)
Grade 2	92	(19.0)	18	(3.7)
Grade 3	50	(10.4)	6	(1.2)
Grade 4	3	(0.6)	0	(0.0)
with no adverse events	300	(62.1)	440	(90.5)
Adrenal Insufficiency	**13**	**(2.7)**	**0**	**(0.0)**
Grade 1	1	(0.2)	0	(0.0)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	5	(1.0)	0	(0.0)
Adrenal insufficiency	13	(2.7)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	7	(1.4)	0	(0.0)
Grade 3	5	(1.0)	0	(0.0)
Arthritis	**2**	**(0.4)**	**2**	**(0.4)**
Grade 2	1	(0.2)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Grade 2	1	(0.2)	2	(0.4)
Grade 3	1	(0.2)	0	(0.0)
Colitis	**20**	**(4.1)**	**5**	**(1.0)**
Grade 1	5	(1.0)	2	(0.4)
Grade 2	7	(1.4)	3	(0.6)
Grade 3	8	(1.7)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Colitis	16	(3.3)	5	(1.0)
Grade 1	4	(0.8)	2	(0.4)
Grade 2	7	(1.4)	3	(0.6)
Grade 3	5	(1.0)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hepatitis	**11**	**(2.3)**	**3**	**(0.6)**
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	1	(0.2)
Grade 3	9	(1.9)	2	(0.4)
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	7	(1.4)	2	(0.4)
Hepatitis	3	(0.6)	1	(0.2)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Hyperthyroidism	**51**	**(10.6)**	**3**	**(0.6)**
Grade 1	35	(7.2)	3	(0.6)
Grade 2	15	(3.1)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hyperthyroidism	51	(10.6)	3	(0.6)
Grade 1	35	(7.2)	3	(0.6)
Grade 2	15	(3.1)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypophysitis	**12**	**(2.5)**	**0**	**(0.0)**
Grade 1	1	(0.2)	0	(0.0)
Grade 2	8	(1.7)	0	(0.0)
Grade 3	3	(0.6)	0	(0.0)
Hypophysitis	7	(1.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	5	(1.0)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Hypopituitarism	5	(1.0)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Hypopituitarism	5	(1.0)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hypothyroidism	**83**	**(17.2)**	**18**	**(3.7)**
Grade 1	27	(5.6)	12	(2.5)
Grade 2	56	(11.6)	6	(1.2)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Hypothyroidism	82	(17.0)	17	(3.5)
Grade 1	27	(5.6)	12	(2.5)
Grade 2	55	(11.4)	5	(1.0)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)
Grade 2	0	(0.0)	1	(0.2)
Infusion Reactions	**3**	**(0.6)**	**7**	**(1.4)**
Grade 1	1	(0.2)	3	(0.6)
Grade 2	2	(0.4)	4	(0.8)
Drug hypersensitivity	1	(0.2)	2	(0.4)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	1	(0.2)	1	(0.2)
Hypersensitivity	0	(0.0)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Infusion related reaction	2	(0.4)	4	(0.8)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	3	(0.6)
Myasthenic Syndrome	**2**	**(0.4)**	**0**	**(0.0)**
Grade 3	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Myelitis	**1**	**(0.2)**	**0**	**(0.0)**
Grade 3	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Myocarditis	**1**	**(0.2)**	**1**	**(0.2)**
Grade 2	1	(0.2)	0	(0.0)
Grade 3	0	(0.0)	1	(0.2)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Grade 3	0	(0.0)	1	(0.2)
Myocarditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Myositis	**6**	**(1.2)**	**1**	**(0.2)**
Grade 1	1	(0.2)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Myopathy	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Grade 1	0	(0.0)	1	(0.2)
Grade 2	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Nephritis	**7**	**(1.4)**	**0**	**(0.0)**
Grade 1	1	(0.2)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Grade 3	3	(0.6)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Glomerulonephritis acute	1	(0.2)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Nephritis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pancreatitis	**2**	**(0.4)**	**0**	**(0.0)**
Grade 3	2	(0.4)	0	(0.0)
Pancreatitis	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Pneumonitis	**13**	**(2.7)**	**4**	**(0.8)**
Grade 1	5	(1.0)	3	(0.6)
Grade 2	6	(1.2)	1	(0.2)
Grade 3	2	(0.4)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Grade 1	5	(1.0)	3	(0.6)
Grade 2	4	(0.8)	1	(0.2)
Grade 3	1	(0.2)	0	(0.0)
Sarcoidosis	**5**	**(1.0)**	**0**	**(0.0)**
Grade 1	2	(0.4)	0	(0.0)
Grade 2	3	(0.6)	0	(0.0)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Sarcoidosis	3	(0.6)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)
Severe Skin Reactions	**15**	**(3.1)**	**3**	**(0.6)**
Grade 1	1	(0.2)	0	(0.0)
Grade 3	13	(2.7)	3	(0.6)
Grade 4	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Erythema multiforme	1	(0.2)	0	(0.0)
Grade 1	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Grade 3	3	(0.6)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Grade 3	7	(1.4)	2	(0.4)
Rash maculo-papular	2	(0.4)	1	(0.2)
Grade 3	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Grade 3	2	(0.4)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Thyroiditis	**8**	**(1.7)**	**2**	**(0.4)**
Grade 1	3	(0.6)	1	(0.2)
Grade 2	5	(1.0)	1	(0.2)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Grade 1	2	(0.4)	0	(0.0)
Grade 2	3	(0.6)	1	(0.2)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Thyroiditis	2	(0.4)	1	(0.2)
Grade 1	1	(0.2)	1	(0.2)
Grade 2	1	(0.2)	0	(0.0)
Type 1 Diabetes Mellitus	**2**	**(0.4)**	**0**	**(0.0)**
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)
Uveitis	**1**	**(0.2)**	**0**	**(0.0)**
Grade 2	1	(0.2)	0	(0.0)
Iridocyclitis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a bolded term is counted a single time for that bolded term.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-80
Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
with one or more adverse events	0	(0.0)	19	(30.2)
Grade 1	0	(0.0)	8	(12.7)
Grade 2	0	(0.0)	8	(12.7)
Grade 3	0	(0.0)	3	(4.8)
with no adverse events	8	(100.0)	44	(69.8)
Adrenal Insufficiency	**0**	**(0.0)**	**2**	**(3.2)**
Grade 2	0	(0.0)	2	(3.2)
Adrenal insufficiency	0	(0.0)	2	(3.2)
Grade 2	0	(0.0)	2	(3.2)
Hepatitis	**0**	**(0.0)**	**1**	**(1.6)**
Grade 1	0	(0.0)	1	(1.6)
Hepatitis	0	(0.0)	1	(1.6)
Grade 1	0	(0.0)	1	(1.6)
Hyperthyroidism	**0**	**(0.0)**	**9**	**(14.3)**
Grade 1	0	(0.0)	7	(11.1)
Grade 2	0	(0.0)	2	(3.2)
Hyperthyroidism	0	(0.0)	9	(14.3)
Grade 1	0	(0.0)	7	(11.1)
Grade 2	0	(0.0)	2	(3.2)
Hypothyroidism	**0**	**(0.0)**	**6**	**(9.5)**
Grade 1	0	(0.0)	2	(3.2)
Grade 2	0	(0.0)	4	(6.3)
Hypothyroidism	0	(0.0)	6	(9.5)
Grade 1	0	(0.0)	2	(3.2)
Grade 2	0	(0.0)	4	(6.3)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Infusion Reactions	**0**	**(0.0)**	**1**	**(1.6)**
Grade 2	0	(0.0)	1	(1.6)
Hypersensitivity	0	(0.0)	1	(1.6)
Grade 2	0	(0.0)	1	(1.6)
Myasthenic Syndrome	**0**	**(0.0)**	**2**	**(3.2)**
Grade 2	0	(0.0)	1	(1.6)
Grade 3	0	(0.0)	1	(1.6)
Myasthenia gravis	0	(0.0)	2	(3.2)
Grade 2	0	(0.0)	1	(1.6)
Grade 3	0	(0.0)	1	(1.6)
Pancreatitis	**0**	**(0.0)**	**1**	**(1.6)**
Grade 3	0	(0.0)	1	(1.6)
Pancreatitis	0	(0.0)	1	(1.6)
Grade 3	0	(0.0)	1	(1.6)
Pneumonitis	**0**	**(0.0)**	**1**	**(1.6)**
Grade 3	0	(0.0)	1	(1.6)
Pneumonitis	0	(0.0)	1	(1.6)
Grade 3	0	(0.0)	1	(1.6)
Thyroiditis	**0**	**(0.0)**	**1**	**(1.6)**
Grade 1	0	(0.0)	1	(1.6)
Thyroiditis	0	(0.0)	1	(1.6)

Participants With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Thyroiditis	0	(0.0)	1	(1.6)
Grade 1	0	(0.0)	1	(1.6)

Every participant is counted a single time for each applicable specific adverse event. A participant with multiple adverse events within a bolded term is counted a single time for that bolded term.

Only the highest reported grade of a given adverse event is counted for the individual participant.

Grades are based on Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-81
Participants With Adverse Events of Special Interest (AEOSI) by Decreasing incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	183	(37.9)	46	(9.5)
with no adverse events	300	(62.1)	440	(90.5)
Hypothyroidism	82	(17.0)	17	(3.5)
Hyperthyroidism	51	(10.6)	3	(0.6)
Colitis	16	(3.3)	5	(1.0)
Adrenal insufficiency	13	(2.7)	0	(0.0)
Pneumonitis	10	(2.1)	4	(0.8)
Autoimmune hepatitis	8	(1.7)	2	(0.4)
Hypophysitis	7	(1.4)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Autoimmune thyroiditis	5	(1.0)	1	(0.2)
Hypopituitarism	5	(1.0)	0	(0.0)
Myositis	4	(0.8)	1	(0.2)
Hepatitis	3	(0.6)	1	(0.2)
Nephritis	3	(0.6)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Sarcoidosis	3	(0.6)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Immune-mediated arthritis	2	(0.4)	2	(0.4)
Immune-mediated enterocolitis	2	(0.4)	0	(0.0)
Immune-mediated lung disease	2	(0.4)	0	(0.0)
Infusion related reaction	2	(0.4)	4	(0.8)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myopathy	2	(0.4)	0	(0.0)
Pancreatitis	2	(0.4)	0	(0.0)
Pulmonary sarcoidosis	2	(0.4)	0	(0.0)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Thyroiditis	2	(0.4)	1	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Autoimmune hypothyroidism	1	(0.2)	0	(0.0)
Cutaneous sarcoidosis	1	(0.2)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Drug hypersensitivity	1	(0.2)	2	(0.4)

Participants With Adverse Events of Special Interest (AEOSI) by Decreasing incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Erythema multiforme	1	(0.2)	0	(0.0)
Glomerulonephritis acute	1	(0.2)	0	(0.0)
Immune-mediated thyroiditis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Iridocyclitis	1	(0.2)	0	(0.0)
Iritis	1	(0.2)	0	(0.0)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myocarditis	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Hypersensitivity	0	(0.0)	1	(0.2)
Immune-mediated hypothyroidism	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-82
Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Participants in population	**483**	**486**
Participants with AEOSI (%)	183 (37.9)	46 (9.5)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	101.5 (87.6)	149.2 (121.8)
Median	67.0	127.0
Range	1 to 371	1 to 415
Total number of episodes of AEOSI	283	56
Average number of episodes of AEOSI per participant	1.5	1.2
Episode Durations (days)[b]		
Median	109.0	50.0
Range	1 to 1445+	1 to 1225+
Adrenal Insufficiency		
Participants with AEOSI (%)	13 (2.7)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	178.2 (99.1)	
Median	158.0	
Range	22 to 374	
Total number of episodes of AEOSI	14	
Average number of episodes of AEOSI per participant	1.1	
Episode Durations (days)[b]		
Median	568.0	
Range	9 to 1387+	
Arthritis		
Participants with AEOSI (%)	2 (0.4)	2 (0.4)

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Arthritis		
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	127.0 (83.4)	203.5 (258.1)
Median	127.0	203.5
Range	68 to 186	21 to 386
Total number of episodes of AEOSI	3	5
Average number of episodes of AEOSI per participant	1.5	2.5
Episode Durations (days)[b]		
Median	Not reached	43.0
Range	38 to 930+	13 to 882+
Colitis		
Participants with AEOSI (%)	20 (4.1)	5 (1.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	165.9 (114.0)	239.4 (93.6)
Median	119.0	257.0
Range	23 to 367	121 to 371
Total number of episodes of AEOSI	22	6
Average number of episodes of AEOSI per participant	1.1	1.2
Episode Durations (days)[b]		
Median	34.0	17.5
Range	3 to 802	5 to 92
Hepatitis		
Participants with AEOSI (%)	11 (2.3)	3 (0.6)
Time to Onset of First AEOSI (days)[a]		

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Hepatitis		
Mean (SD)	94.0 (96.4)	83.3 (57.5)
Median	43.0	106.0
Range	22 to 334	18 to 126
Total number of episodes of AEOSI	12	3
Average number of episodes of AEOSI per participant	1.1	1.0
Episode Durations (days)[b]		
Median	124.0	36.0
Range	20 to 1445+	29 to 793
Hyperthyroidism		
Participants with AEOSI (%)	51 (10.6)	3 (0.6)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	46.0 (39.5)	231.0 (181.7)
Median	24.0	320.0
Range	19 to 192	22 to 351
Total number of episodes of AEOSI	51	4
Average number of episodes of AEOSI per participant	1.0	1.3
Episode Durations (days)[b]		
Median	49.0	41.0
Range	15 to 1324+	25 to 562+
Hypophysitis		
Participants with AEOSI (%)	12 (2.5)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	177.1 (97.0)	

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Hypophysitis		
Median	190.5	
Range	4 to 295	
Total number of episodes of AEOSI	13	
Average number of episodes of AEOSI per participant	1.1	
Episode Durations (days)[b]		
Median	Not reached	
Range	22 to 1392+	
Hypothyroidism		
Participants with AEOSI (%)	83 (17.2)	18 (3.7)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	123.0 (78.1)	105.5 (73.8)
Median	106.0	72.0
Range	5 to 371	21 to 253
Total number of episodes of AEOSI	85	20
Average number of episodes of AEOSI per participant	1.0	1.1
Episode Durations (days)[b]		
Median	836.0	88.5
Range	12 to 1415+	8 to 1225+
Infusion Reactions		
Participants with AEOSI (%)	3 (0.6)	7 (1.4)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	54.7 (75.5)	151.4 (172.8)
Median	22.0	126.0

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Infusion Reactions		
Range	1 to 141	1 to 415
Total number of episodes of AEOSI	4	7
Average number of episodes of AEOSI per participant	1.3	1.0
Episode Durations (days)[b]		
Median	1.0	1.0
Range	1 to 3	1 to 140
Myasthenic Syndrome		
Participants with AEOSI (%)	2 (0.4)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	40.0 (24.0)	
Median	40.0	
Range	23 to 57	
Total number of episodes of AEOSI	2	
Average number of episodes of AEOSI per participant	1.0	
Episode Durations (days)[b]		
Median	Not reached	
Range	16 to 394+	
Myelitis		
Participants with AEOSI (%)	1 (0.2)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	179.0 ()	
Median	179.0	
Range	179 to 179	

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Myelitis		
Total number of episodes of AEOSI	1	
Average number of episodes of AEOSI per participant	1.0	
Episode Durations (days)[b]		
Median	Not reached	
Range	292+ to 292+	
Myocarditis		
Participants with AEOSI (%)	1 (0.2)	1 (0.2)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	397.0 ()	32.0 ()
Median	397.0	32.0
Range	397 to 397	32 to 32
Total number of episodes of AEOSI	1	1
Average number of episodes of AEOSI per participant	1.0	1.0
Episode Durations (days)[b]		
Median	11.0	24.0
Range	11 to 11	24 to 24
Myositis		
Participants with AEOSI (%)	6 (1.2)	1 (0.2)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	59.3 (39.2)	295.0 ()
Median	49.5	295.0
Range	26 to 135	295 to 295

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Myositis		
Total number of episodes of AEOSI	6	1
Average number of episodes of AEOSI per participant	1.0	1.0
Episode Durations (days)[b]		
Median	64.0	6.0
Range	20 to 205	6 to 6
Nephritis		
Participants with AEOSI (%)	7 (1.4)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	181.4 (110.6)	
Median	129.0	
Range	63 to 323	
Total number of episodes of AEOSI	7	
Average number of episodes of AEOSI per participant	1.0	
Episode Durations (days)[b]		
Median	45.0	
Range	7 to 149	
Pancreatitis		
Participants with AEOSI (%)	2 (0.4)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	260.5 (129.4)	
Median	260.5	
Range	169 to 352	
Total number of episodes of AEOSI	2	

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Pancreatitis		
Average number of episodes of AEOSI per participant	1.0	
Episode Durations (days)[b]		
Median	Not reached	
Range	10 to 903+	
Pneumonitis		
Participants with AEOSI (%)	13 (2.7)	4 (0.8)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	211.8 (113.8)	217.5 (103.4)
Median	174.0	176.0
Range	25 to 397	147 to 371
Total number of episodes of AEOSI	16	4
Average number of episodes of AEOSI per participant	1.2	1.0
Episode Durations (days)[b]		
Median	58.0	101.5
Range	4 to 946+	31 to 694+
Sarcoidosis		
Participants with AEOSI (%)	5 (1.0)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	155.8 (52.4)	
Median	176.0	
Range	63 to 189	
Total number of episodes of AEOSI	6	
Average number of episodes of AEOSI per participant	1.2	

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Sarcoidosis		
Episode Durations (days)[b]		
Median	140.5	
Range	3 to 989	
Severe Skin Reactions		
Participants with AEOSI (%)	15 (3.1)	3 (0.6)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	73.6 (100.1)	163.0 (198.5)
Median	38.0	93.0
Range	2 to 378	9 to 387
Total number of episodes of AEOSI	24	3
Average number of episodes of AEOSI per participant	1.6	1.0
Episode Durations (days)[b]		
Median	72.5	35.0
Range	3 to 1125+	24 to 43
Thyroiditis		
Participants with AEOSI (%)	8 (1.7)	2 (0.4)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	38.3 (23.9)	55.0 (9.9)
Median	34.0	55.0
Range	10 to 85	48 to 62
Total number of episodes of AEOSI	8	2
Average number of episodes of AEOSI per participant	1.0	1.0
Episode Durations (days)[b]		

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Thyroiditis		
Median	Not reached	61.5
Range	22 to 1330+	59 to 64
Type 1 Diabetes Mellitus		
Participants with AEOSI (%)	2 (0.4)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	141.5 (68.6)	
Median	141.5	
Range	93 to 190	
Total number of episodes of AEOSI	2	
Average number of episodes of AEOSI per participant	1.0	
Episode Durations (days)[b]		
Median	148.0	
Range	19 to 277	
Uveitis		
Participants with AEOSI (%)	1 (0.2)	0 (0.0)
Time to Onset of First AEOSI (days)[a]		
Mean (SD)	175.0 ()	
Median	175.0	
Range	175 to 175	
Total number of episodes of AEOSI	4	
Average number of episodes of AEOSI per participant	4.0	
Episode Durations (days)[b]		
Median	19.5	

Time to Onset and Duration of AEOSI
(APaT Population)

	Pembrolizumab	Placebo
Uveitis		
Range	11 to 29	

(%) = Number of participants with AEOSI / Number of participants in population.

[a] Time to onset statistics are based on number of participants with AEOSI.

[b] From product-limit (Kaplan-Meier) method for censored data. If an adverse event is not resolved at the time of analysis or the participant died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.

+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.

SD = Standard Deviation.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-83
Summary of Concomitant Corticosteroid Use for AEOSI
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
Participants with one or more events	183		46	
Treated with systemic corticosteroid	75	(41.0)	9	(19.6)
Not treated with systemic corticosteroid	108	(59.0)	37	(80.4)
Adrenal Insufficiency				
Participants with one or more events	13		0	
Treated with systemic corticosteroid	12	(92.3)	0	(0.0)
Not treated with systemic corticosteroid	1	(7.7)	0	(0.0)
Arthritis				
Participants with one or more events	2		2	
Treated with systemic corticosteroid	2	(100.0)	1	(50.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(50.0)
Colitis				
Participants with one or more events	20		5	
Treated with systemic corticosteroid	14	(70.0)	0	(0.0)
Not treated with systemic corticosteroid	6	(30.0)	5	(100.0)
Hepatitis				
Participants with one or more events	11		3	
Treated with systemic corticosteroid	10	(90.9)	3	(100.0)
Not treated with systemic corticosteroid	1	(9.1)	0	(0.0)
Hyperthyroidism				
Participants with one or more events	51		3	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	51	(100.0)	3	(100.0)
Hypophysitis				
Participants with one or more events	12		0	
Treated with systemic corticosteroid	12	(100.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Hypothyroidism				

Summary of Concomitant Corticosteroid Use for AEOSI
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants with one or more events	83		18	
Treated with systemic corticosteroid	1	(1.2)	0	(0.0)
Not treated with systemic corticosteroid	82	(98.8)	18	(100.0)
Infusion Reactions				
Participants with one or more events	3		7	
Treated with systemic corticosteroid	0	(0.0)	2	(28.6)
Not treated with systemic corticosteroid	3	(100.0)	5	(71.4)
Myasthenic Syndrome				
Participants with one or more events	2		0	
Treated with systemic corticosteroid	1	(50.0)	0	(0.0)
Not treated with systemic corticosteroid	1	(50.0)	0	(0.0)
Myelitis				
Participants with one or more events	1		0	
Treated with systemic corticosteroid	1	(100.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Myocarditis				
Participants with one or more events	1		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	1	(100.0)	1	(100.0)
Myositis				
Participants with one or more events	6		1	
Treated with systemic corticosteroid	4	(66.7)	0	(0.0)
Not treated with systemic corticosteroid	2	(33.3)	1	(100.0)
Nephritis				
Participants with one or more events	7		0	
Treated with systemic corticosteroid	5	(71.4)	0	(0.0)
Not treated with systemic corticosteroid	2	(28.6)	0	(0.0)
Pancreatitis				
Participants with one or more events	2		0	

Summary of Concomitant Corticosteroid Use for AEOSI (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Treated with systemic corticosteroid	1	(50.0)	0	(0.0)
Not treated with systemic corticosteroid	1	(50.0)	0	(0.0)
Pneumonitis				
Participants with one or more events	13		4	
Treated with systemic corticosteroid	8	(61.5)	1	(25.0)
Not treated with systemic corticosteroid	5	(38.5)	3	(75.0)
Sarcoidosis				
Participants with one or more events	5		0	
Treated with systemic corticosteroid	1	(20.0)	0	(0.0)
Not treated with systemic corticosteroid	4	(80.0)	0	(0.0)
Severe Skin Reactions				
Participants with one or more events	15		3	
Treated with systemic corticosteroid	9	(60.0)	2	(66.7)
Not treated with systemic corticosteroid	6	(40.0)	1	(33.3)
Thyroiditis				
Participants with one or more events	8		2	
Treated with systemic corticosteroid	1	(12.5)	0	(0.0)
Not treated with systemic corticosteroid	7	(87.5)	2	(100.0)
Type 1 Diabetes Mellitus				
Participants with one or more events	2		0	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	2	(100.0)	0	(0.0)
Uveitis				
Participants with one or more events	1		0	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)

Summary of Concomitant Corticosteroid Use for AEOSI (APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Not treated with systemic corticosteroid	1	(100.0)	0	(0.0)

The number of participants with one or more events is used as the denominator for the percentage calculation.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae; adcm]

Table 14.3-84
Summary of Concomitant Corticosteroid Use for AEOSI
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Participants in population	8		63	
Participants with one or more events	0		19	
Treated with systemic corticosteroid	0	(0.0)	4	(21.1)
Not treated with systemic corticosteroid	0	(0.0)	15	(78.9)
Adrenal Insufficiency				
Participants with one or more events	0		2	
Treated with systemic corticosteroid	0	(0.0)	1	(50.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(50.0)
Hepatitis				
Participants with one or more events	0		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)
Hyperthyroidism				
Participants with one or more events	0		9	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	9	(100.0)
Hypothyroidism				
Participants with one or more events	0		6	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	6	(100.0)
Infusion Reactions				
Participants with one or more events	0		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)
Myasthenic Syndrome				
Participants with one or more events	0		2	
Treated with systemic corticosteroid	0	(0.0)	2	(100.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)

Summary of Concomitant Corticosteroid Use for AEOSI
(APaT Population - Part 2)

	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
	n	(%)	n	(%)
Pancreatitis				
Participants with one or more events	0		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)
Pneumonitis				
Participants with one or more events	0		1	
Treated with systemic corticosteroid	0	(0.0)	1	(100.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Thyroiditis				
Participants with one or more events	0		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)

The number of participants with one or more events is used as the denominator for the percentage calculation.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae; adcm]

Table 14.3-85
Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
Total Episodes	283	56
High Starting Dose (%) [a], n (%)	**58 (20.5)**	**8 (14.3)**
Starting dose (mg/day)		
Mean (SD)	103 (85.1)	69 (23.9)
Median (Range)	80 (40-544)	65 (40-100)
Duration[b](days)		
Mean (SD)	15 (63.3)	3 (2.0)
Median (Range)	5 (1-486)	2 (1-6)
Low Starting Dose (%) [a], n (%)	**30 (10.6)**	**4 (7.1)**
Starting dose (mg/day)		
Mean (SD)	17 (11.9)	14 (7.5)
Median (Range)	20 (0-38)	15 (5-20)
Duration[b](days)		
Mean (SD)	109 (233.3)	31 (44.0)
Median (Range)	8 (1-944)	12 (5-97)
Not Treated with Systemic Corticosteroid, n (%)	**195 (68.9)**	**44 (78.6)**
Adrenal Insufficiency		
Total Episodes	14	0
High Starting Dose (%) [a], n (%)	**3 (21.4)**	**NA**
Starting dose (mg/day)		
Mean (SD)	89 (19.3)	NA
Median (Range)	100 (67-100)	NA
Duration[b](days)		
Mean (SD)	2 (1.7)	NA
Median (Range)	1 (1-4)	NA
Low Starting Dose (%) [a], n (%)	**9 (64.3)**	**NA**
Starting dose (mg/day)		
Mean (SD)	13 (11.1)	NA
Median (Range)	8 (0-25)	NA
Duration[b](days)		
Mean (SD)	92 (191.3)	NA
Median (Range)	9 (1-576)	NA
Not Treated with Systemic Corticosteroid, n (%)	**2 (14.3)**	**NA**
Arthritis		
Total Episodes	3	5

Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
High Starting Dose (%) [a], n (%)	**1 (33.3)**	**1 (20.0)**
Starting dose (mg/day)		
Mean (SD)	75	80
Median (Range)	75 (75-75)	80 (80-80)
Duration[b](days)		
Mean (SD)	2	2
Median (Range)	2 (2-2)	2 (2-2)
Low Starting Dose (%) [a], n (%)	**2 (66.7)**	**3 (60.0)**
Starting dose (mg/day)		
Mean (SD)	23 (3.5)	12 (7.6)
Median (Range)	23 (20-25)	10 (5-20)
Duration[b](days)		
Mean (SD)	8 (0.7)	40 (49.5)
Median (Range)	8 (7-8)	15 (8-97)
Not Treated with Systemic Corticosteroid, n (%)	**0 (0.0)**	**1 (20.0)**
Colitis		
Total Episodes	22	6
High Starting Dose (%) [a], n (%)	**14 (63.6)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	105 (128.3)	NA
Median (Range)	75 (40-544)	NA
Duration[b](days)		
Mean (SD)	6 (4.4)	NA
Median (Range)	5 (1-14)	NA
Low Starting Dose (%) [a], n (%)	**1 (4.5)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	38	NA
Median (Range)	38 (38-38)	NA
Duration[b](days)		
Mean (SD)	3	NA
Median (Range)	3 (3-3)	NA
Not Treated with Systemic Corticosteroid, n (%)	**7 (31.8)**	**6 (100.0)**
Hepatitis		
Total Episodes	12	3
High Starting Dose (%) [a], n (%)	**10 (83.3)**	**3 (100.0)**
Starting dose (mg/day)		

Summary of Concomitant Corticosteroid Use for AEOSI Episodes (APaT Population)

	Pembrolizumab	Placebo
Mean (SD)	79 (26.3)	81 (27.0)
Median (Range)	78 (40-120)	93 (50-100)
Duration[b](days)		
Mean (SD)	5 (2.5)	3 (2.1)
Median (Range)	7 (1-8)	4 (1-5)
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**2 (16.7)**	**0 (0.0)**
Hyperthyroidism		
Total Episodes	51	4
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**51 (100.0)**	**4 (100.0)**
Hypophysitis		
Total Episodes	13	0
High Starting Dose (%) [a], n (%)	**3 (23.1)**	**NA**
Starting dose (mg/day)		
Mean (SD)	137 (77.7)	NA
Median (Range)	160 (50-200)	NA
Duration[b](days)		
Mean (SD)	5 (1.5)	NA
Median (Range)	5 (4-7)	NA
Low Starting Dose (%) [a], n (%)	**9 (69.2)**	**NA**
Starting dose (mg/day)		
Mean (SD)	11 (10.5)	NA
Median (Range)	8 (3-33)	NA
Duration[b](days)		
Mean (SD)	236 (357.1)	NA
Median (Range)	57 (1-944)	NA
Not Treated with Systemic Corticosteroid, n (%)	**1 (7.7)**	**NA**
Hypothyroidism		
Total Episodes	85	20
High Starting Dose (%) [a], n (%)	**1 (1.2)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	60	NA
Median (Range)	60 (60-60)	NA

Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
Duration[b](days)		
Mean (SD)	4	NA
Median (Range)	4 (4-4)	NA
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**84 (98.8)**	**20 (100.0)**
Infusion Reactions		
Total Episodes	4	7
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**2 (28.6)**
Starting dose (mg/day)		
Mean (SD)	NA	45 (7.1)
Median (Range)	NA	45 (40-50)
Duration[b](days)		
Mean (SD)	NA	1 (0.0)
Median (Range)	NA	1 (1-1)
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**4 (100.0)**	**5 (71.4)**
Myasthenic Syndrome		
Total Episodes	2	0
High Starting Dose (%) [a], n (%)	**1 (50.0)**	**NA**
Starting dose (mg/day)		
Mean (SD)	80	NA
Median (Range)	80 (80-80)	NA
Duration[b](days)		
Mean (SD)	14	NA
Median (Range)	14 (14-14)	NA
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Not Treated with Systemic Corticosteroid, n (%)	**1 (50.0)**	**NA**
Myelitis		
Total Episodes	1	0
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Low Starting Dose (%) [a], n (%)	**1 (100.0)**	**NA**
Starting dose (mg/day)		
Mean (SD)	1	NA
Median (Range)	1 (1-1)	NA
Duration[b](days)		

Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
Mean (SD)	4	NA
Median (Range)	4 (4-4)	NA
Not Treated with Systemic Corticosteroid, n (%)	**0 (0.0)**	**NA**
Myocarditis		
Total Episodes	1	1
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**1 (100.0)**	**1 (100.0)**
Myositis		
Total Episodes	6	1
High Starting Dose (%) [a], n (%)	**3 (50.0)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	130 (82.6)	NA
Median (Range)	90 (75-225)	NA
Duration[b](days)		
Mean (SD)	9 (13.0)	NA
Median (Range)	2 (1-24)	NA
Low Starting Dose (%) [a], n (%)	**1 (16.7)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	25	NA
Median (Range)	25 (25-25)	NA
Duration[b](days)		
Mean (SD)	209	NA
Median (Range)	209 (209-209)	NA
Not Treated with Systemic Corticosteroid, n (%)	**2 (33.3)**	**1 (100.0)**
Nephritis		
Total Episodes	7	0
High Starting Dose (%) [a], n (%)	**5 (71.4)**	**NA**
Starting dose (mg/day)		
Mean (SD)	160 (92.3)	NA
Median (Range)	156 (75-313)	NA
Duration[b](days)		
Mean (SD)	7 (7.9)	NA
Median (Range)	6 (1-21)	NA
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**

Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
Not Treated with Systemic Corticosteroid, n (%)	**2 (28.6)**	**NA**
Pancreatitis		
Total Episodes	2	0
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Low Starting Dose (%) [a], n (%)	**1 (50.0)**	**NA**
Starting dose (mg/day)		
Mean (SD)	35	NA
Median (Range)	35 (35-35)	NA
Duration[b](days)		
Mean (SD)	64	NA
Median (Range)	64 (64-64)	NA
Not Treated with Systemic Corticosteroid, n (%)	**1 (50.0)**	**NA**
Pneumonitis		
Total Episodes	16	4
High Starting Dose (%) [a], n (%)	**9 (56.3)**	**1 (25.0)**
Starting dose (mg/day)		
Mean (SD)	84 (37.8)	90
Median (Range)	90 (40-140)	90 (90-90)
Duration[b](days)		
Mean (SD)	9 (8.5)	6
Median (Range)	7 (2-31)	6 (6-6)
Low Starting Dose (%) [a], n (%)	**1 (6.3)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	4	NA
Median (Range)	4 (4-4)	NA
Duration[b](days)		
Mean (SD)	8	NA
Median (Range)	8 (8-8)	NA
Not Treated with Systemic Corticosteroid, n (%)	**6 (37.5)**	**3 (75.0)**
Sarcoidosis		
Total Episodes	6	0
High Starting Dose (%) [a], n (%)	**1 (16.7)**	**NA**
Starting dose (mg/day)		
Mean (SD)	50	NA
Median (Range)	50 (50-50)	NA

Summary of Concomitant Corticosteroid Use for AEOSI Episodes
(APaT Population)

	Pembrolizumab	Placebo
Duration[b](days)		
Mean (SD)	35	NA
Median (Range)	35 (35-35)	NA
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Not Treated with Systemic Corticosteroid, n (%)	**5 (83.3)**	**NA**
Severe Skin Reactions		
Total Episodes	24	3
High Starting Dose (%) [a], n (%)	**6 (25.0)**	**1 (33.3)**
Starting dose (mg/day)		
Mean (SD)	124 (124.8)	50
Median (Range)	80 (50-375)	50 (50-50)
Duration[b](days)		
Mean (SD)	85 (196.4)	2
Median (Range)	5 (3-486)	2 (2-2)
Low Starting Dose (%) [a], n (%)	**5 (20.8)**	**1 (33.3)**
Starting dose (mg/day)		
Mean (SD)	27 (4.5)	20
Median (Range)	30 (20-30)	20 (20-20)
Duration[b](days)		
Mean (SD)	6 (4.2)	5
Median (Range)	5 (1-12)	5 (5-5)
Not Treated with Systemic Corticosteroid, n (%)	**13 (54.2)**	**1 (33.3)**
Thyroiditis		
Total Episodes	8	2
High Starting Dose (%) [a], n (%)	**1 (12.5)**	**0 (0.0)**
Starting dose (mg/day)		
Mean (SD)	50	NA
Median (Range)	50 (50-50)	NA
Duration[b](days)		
Mean (SD)	5	NA
Median (Range)	5 (5-5)	NA
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid, n (%)	**7 (87.5)**	**2 (100.0)**
Type 1 Diabetes Mellitus		
Total Episodes	2	0

Summary of Concomitant Corticosteroid Use for AEOSI Episodes (APaT Population)

	Pembrolizumab	Placebo
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Not Treated with Systemic Corticosteroid, n (%)	**2 (100.0)**	**NA**
Uveitis		
Total Episodes	4	0
High Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Low Starting Dose (%) [a], n (%)	**0 (0.0)**	**NA**
Not Treated with Systemic Corticosteroid, n (%)	**4 (100.0)**	**NA**

The number of total episodes in each category is used as the denominator for the percentage calculation.

[a] High starting dose corticosteroid treatment is defined as ≥ 40 mg/day prednisone or equivalent, Low starting dose corticosteroid treatment is defined as < 40 mg/day prednisone or equivalent.

[b] Ongoing corticosteroid treatment is censored at the cutoff date or date of death, whichever occurs first.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days and serious adverse events up to 90 days of last dose of the initial treatment phase are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae; adcm]

Table 14.3-86
Summary of Outcome for Participants With AEOSI
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Participants in population		483		486	
With one or more AEOSI	**Overall**	**183**	**(37.9)**	**46**	**(9.5)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	45	(24.6)	6	(13.0)
	Resolving	22	(12.0)	1	(2.2)
	Unknown	1	(0.5)	0	(0.0)
	Sequelae	4	(2.2)	0	(0.0)
	Resolved	111	(60.7)	39	(84.8)
Hypothyroidism	**Overall**	**83**	**(17.2)**	**18**	**(3.7)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	27	(32.5)	3	(16.7)
	Resolving	13	(15.7)	1	(5.6)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	1	(1.2)	0	(0.0)
	Resolved	42	(50.6)	14	(77.8)
Hyperthyroidism	**Overall**	**51**	**(10.6)**	**3**	**(0.6)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(2.0)	1	(33.3)
	Resolving	1	(2.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	49	(96.1)	2	(66.7)
Colitis	**Overall**	**20**	**(4.1)**	**5**	**(1.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	20	(100.0)	5	(100.0)

Summary of Outcome for Participants With AEOSI
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Severe Skin Reactions	**Overall**	**15**	**(3.1)**	**3**	**(0.6)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	1	(6.7)	0	(0.0)
	Unknown	1	(6.7)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	13	(86.7)	3	(100.0)
Adrenal Insufficiency	**Overall**	**13**	**(2.7)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	4	(30.8)	0	(0.0)
	Resolving	2	(15.4)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	1	(7.7)	0	(0.0)
	Resolved	6	(46.2)	0	(0.0)
Pneumonitis	**Overall**	**13**	**(2.7)**	**4**	**(0.8)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(7.7)	1	(25.0)
	Resolving	1	(7.7)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	11	(84.6)	3	(75.0)
Hypophysitis	**Overall**	**12**	**(2.5)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	7	(58.3)	0	(0.0)
	Resolving	2	(16.7)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	3	(25.0)	0	(0.0)

Summary of Outcome for Participants With AEOSI
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Hepatitis	**Overall**	**11**	**(2.3)**	**3**	**(0.6)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(9.1)	0	(0.0)
	Resolving	2	(18.2)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	8	(72.7)	3	(100.0)
Thyroiditis	**Overall**	**8**	**(1.7)**	**2**	**(0.4)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	2	(25.0)	0	(0.0)
	Resolving	2	(25.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	4	(50.0)	2	(100.0)
Nephritis	**Overall**	**7**	**(1.4)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	7	(100.0)	0	(0.0)
Myositis	**Overall**	**6**	**(1.2)**	**1**	**(0.2)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	6	(100.0)	1	(100.0)

Summary of Outcome for Participants With AEOSI
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Sarcoidosis	**Overall**	**5**	**(1.0)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	1	(20.0)	0	(0.0)
	Resolved	4	(80.0)	0	(0.0)
Infusion Reactions	**Overall**	**3**	**(0.6)**	**7**	**(1.4)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	3	(100.0)	7	(100.0)
Arthritis	**Overall**	**2**	**(0.4)**	**2**	**(0.4)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	2	(100.0)	2	(100.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	0	(0.0)	0	(0.0)
Myasthenic Syndrome	**Overall**	**2**	**(0.4)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(50.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	1	(50.0)	0	(0.0)

Summary of Outcome for Participants With AEOSI
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Pancreatitis	**Overall**	**2**	**(0.4)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(50.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	1	(50.0)	0	(0.0)
Type 1 Diabetes Mellitus	**Overall**	**2**	**(0.4)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	1	(50.0)	0	(0.0)
	Resolved	1	(50.0)	0	(0.0)
Myelitis	**Overall**	**1**	**(0.2)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	1	(100.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	0	(0.0)	0	(0.0)
Myocarditis	**Overall**	**1**	**(0.2)**	**1**	**(0.2)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	1	(100.0)	1	(100.0)

Summary of Outcome for Participants With AEOSI (Incidence > 0% in One or More Treatment Groups) (APaT Population)

		Pembrolizumab		Placebo	
	Outcome	n	(%)	n	(%)
Uveitis	**Overall**	**1**	**(0.2)**	**0**	**(0.0)**
	Fatal	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)
	Sequelae	0	(0.0)	0	(0.0)
	Resolved	1	(100.0)	0	(0.0)

Every participant is counted once for each specific AEOSI according to the worst outcome; the ordering of the outcomes is as follows: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.

"Participants in population" is used for percentage calculation for the Overall row in each section. Within each section, the overall total is used for percentage calculation for each outcome.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-87
Participants With Grade 3-5 Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	53	(11.0)	6	(1.2)
with no adverse events	430	(89.0)	480	(98.8)
Adrenal Insufficiency	**5**	**(1.0)**	**0**	**(0.0)**
Adrenal insufficiency	5	(1.0)	0	(0.0)
Arthritis	**1**	**(0.2)**	**0**	**(0.0)**
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Colitis	**8**	**(1.7)**	**0**	**(0.0)**
Autoimmune colitis	2	(0.4)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Hepatitis	**9**	**(1.9)**	**2**	**(0.4)**
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Hepatitis	2	(0.4)	0	(0.0)
Hyperthyroidism	**1**	**(0.2)**	**0**	**(0.0)**
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	**3**	**(0.6)**	**0**	**(0.0)**
Hypophysitis	1	(0.2)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Myasthenic Syndrome	**2**	**(0.4)**	**0**	**(0.0)**
Myasthenia gravis	2	(0.4)	0	(0.0)
Myelitis	**1**	**(0.2)**	**0**	**(0.0)**
Myelitis transverse	1	(0.2)	0	(0.0)
Myocarditis	**0**	**(0.0)**	**1**	**(0.2)**
Autoimmune myocarditis	0	(0.0)	1	(0.2)
Myositis	**3**	**(0.6)**	**0**	**(0.0)**
Myopathy	1	(0.2)	0	(0.0)

Participants With Grade 3-5 Adverse Events of Special Interest (AEOSI)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Myositis	**3**	**(0.6)**	**0**	**(0.0)**
Myositis	2	(0.4)	0	(0.0)
Nephritis	**3**	**(0.6)**	**0**	**(0.0)**
Autoimmune nephritis	2	(0.4)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Pancreatitis	**2**	**(0.4)**	**0**	**(0.0)**
Pancreatitis	2	(0.4)	0	(0.0)
Pneumonitis	**2**	**(0.4)**	**0**	**(0.0)**
Interstitial lung disease	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Severe Skin Reactions	**14**	**(2.9)**	**3**	**(0.6)**
Dermatitis bullous	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Rash	7	(1.4)	2	(0.4)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)
Type 1 Diabetes Mellitus	**2**	**(0.4)**	**0**	**(0.0)**
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)

Every participant is counted a single time for each applicable row and column.
NCI CTCAE version 4.03.
Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.
Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-88
Participants With Grade 3-5 Adverse Events of Special Interest (AEOSI) by Decreasing incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Participants in population	483		486	
with one or more adverse events	53	(11.0)	6	(1.2)
with no adverse events	430	(89.0)	480	(98.8)
Autoimmune hepatitis	7	(1.4)	2	(0.4)
Rash	7	(1.4)	2	(0.4)
Adrenal insufficiency	5	(1.0)	0	(0.0)
Colitis	5	(1.0)	0	(0.0)
Pruritus	3	(0.6)	0	(0.0)
Autoimmune colitis	2	(0.4)	0	(0.0)
Autoimmune nephritis	2	(0.4)	0	(0.0)
Hepatitis	2	(0.4)	0	(0.0)
Hypopituitarism	2	(0.4)	0	(0.0)
Myasthenia gravis	2	(0.4)	0	(0.0)
Myositis	2	(0.4)	0	(0.0)
Pancreatitis	2	(0.4)	0	(0.0)
Rash maculo-papular	2	(0.4)	1	(0.2)
Rash pruritic	2	(0.4)	0	(0.0)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)
Dermatitis bullous	1	(0.2)	0	(0.0)
Hyperthyroidism	1	(0.2)	0	(0.0)
Hypophysitis	1	(0.2)	0	(0.0)
Immune-mediated arthritis	1	(0.2)	0	(0.0)
Immune-mediated enterocolitis	1	(0.2)	0	(0.0)
Interstitial lung disease	1	(0.2)	0	(0.0)
Myelitis transverse	1	(0.2)	0	(0.0)
Myopathy	1	(0.2)	0	(0.0)
Nephritis	1	(0.2)	0	(0.0)
Pemphigoid	1	(0.2)	0	(0.0)
Pneumonitis	1	(0.2)	0	(0.0)
Rash pustular	1	(0.2)	0	(0.0)

Participants With Grade 3-5 Adverse Events of Special Interest (AEOSI) by Decreasing incidence
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Autoimmune myocarditis	0	(0.0)	1	(0.2)

Every participant is counted a single time for each applicable row and column.

NCI CTCAE version 4.03.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-89
Exposure-Adjusted Grade 3-5 AEOSI Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Number of participants exposed	483	486
Total exposure[b] in person-months	4945.05	5420.53
Adrenal Insufficiency	**5 (0.10)**	**0 (0.00)**
Adrenal insufficiency	5 (0.10)	0 (0.00)
Arthritis	**1 (0.02)**	**0 (0.00)**
Immune-mediated arthritis	1 (0.02)	0 (0.00)
Colitis	**8 (0.16)**	**0 (0.00)**
Autoimmune colitis	2 (0.04)	0 (0.00)
Colitis	5 (0.10)	0 (0.00)
Immune-mediated enterocolitis	1 (0.02)	0 (0.00)
Hepatitis	**9 (0.18)**	**2 (0.04)**
Autoimmune hepatitis	7 (0.14)	2 (0.04)
Hepatitis	2 (0.04)	0 (0.00)
Hyperthyroidism	**1 (0.02)**	**0 (0.00)**
Hyperthyroidism	1 (0.02)	0 (0.00)
Hypophysitis	**3 (0.06)**	**0 (0.00)**
Hypophysitis	1 (0.02)	0 (0.00)
Hypopituitarism	2 (0.04)	0 (0.00)
Myasthenic Syndrome	**2 (0.04)**	**0 (0.00)**
Myasthenia gravis	2 (0.04)	0 (0.00)
Myelitis	**1 (0.02)**	**0 (0.00)**
Myelitis transverse	1 (0.02)	0 (0.00)
Myocarditis	**0 (0.00)**	**1 (0.02)**
Autoimmune myocarditis	0 (0.00)	1 (0.02)
Myositis	**3 (0.06)**	**0 (0.00)**
Myopathy	1 (0.02)	0 (0.00)
Myositis	2 (0.04)	0 (0.00)
Nephritis	**3 (0.06)**	**0 (0.00)**
Autoimmune nephritis	2 (0.04)	0 (0.00)
Nephritis	1 (0.02)	0 (0.00)
Pancreatitis	**2 (0.04)**	**0 (0.00)**
Pancreatitis	2 (0.04)	0 (0.00)
Pneumonitis	**2 (0.04)**	**0 (0.00)**
Interstitial lung disease	1 (0.02)	0 (0.00)
Pneumonitis	1 (0.02)	0 (0.00)
Severe Skin Reactions	**18 (0.36)**	**3 (0.06)**

Exposure-Adjusted Grade 3-5 AEOSI Adverse Events
(Including Multiple Occurrences of Events)
(Incidence > 0% in One or More Treatment Groups)
(APaT Population)

	Event Count and Rate (Events/100 person-months)[a]	
	Pembrolizumab	Placebo
Severe Skin Reactions	**18 (0.36)**	**3 (0.06)**
Dermatitis bullous	1 (0.02)	0 (0.00)
Pemphigoid	1 (0.02)	0 (0.00)
Pruritus	3 (0.06)	0 (0.00)
Rash	7 (0.14)	2 (0.04)
Rash maculo-papular	3 (0.06)	1 (0.02)
Rash pruritic	2 (0.04)	0 (0.00)
Rash pustular	1 (0.02)	0 (0.00)
Type 1 Diabetes Mellitus	**2 (0.04)**	**0 (0.00)**
Type 1 diabetes mellitus	2 (0.04)	0 (0.00)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the interval between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

Adverse events occurred after the first dose of second course are excluded.

Non-serious adverse events up to 30 days of last treatment and serious adverse events up to 90 days of last treatment are included.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

Table 14.3-90
Exposure-Adjusted Adverse Event Summary
(Including Multiple Occurrences of Events)
AEOSI
(APaT Population - Part 2)

	Event Count and Rate (Events/100 person-months)[a]			
	Pembrolizumab Rechallenge		Crossover to Pembrolizumab	
Number of participants exposed	8		63	
Total exposure[b] in person-months	58.19		646.92	
Total events (rate)				
adverse events	0	(0.00)	25	(3.86)
drug-related[c] adverse events	0	(0.00)	19	(2.94)
toxicity grade 3-5 adverse events	0	(0.00)	3	(0.46)
toxicity grade 3-5 drug-related adverse events	0	(0.00)	3	(0.46)
serious adverse events	0	(0.00)	2	(0.31)
serious drug-related adverse events	0	(0.00)	2	(0.31)
adverse events leading to death	0	(0.00)	0	(0.00)
drug-related adverse events leading to death	0	(0.00)	0	(0.00)
adverse events resulting in drug discontinuation	0	(0.00)	3	(0.46)
drug-related adverse events resulting in drug discontinuation	0	(0.00)	3	(0.46)
serious adverse events resulting in drug discontinuation	0	(0.00)	2	(0.31)
serious drug-related adverse events resulting in drug discontinuation	0	(0.00)	2	(0.31)

[a] Event rate per 100 person-months of exposure = event count *100/person-months of exposure.

[b] Drug exposure is defined as the between the first dose date + 1 day and the earlier of the last dose date + 30 or the database cutoff date.

[c] Determined by the investigator to be related to the drug.

AEs were followed 30 days after last dose of study treatment in Part 2. SAEs were followed 90 days after last dose of study treatment in Part 2.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adae]

14.4 Clinical Laboratory Evaluation

Table 14.4-1
Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Activated Partial Thromboplastin Time Increased (Activated partial thromboplastin time prolonged)						
Grade 0	120 (87.6)	11 (8.0)	0 (0.0)	0 (0.0)	0 (0.0)	131 (95.6)
Grade 1	3 (2.2)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	5 (3.6)
Grade 2	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)
Total	123 (89.8)	13 (9.5)	1 (0.7)	0 (0.0)	0 (0.0)	137 (100.0)
Alanine Aminotransferase Increased (Alanine aminotransferase increased)						
Grade 0	300 (62.4)	112 (23.3)	8 (1.7)	9 (1.9)	0 (0.0)	429 (89.2)
Grade 1	7 (1.5)	36 (7.5)	4 (0.8)	5 (1.0)	0 (0.0)	52 (10.8)
Total	307 (63.8)	148 (30.8)	12 (2.5)	14 (2.9)	0 (0.0)	481 (100.0)
Albumin Decreased (Hypoalbuminemia)						
Grade 0	418 (87.6)	43 (9.0)	7 (1.5)	2 (0.4)	0 (0.0)	470 (98.5)
Grade 1	1 (0.2)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.5)
Total	419 (87.8)	49 (10.3)	7 (1.5)	2 (0.4)	0 (0.0)	477 (100.0)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)						
Grade 0	405 (84.9)	49 (10.3)	2 (0.4)	1 (0.2)	0 (0.0)	457 (95.8)
Grade 1	3 (0.6)	15 (3.1)	2 (0.4)	0 (0.0)	0 (0.0)	20 (4.2)
Total	408 (85.5)	64 (13.4)	4 (0.8)	1 (0.2)	0 (0.0)	477 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Activated Partial Thromboplastin Time Increased (Activated partial thromboplastin time prolonged)						
Grade 0	147 (83.5)	14 (8.0)	2 (1.1)	0 (0.0)	0 (0.0)	163 (92.6)
Grade 1	4 (2.3)	8 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	12 (6.8)
Grade 2	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
Total	151 (85.8)	22 (12.5)	3 (1.7)	0 (0.0)	0 (0.0)	176 (100.0)
Alanine Aminotransferase Increased (Alanine aminotransferase increased)						
Grade 0	369 (76.7)	66 (13.7)	4 (0.8)	2 (0.4)	0 (0.0)	441 (91.7)
Grade 1	9 (1.9)	30 (6.2)	0 (0.0)	1 (0.2)	0 (0.0)	40 (8.3)
Total	378 (78.6)	96 (20.0)	4 (0.8)	3 (0.6)	0 (0.0)	481 (100.0)
Albumin Decreased (Hypoalbuminemia)						
Grade 0	447 (93.3)	25 (5.2)	2 (0.4)	1 (0.2)	0 (0.0)	475 (99.2)
Grade 1	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.8)
Total	449 (93.7)	27 (5.6)	2 (0.4)	1 (0.2)	0 (0.0)	479 (100.0)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)						
Grade 0	427 (89.0)	32 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	459 (95.6)
Grade 1	0 (0.0)	20 (4.2)	1 (0.2)	0 (0.0)	0 (0.0)	21 (4.4)
Total	427 (89.0)	52 (10.8)	1 (0.2)	0 (0.0)	0 (0.0)	480 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Amylase Increased (Serum amylase increased)						
Grade 0	91 (76.5)	16 (13.4)	2 (1.7)	0 (0.0)	0 (0.0)	109 (91.6)
Grade 1	2 (1.7)	5 (4.2)	0 (0.0)	0 (0.0)	1 (0.8)	8 (6.7)
Grade 2	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.7)
Total	95 (79.8)	21 (17.6)	2 (1.7)	0 (0.0)	1 (0.8)	119 (100.0)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)						
Grade 0	332 (69.2)	101 (21.0)	9 (1.9)	7 (1.5)	0 (0.0)	449 (93.5)
Grade 1	7 (1.5)	19 (4.0)	3 (0.6)	1 (0.2)	0 (0.0)	30 (6.3)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	340 (70.8)	120 (25.0)	12 (2.5)	8 (1.7)	0 (0.0)	480 (100.0)
Bilirubin Increased (Blood bilirubin increased)						
Grade 0	412 (85.7)	31 (6.4)	2 (0.4)	0 (0.0)	0 (0.0)	445 (92.5)
Grade 1	4 (0.8)	13 (2.7)	14 (2.9)	0 (0.0)	0 (0.0)	31 (6.4)
Grade 2	1 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	5 (1.0)
Total	417 (86.7)	46 (9.6)	18 (3.7)	0 (0.0)	0 (0.0)	481 (100.0)
Calcium Decreased (Hypocalcemia)						
Grade 0	379 (79.8)	67 (14.1)	3 (0.6)	1 (0.2)	1 (0.2)	451 (94.9)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline (APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Amylase Increased (Serum amylase increased)						
Grade 0	110 (75.9)	20 (13.8)	3 (2.1)	1 (0.7)	1 (0.7)	135 (93.1)
Grade 1	0 (0.0)	7 (4.8)	3 (2.1)	0 (0.0)	0 (0.0)	10 (6.9)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	110 (75.9)	27 (18.6)	6 (4.1)	1 (0.7)	1 (0.7)	145 (100.0)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)						
Grade 0	389 (81.0)	57 (11.9)	3 (0.6)	4 (0.8)	0 (0.0)	453 (94.4)
Grade 1	4 (0.8)	21 (4.4)	1 (0.2)	1 (0.2)	0 (0.0)	27 (5.6)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	393 (81.9)	78 (16.3)	4 (0.8)	5 (1.0)	0 (0.0)	480 (100.0)
Bilirubin Increased (Blood bilirubin increased)						
Grade 0	408 (84.8)	38 (7.9)	10 (2.1)	0 (0.0)	0 (0.0)	456 (94.8)
Grade 1	0 (0.0)	13 (2.7)	10 (2.1)	0 (0.0)	0 (0.0)	23 (4.8)
Grade 2	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.4)
Total	408 (84.8)	51 (10.6)	21 (4.4)	1 (0.2)	0 (0.0)	481 (100.0)
Calcium Decreased (Hypocalcemia)						
Grade 0	392 (81.2)	63 (13.0)	5 (1.0)	0 (0.0)	0 (0.0)	460 (95.2)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Calcium Decreased (Hypocalcemia)						
Grade 1	6 (1.3)	16 (3.4)	2 (0.4)	0 (0.0)	0 (0.0)	24 (5.1)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	385 (81.1)	83 (17.5)	5 (1.1)	1 (0.2)	1 (0.2)	475 (100.0)
Calcium Increased (Hypercalcemia)						
Grade 0	379 (79.8)	67 (14.1)	3 (0.6)	1 (0.2)	1 (0.2)	451 (94.9)
Grade 1	6 (1.3)	16 (3.4)	2 (0.4)	0 (0.0)	0 (0.0)	24 (5.1)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	385 (81.1)	83 (17.5)	5 (1.1)	1 (0.2)	1 (0.2)	475 (100.0)
Cholesterol Increased (Cholesterol high)						
Grade 0	34 (45.3)	14 (18.7)	1 (1.3)	0 (0.0)	0 (0.0)	49 (65.3)
Grade 1	4 (5.3)	16 (21.3)	5 (6.7)	0 (0.0)	0 (0.0)	25 (33.3)
Grade 2	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
Total	38 (50.7)	31 (41.3)	6 (8.0)	0 (0.0)	0 (0.0)	75 (100.0)
Creatine Kinase Increased (CPK increased)						
Grade 0	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
Total	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline (APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Calcium Decreased (Hypocalcemia)						
Grade 1	6 (1.2)	15 (3.1)	1 (0.2)	0 (0.0)	0 (0.0)	22 (4.6)
Grade 2	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	399 (82.6)	78 (16.1)	6 (1.2)	0 (0.0)	0 (0.0)	483 (100.0)
Calcium Increased (Hypercalcemia)						
Grade 0	392 (81.2)	63 (13.0)	5 (1.0)	0 (0.0)	0 (0.0)	460 (95.2)
Grade 1	6 (1.2)	15 (3.1)	1 (0.2)	0 (0.0)	0 (0.0)	22 (4.6)
Grade 2	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	399 (82.6)	78 (16.1)	6 (1.2)	0 (0.0)	0 (0.0)	483 (100.0)
Cholesterol Increased (Cholesterol high)						
Grade 0	44 (48.4)	15 (16.5)	0 (0.0)	0 (0.0)	0 (0.0)	59 (64.8)
Grade 1	2 (2.2)	23 (25.3)	3 (3.3)	0 (0.0)	0 (0.0)	28 (30.8)
Grade 2	1 (1.1)	0 (0.0)	3 (3.3)	0 (0.0)	0 (0.0)	4 (4.4)
Total	47 (51.6)	38 (41.8)	6 (6.6)	0 (0.0)	0 (0.0)	91 (100.0)
Creatine Kinase Increased (CPK increased)						
Grade 0	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)
Total	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Creatinine Increased (Creatinine increased)						
Grade 0	377 (78.4)	65 (13.5)	9 (1.9)	1 (0.2)	1 (0.2)	453 (94.2)
Grade 1	3 (0.6)	20 (4.2)	5 (1.0)	0 (0.0)	0 (0.0)	28 (5.8)
Total	380 (79.0)	85 (17.7)	14 (2.9)	1 (0.2)	1 (0.2)	481 (100.0)
Gamma Glutamyl Transferase Increased (GGT increased)						
Grade 0	123 (65.8)	27 (14.4)	7 (3.7)	4 (2.1)	1 (0.5)	162 (86.6)
Grade 1	0 (0.0)	16 (8.6)	5 (2.7)	0 (0.0)	1 (0.5)	22 (11.8)
Grade 2	0 (0.0)	0 (0.0)	3 (1.6)	0 (0.0)	0 (0.0)	3 (1.6)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	123 (65.8)	43 (23.0)	15 (8.0)	4 (2.1)	2 (1.1)	187 (100.0)
Glucose Decreased (Hypoglycemia)						
Grade 0	117 (24.5)	169 (35.4)	16 (3.3)	6 (1.3)	1 (0.2)	309 (64.6)
Grade 1	8 (1.7)	116 (24.3)	23 (4.8)	5 (1.0)	0 (0.0)	152 (31.8)
Grade 2	0 (0.0)	2 (0.4)	6 (1.3)	3 (0.6)	1 (0.2)	12 (2.5)
Grade 3	0 (0.0)	0 (0.0)	1 (0.2)	4 (0.8)	0 (0.0)	5 (1.0)
Total	125 (26.2)	287 (60.0)	46 (9.6)	18 (3.8)	2 (0.4)	478 (100.0)
Glucose Increased (Hyperglycemia)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Creatinine Increased (Creatinine increased)						
Grade 0	398 (82.2)	52 (10.7)	0 (0.0)	0 (0.0)	0 (0.0)	450 (93.0)
Grade 1	2 (0.4)	26 (5.4)	6 (1.2)	0 (0.0)	0 (0.0)	34 (7.0)
Total	400 (82.6)	78 (16.1)	6 (1.2)	0 (0.0)	0 (0.0)	484 (100.0)
Gamma Glutamyl Transferase Increased (GGT increased)						
Grade 0	141 (70.9)	22 (11.1)	2 (1.0)	1 (0.5)	0 (0.0)	166 (83.4)
Grade 1	6 (3.0)	18 (9.0)	3 (1.5)	3 (1.5)	0 (0.0)	30 (15.1)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)	2 (1.0)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)
Total	147 (73.9)	40 (20.1)	5 (2.5)	7 (3.5)	0 (0.0)	199 (100.0)
Glucose Decreased (Hypoglycemia)						
Grade 0	139 (29.2)	163 (34.2)	14 (2.9)	1 (0.2)	0 (0.0)	317 (66.6)
Grade 1	3 (0.6)	104 (21.8)	19 (4.0)	2 (0.4)	1 (0.2)	129 (27.1)
Grade 2	1 (0.2)	3 (0.6)	9 (1.9)	7 (1.5)	2 (0.4)	22 (4.6)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.7)	0 (0.0)	8 (1.7)
Total	143 (30.0)	270 (56.7)	42 (8.8)	18 (3.8)	3 (0.6)	476 (100.0)
Glucose Increased (Hyperglycemia)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Glucose Increased (Hyperglycemia)						
Grade 0	117 (24.5)	169 (35.4)	16 (3.3)	6 (1.3)	1 (0.2)	309 (64.6)
Grade 1	8 (1.7)	116 (24.3)	23 (4.8)	5 (1.0)	0 (0.0)	152 (31.8)
Grade 2	0 (0.0)	2 (0.4)	6 (1.3)	3 (0.6)	1 (0.2)	12 (2.5)
Grade 3	0 (0.0)	0 (0.0)	1 (0.2)	4 (0.8)	0 (0.0)	5 (1.0)
Total	125 (26.2)	287 (60.0)	46 (9.6)	18 (3.8)	2 (0.4)	478 (100.0)
Hemoglobin Decreased (Anemia)						
Grade 0	316 (65.8)	104 (21.7)	2 (0.4)	2 (0.4)	0 (0.0)	424 (88.3)
Grade 1	3 (0.6)	47 (9.8)	4 (0.8)	0 (0.0)	0 (0.0)	54 (11.3)
Grade 2	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
Total	319 (66.5)	151 (31.5)	8 (1.7)	2 (0.4)	0 (0.0)	480 (100.0)
Hemoglobin Increased (Hemoglobin increased)						
Grade 0	316 (65.8)	104 (21.7)	2 (0.4)	2 (0.4)	0 (0.0)	424 (88.3)
Grade 1	3 (0.6)	47 (9.8)	4 (0.8)	0 (0.0)	0 (0.0)	54 (11.3)
Grade 2	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.4)
Total	319 (66.5)	151 (31.5)	8 (1.7)	2 (0.4)	0 (0.0)	480 (100.0)
Leukocytes Decreased (White blood cell decreased)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Glucose Increased (Hyperglycemia)						
Grade 0	139 (29.2)	163 (34.2)	14 (2.9)	1 (0.2)	0 (0.0)	317 (66.6)
Grade 1	3 (0.6)	104 (21.8)	19 (4.0)	2 (0.4)	1 (0.2)	129 (27.1)
Grade 2	1 (0.2)	3 (0.6)	9 (1.9)	7 (1.5)	2 (0.4)	22 (4.6)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.7)	0 (0.0)	8 (1.7)
Total	143 (30.0)	270 (56.7)	42 (8.8)	18 (3.8)	3 (0.6)	476 (100.0)
Hemoglobin Decreased (Anemia)						
Grade 0	352 (72.6)	75 (15.5)	0 (0.0)	0 (0.0)	0 (0.0)	427 (88.0)
Grade 1	7 (1.4)	50 (10.3)	1 (0.2)	0 (0.0)	0 (0.0)	58 (12.0)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	359 (74.0)	125 (25.8)	1 (0.2)	0 (0.0)	0 (0.0)	485 (100.0)
Hemoglobin Increased (Hemoglobin increased)						
Grade 0	352 (72.6)	75 (15.5)	0 (0.0)	0 (0.0)	0 (0.0)	427 (88.0)
Grade 1	7 (1.4)	50 (10.3)	1 (0.2)	0 (0.0)	0 (0.0)	58 (12.0)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	359 (74.0)	125 (25.8)	1 (0.2)	0 (0.0)	0 (0.0)	485 (100.0)
Leukocytes Decreased (White blood cell decreased)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Leukocytes Decreased (White blood cell decreased)						
Grade 0	432 (90.0)	36 (7.5)	1 (0.2)	0 (0.0)	0 (0.0)	469 (97.7)
Grade 1	5 (1.0)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.3)
Total	437 (91.0)	42 (8.8)	1 (0.2)	0 (0.0)	0 (0.0)	480 (100.0)
Lymphocytes Decreased (Lymphocyte count decreased)						
Grade 0	350 (73.4)	53 (11.1)	16 (3.4)	9 (1.9)	6 (1.3)	434 (91.0)
Grade 1	2 (0.4)	24 (5.0)	11 (2.3)	0 (0.0)	0 (0.0)	37 (7.8)
Grade 2	0 (0.0)	0 (0.0)	5 (1.0)	0 (0.0)	0 (0.0)	5 (1.0)
Grade 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
Total	352 (73.8)	77 (16.1)	32 (6.7)	9 (1.9)	7 (1.5)	477 (100.0)
Magnesium Decreased (Hypomagnesemia)						
Grade 0	360 (84.9)	46 (10.8)	2 (0.5)	1 (0.2)	0 (0.0)	409 (96.5)
Grade 1	2 (0.5)	10 (2.4)	2 (0.5)	0 (0.0)	0 (0.0)	14 (3.3)
Grade 2	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	362 (85.4)	56 (13.2)	5 (1.2)	1 (0.2)	0 (0.0)	424 (100.0)
Magnesium Increased (Hypermagnesemia)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Leukocytes Decreased (White blood cell decreased)						
Grade 0	417 (86.0)	44 (9.1)	2 (0.4)	0 (0.0)	0 (0.0)	463 (95.5)
Grade 1	4 (0.8)	16 (3.3)	2 (0.4)	0 (0.0)	0 (0.0)	22 (4.5)
Total	421 (86.8)	60 (12.4)	4 (0.8)	0 (0.0)	0 (0.0)	485 (100.0)
Lymphocytes Decreased (Lymphocyte count decreased)						
Grade 0	342 (70.8)	65 (13.5)	12 (2.5)	6 (1.2)	10 (2.1)	435 (90.1)
Grade 1	4 (0.8)	32 (6.6)	2 (0.4)	1 (0.2)	0 (0.0)	39 (8.1)
Grade 2	2 (0.4)	1 (0.2)	3 (0.6)	3 (0.6)	0 (0.0)	9 (1.9)
Grade 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	348 (72.0)	98 (20.3)	17 (3.5)	10 (2.1)	10 (2.1)	483 (100.0)
Magnesium Decreased (Hypomagnesemia)						
Grade 0	374 (84.0)	43 (9.7)	3 (0.7)	0 (0.0)	1 (0.2)	421 (94.6)
Grade 1	5 (1.1)	13 (2.9)	2 (0.4)	0 (0.0)	0 (0.0)	20 (4.5)
Grade 2	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	3 (0.7)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	380 (85.4)	57 (12.8)	7 (1.6)	0 (0.0)	1 (0.2)	445 (100.0)
Magnesium Increased (Hypermagnesemia)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Magnesium Increased (Hypermagnesemia)						
Grade 0	360 (84.9)	46 (10.8)	2 (0.5)	1 (0.2)	0 (0.0)	409 (96.5)
Grade 1	2 (0.5)	10 (2.4)	2 (0.5)	0 (0.0)	0 (0.0)	14 (3.3)
Grade 2	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	362 (85.4)	56 (13.2)	5 (1.2)	1 (0.2)	0 (0.0)	424 (100.0)
Neutrophils Decreased (Neutrophil count decreased)						
Grade 0	431 (90.5)	18 (3.8)	10 (2.1)	0 (0.0)	2 (0.4)	461 (96.8)
Grade 1	3 (0.6)	9 (1.9)	1 (0.2)	0 (0.0)	0 (0.0)	13 (2.7)
Grade 2	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
Total	435 (91.4)	28 (5.9)	11 (2.3)	0 (0.0)	2 (0.4)	476 (100.0)
Phosphate Decreased (Hypophosphatemia)						
Grade 0	301 (71.7)	10 (2.4)	62 (14.8)	12 (2.9)	0 (0.0)	385 (91.7)
Grade 1	0 (0.0)	1 (0.2)	2 (0.5)	1 (0.2)	0 (0.0)	4 (1.0)
Grade 2	3 (0.7)	4 (1.0)	13 (3.1)	6 (1.4)	0 (0.0)	26 (6.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0 (0.0)	5 (1.2)
Total	304 (72.4)	15 (3.6)	77 (18.3)	24 (5.7)	0 (0.0)	420 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Magnesium Increased (Hypermagnesemia)						
Grade 0	374 (84.0)	43 (9.7)	3 (0.7)	0 (0.0)	1 (0.2)	421 (94.6)
Grade 1	5 (1.1)	13 (2.9)	2 (0.4)	0 (0.0)	0 (0.0)	20 (4.5)
Grade 2	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	3 (0.7)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	380 (85.4)	57 (12.8)	7 (1.6)	0 (0.0)	1 (0.2)	445 (100.0)
Neutrophils Decreased (Neutrophil count decreased)						
Grade 0	423 (87.6)	35 (7.2)	11 (2.3)	1 (0.2)	0 (0.0)	470 (97.3)
Grade 1	2 (0.4)	7 (1.4)	1 (0.2)	0 (0.0)	0 (0.0)	10 (2.1)
Grade 2	0 (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	3 (0.6)
Total	425 (88.0)	43 (8.9)	13 (2.7)	2 (0.4)	0 (0.0)	483 (100.0)
Phosphate Decreased (Hypophosphatemia)						
Grade 0	299 (68.4)	7 (1.6)	70 (16.0)	15 (3.4)	0 (0.0)	391 (89.5)
Grade 1	2 (0.5)	1 (0.2)	8 (1.8)	0 (0.0)	0 (0.0)	11 (2.5)
Grade 2	6 (1.4)	2 (0.5)	16 (3.7)	6 (1.4)	0 (0.0)	30 (6.9)
Grade 3	2 (0.5)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	5 (1.1)
Total	309 (70.7)	10 (2.3)	96 (22.0)	22 (5.0)	0 (0.0)	437 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Platelets Decreased (Platelet count decreased)						
Grade 0	445 (92.9)	20 (4.2)	2 (0.4)	1 (0.2)	0 (0.0)	468 (97.7)
Grade 1	1 (0.2)	10 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.3)
Total	446 (93.1)	30 (6.3)	2 (0.4)	1 (0.2)	0 (0.0)	479 (100.0)
Potassium Decreased (Hypokalemia)						
Grade 0	351 (73.4)	83 (17.4)	13 (2.7)	4 (0.8)	6 (1.3)	457 (95.6)
Grade 1	3 (0.6)	11 (2.3)	4 (0.8)	1 (0.2)	0 (0.0)	19 (4.0)
Grade 2	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	355 (74.3)	95 (19.9)	17 (3.6)	5 (1.0)	6 (1.3)	478 (100.0)
Potassium Increased (Hyperkalemia)						
Grade 0	351 (73.4)	83 (17.4)	13 (2.7)	4 (0.8)	6 (1.3)	457 (95.6)
Grade 1	3 (0.6)	11 (2.3)	4 (0.8)	1 (0.2)	0 (0.0)	19 (4.0)
Grade 2	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	355 (74.3)	95 (19.9)	17 (3.6)	5 (1.0)	6 (1.3)	478 (100.0)
Prothrombin Intl. Normalized Ratio Increased (INR increased)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Platelets Decreased (Platelet count decreased)						
Grade 0	444 (91.5)	26 (5.4)	1 (0.2)	0 (0.0)	0 (0.0)	471 (97.1)
Grade 1	3 (0.6)	11 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	14 (2.9)
Total	447 (92.2)	37 (7.6)	1 (0.2)	0 (0.0)	0 (0.0)	485 (100.0)
Potassium Decreased (Hypokalemia)						
Grade 0	357 (74.2)	85 (17.7)	14 (2.9)	2 (0.4)	3 (0.6)	461 (95.8)
Grade 1	2 (0.4)	15 (3.1)	0 (0.0)	1 (0.2)	0 (0.0)	18 (3.7)
Grade 2	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
Total	360 (74.8)	100 (20.8)	14 (2.9)	4 (0.8)	3 (0.6)	481 (100.0)
Potassium Increased (Hyperkalemia)						
Grade 0	357 (74.2)	85 (17.7)	14 (2.9)	2 (0.4)	3 (0.6)	461 (95.8)
Grade 1	2 (0.4)	15 (3.1)	0 (0.0)	1 (0.2)	0 (0.0)	18 (3.7)
Grade 2	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
Total	360 (74.8)	100 (20.8)	14 (2.9)	4 (0.8)	3 (0.6)	481 (100.0)
Prothrombin Intl. Normalized Ratio Increased (INR increased)						

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Prothrombin Intl. Normalized Ratio Increased (INR increased)						
Grade 0	116 (89.2)	7 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)	123 (94.6)
Grade 1	2 (1.5)	5 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	7 (5.4)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	118 (90.8)	12 (9.2)	0 (0.0)	0 (0.0)	0 (0.0)	130 (100.0)
Sodium Decreased (Hyponatremia)						
Grade 0	370 (77.6)	80 (16.8)	1 (0.2)	6 (1.3)	1 (0.2)	458 (96.0)
Grade 1	7 (1.5)	10 (2.1)	0 (0.0)	0 (0.0)	1 (0.2)	18 (3.8)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	378 (79.2)	90 (18.9)	1 (0.2)	6 (1.3)	2 (0.4)	477 (100.0)
Sodium Increased (Hypernatremia)						
Grade 0	370 (77.6)	80 (16.8)	1 (0.2)	6 (1.3)	1 (0.2)	458 (96.0)
Grade 1	7 (1.5)	10 (2.1)	0 (0.0)	0 (0.0)	1 (0.2)	18 (3.8)
Grade 3	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	378 (79.2)	90 (18.9)	1 (0.2)	6 (1.3)	2 (0.4)	477 (100.0)
Triacylglycerol Lipase Increased (Lipase increased)						
Grade 0	90 (74.4)	13 (10.7)	5 (4.1)	2 (1.7)	2 (1.7)	112 (92.6)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Prothrombin Intl. Normalized Ratio Increased (INR increased)						
Grade 0	155 (89.1)	9 (5.2)	2 (1.1)	0 (0.0)	0 (0.0)	166 (95.4)
Grade 1	2 (1.1)	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)
Grade 2	0 (0.0)	0 (0.0)	1 (0.6)	3 (1.7)	0 (0.0)	4 (2.3)
Total	157 (90.2)	11 (6.3)	3 (1.7)	3 (1.7)	0 (0.0)	174 (100.0)
Sodium Decreased (Hyponatremia)						
Grade 0	397 (82.4)	69 (14.3)	1 (0.2)	1 (0.2)	0 (0.0)	468 (97.1)
Grade 1	7 (1.5)	6 (1.2)	0 (0.0)	1 (0.2)	0 (0.0)	14 (2.9)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	404 (83.8)	75 (15.6)	1 (0.2)	2 (0.4)	0 (0.0)	482 (100.0)
Sodium Increased (Hypernatremia)						
Grade 0	397 (82.4)	69 (14.3)	1 (0.2)	1 (0.2)	0 (0.0)	468 (97.1)
Grade 1	7 (1.5)	6 (1.2)	0 (0.0)	1 (0.2)	0 (0.0)	14 (2.9)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	404 (83.8)	75 (15.6)	1 (0.2)	2 (0.4)	0 (0.0)	482 (100.0)
Triacylglycerol Lipase Increased (Lipase increased)						
Grade 0	100 (74.1)	12 (8.9)	7 (5.2)	6 (4.4)	0 (0.0)	125 (92.6)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(APaT Population)

	Pembrolizumab (N=483)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Triacylglycerol Lipase Increased (Lipase increased)						
Grade 1	0 (0.0)	2 (1.7)	2 (1.7)	0 (0.0)	2 (1.7)	6 (5.0)
Grade 2	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.7)
Grade 3	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Total	92 (76.0)	16 (13.2)	7 (5.8)	2 (1.7)	4 (3.3)	121 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline (APaT Population)

	Placebo (N=486)					
	Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Triacylglycerol Lipase Increased (Lipase increased)						
Grade 1	1 (0.7)	2 (1.5)	2 (1.5)	1 (0.7)	0 (0.0)	6 (4.4)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	1 (0.7)	3 (2.2)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Total	101 (74.8)	14 (10.4)	9 (6.7)	10 (7.4)	1 (0.7)	135 (100.0)

Number of subjects with at least one baseline and post-baseline laboratory measurement is used as the denominator in percentage calculation.

A toxicity lab grade appears on this report only if its incidence in one or more of the columns per treatment group is greater than or equal 1; otherwise, the toxicity grade does not display.

NCI CTCAE version 4.03.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; adlbgrd]

Table 14.4-2
Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Activated Partial Thromboplastin Time Increased (Activated partial thromboplastin time prolonged)						
Subjects with Baseline and Post-baseline Measurements	137		176		313	
Grade 1	11	(8.0)	14	(8.0)	25	(8.0)
Grade 2	0	(0.0)	2	(1.1)	2	(0.6)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	0	(0.0)	0	(0.0)
All Grades	11	(8.0)	16	(9.1)	27	(8.6)
Alanine Aminotransferase Increased (Alanine aminotransferase increased)						
Subjects with Baseline and Post-baseline Measurements	481		481		962	
Grade 1	112	(23.3)	66	(13.7)	178	(18.5)
Grade 2	12	(2.5)	4	(0.8)	16	(1.7)
Grade 3	14	(2.9)	3	(0.6)	17	(1.8)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	14	(2.9)	3	(0.6)	17	(1.8)
All Grades	138	(28.7)	73	(15.2)	211	(21.9)
Albumin Decreased (Hypoalbuminemia)						
Subjects with Baseline and Post-baseline Measurements	477		479		956	
Grade 1	43	(9.0)	25	(5.2)	68	(7.1)
Grade 2	7	(1.5)	2	(0.4)	9	(0.9)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	2	(0.4)	1	(0.2)	3	(0.3)
All Grades	52	(10.9)	28	(5.8)	80	(8.4)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)						
Subjects with Baseline and Post-baseline Measurements	477		480		957	
Grade 1	49	(10.3)	32	(6.7)	81	(8.5)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	1	(0.2)	0	(0.0)	1	(0.1)
All Grades	54	(11.3)	33	(6.9)	87	(9.1)
Amylase Increased (Serum amylase increased)						
Subjects with Baseline and Post-baseline Measurements	119		145		264	
Grade 1	16	(13.4)	20	(13.8)	36	(13.6)
Grade 2	2	(1.7)	6	(4.1)	8	(3.0)
Grade 3	0	(0.0)	1	(0.7)	1	(0.4)
Grade 4	1	(0.8)	1	(0.7)	2	(0.8)
Grade 3-4	1	(0.8)	2	(1.4)	3	(1.1)
All Grades	19	(16.0)	28	(19.3)	47	(17.8)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)						
Subjects with Baseline and Post-baseline Measurements	480		480		960	
Grade 1	101	(21.0)	57	(11.9)	158	(16.5)
Grade 2	12	(2.5)	4	(0.8)	16	(1.7)
Grade 3	8	(1.7)	5	(1.0)	13	(1.4)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	8	(1.7)	5	(1.0)	13	(1.4)
All Grades	121	(25.2)	66	(13.8)	187	(19.5)
Bilirubin Increased (Blood bilirubin increased)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Bilirubin Increased (Blood bilirubin increased)						
Subjects with Baseline and Post-baseline Measurements	481		481		962	
Grade 1	31	(6.4)	38	(7.9)	69	(7.2)
Grade 2	16	(3.3)	20	(4.2)	36	(3.7)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	1	(0.2)	1	(0.1)
All Grades	47	(9.8)	59	(12.3)	106	(11.0)
Calcium Decreased (Hypocalcemia)						
Subjects with Baseline and Post-baseline Measurements	475		483		958	
Grade 1	67	(14.1)	63	(13.0)	130	(13.6)
Grade 2	5	(1.1)	6	(1.2)	11	(1.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	2	(0.4)	0	(0.0)	2	(0.2)
All Grades	74	(15.6)	69	(14.3)	143	(14.9)
Calcium Increased (Hypercalcemia)						
Subjects with Baseline and Post-baseline Measurements	475		483		958	
Grade 1	67	(14.1)	63	(13.0)	130	(13.6)
Grade 2	5	(1.1)	6	(1.2)	11	(1.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	2	(0.4)	0	(0.0)	2	(0.2)
All Grades	74	(15.6)	69	(14.3)	143	(14.9)
Cholesterol Increased (Cholesterol high)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Cholesterol Increased (Cholesterol high)						
Subjects with Baseline and Post-baseline Measurements	75		91		166	
Grade 1	14	(18.7)	15	(16.5)	29	(17.5)
Grade 2	6	(8.0)	3	(3.3)	9	(5.4)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	0	(0.0)	0	(0.0)
All Grades	20	(26.7)	18	(19.8)	38	(22.9)
Creatinine Increased (Creatinine increased)						
Subjects with Baseline and Post-baseline Measurements	481		484		965	
Grade 1	65	(13.5)	52	(10.7)	117	(12.1)
Grade 2	14	(2.9)	6	(1.2)	20	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	2	(0.4)	0	(0.0)	2	(0.2)
All Grades	81	(16.8)	58	(12.0)	139	(14.4)
Gamma Glutamyl Transferase Increased (GGT increased)						
Subjects with Baseline and Post-baseline Measurements	187		199		386	
Grade 1	27	(14.4)	22	(11.1)	49	(12.7)
Grade 2	12	(6.4)	5	(2.5)	17	(4.4)
Grade 3	4	(2.1)	6	(3.0)	10	(2.6)
Grade 4	2	(1.1)	0	(0.0)	2	(0.5)
Grade 3-4	6	(3.2)	6	(3.0)	12	(3.1)
All Grades	45	(24.1)	33	(16.6)	78	(20.2)
Glucose Decreased (Hypoglycemia)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Glucose Decreased (Hypoglycemia)						
Subjects with Baseline and Post-baseline Measurements	478		476		954	
Grade 1	169	(35.4)	163	(34.2)	332	(34.8)
Grade 2	39	(8.2)	33	(6.9)	72	(7.5)
Grade 3	14	(2.9)	10	(2.1)	24	(2.5)
Grade 4	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3-4	16	(3.3)	13	(2.7)	29	(3.0)
All Grades	224	(46.9)	209	(43.9)	433	(45.4)
Glucose Increased (Hyperglycemia)						
Subjects with Baseline and Post-baseline Measurements	478		476		954	
Grade 1	169	(35.4)	163	(34.2)	332	(34.8)
Grade 2	39	(8.2)	33	(6.9)	72	(7.5)
Grade 3	14	(2.9)	10	(2.1)	24	(2.5)
Grade 4	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3-4	16	(3.3)	13	(2.7)	29	(3.0)
All Grades	224	(46.9)	209	(43.9)	433	(45.4)
Hemoglobin Decreased (Anemia)						
Subjects with Baseline and Post-baseline Measurements	480		485		965	
Grade 1	104	(21.7)	75	(15.5)	179	(18.5)
Grade 2	6	(1.3)	1	(0.2)	7	(0.7)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	2	(0.4)	0	(0.0)	2	(0.2)
All Grades	112	(23.3)	76	(15.7)	188	(19.5)
Hemoglobin Increased (Hemoglobin increased)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Hemoglobin Increased (Hemoglobin increased)						
Subjects with Baseline and Post-baseline Measurements	480		485		965	
Grade 1	104	(21.7)	75	(15.5)	179	(18.5)
Grade 2	6	(1.3)	1	(0.2)	7	(0.7)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	2	(0.4)	0	(0.0)	2	(0.2)
All Grades	112	(23.3)	76	(15.7)	188	(19.5)
Leukocytes Decreased (White blood cell decreased)						
Subjects with Baseline and Post-baseline Measurements	480		485		965	
Grade 1	36	(7.5)	44	(9.1)	80	(8.3)
Grade 2	1	(0.2)	4	(0.8)	5	(0.5)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	0	(0.0)	0	(0.0)
All Grades	37	(7.7)	48	(9.9)	85	(8.8)
Lymphocytes Decreased (Lymphocyte count decreased)						
Subjects with Baseline and Post-baseline Measurements	477		483		960	
Grade 1	53	(11.1)	65	(13.5)	118	(12.3)
Grade 2	27	(5.7)	14	(2.9)	41	(4.3)
Grade 3	9	(1.9)	10	(2.1)	19	(2.0)
Grade 4	6	(1.3)	10	(2.1)	16	(1.7)
Grade 3-4	15	(3.1)	20	(4.1)	35	(3.6)
All Grades	95	(19.9)	99	(20.5)	194	(20.2)
Magnesium Decreased (Hypomagnesemia)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Magnesium Decreased (Hypomagnesemia)						
Subjects with Baseline and Post-baseline Measurements	424		445		869	
Grade 1	46	(10.8)	43	(9.7)	89	(10.2)
Grade 2	4	(0.9)	5	(1.1)	9	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3-4	1	(0.2)	1	(0.2)	2	(0.2)
All Grades	51	(12.0)	49	(11.0)	100	(11.5)
Magnesium Increased (Hypermagnesemia)						
Subjects with Baseline and Post-baseline Measurements	424		445		869	
Grade 1	46	(10.8)	43	(9.7)	89	(10.2)
Grade 2	4	(0.9)	5	(1.1)	9	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3-4	1	(0.2)	1	(0.2)	2	(0.2)
All Grades	51	(12.0)	49	(11.0)	100	(11.5)
Neutrophils Decreased (Neutrophil count decreased)						
Subjects with Baseline and Post-baseline Measurements	476		483		959	
Grade 1	18	(3.8)	35	(7.2)	53	(5.5)
Grade 2	11	(2.3)	12	(2.5)	23	(2.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3-4	2	(0.4)	2	(0.4)	4	(0.4)
All Grades	31	(6.5)	49	(10.1)	80	(8.3)
Phosphate Decreased (Hypophosphatemia)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Phosphate Decreased (Hypophosphatemia)						
Subjects with Baseline and Post-baseline Measurements	420		437		857	
Grade 1	10	(2.4)	7	(1.6)	17	(2.0)
Grade 2	64	(15.2)	78	(17.8)	142	(16.6)
Grade 3	19	(4.5)	21	(4.8)	40	(4.7)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	19	(4.5)	21	(4.8)	40	(4.7)
All Grades	93	(22.1)	106	(24.3)	199	(23.2)
Platelets Decreased (Platelet count decreased)						
Subjects with Baseline and Post-baseline Measurements	479		485		964	
Grade 1	20	(4.2)	26	(5.4)	46	(4.8)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	1	(0.2)	0	(0.0)	1	(0.1)
All Grades	23	(4.8)	27	(5.6)	50	(5.2)
Potassium Decreased (Hypokalemia)						
Subjects with Baseline and Post-baseline Measurements	478		481		959	
Grade 1	83	(17.4)	85	(17.7)	168	(17.5)
Grade 2	17	(3.6)	14	(2.9)	31	(3.2)
Grade 3	5	(1.0)	3	(0.6)	8	(0.8)
Grade 4	6	(1.3)	3	(0.6)	9	(0.9)
Grade 3-4	11	(2.3)	6	(1.2)	17	(1.8)
All Grades	111	(23.2)	105	(21.8)	216	(22.5)
Potassium Increased (Hyperkalemia)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Potassium Increased (Hyperkalemia)						
Subjects with Baseline and Post-baseline Measurements	478		481		959	
Grade 1	83	(17.4)	85	(17.7)	168	(17.5)
Grade 2	17	(3.6)	14	(2.9)	31	(3.2)
Grade 3	5	(1.0)	3	(0.6)	8	(0.8)
Grade 4	6	(1.3)	3	(0.6)	9	(0.9)
Grade 3-4	11	(2.3)	6	(1.2)	17	(1.8)
All Grades	111	(23.2)	105	(21.8)	216	(22.5)
Prothrombin Intl. Normalized Ratio Increased (INR increased)						
Subjects with Baseline and Post-baseline Measurements	130		174		304	
Grade 1	7	(5.4)	9	(5.2)	16	(5.3)
Grade 2	0	(0.0)	2	(1.1)	2	(0.7)
Grade 3	0	(0.0)	3	(1.7)	3	(1.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	3	(1.7)	3	(1.0)
All Grades	7	(5.4)	14	(8.0)	21	(6.9)
Sodium Decreased (Hyponatremia)						
Subjects with Baseline and Post-baseline Measurements	477		482		959	
Grade 1	80	(16.8)	69	(14.3)	149	(15.5)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	6	(1.3)	2	(0.4)	8	(0.8)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3-4	8	(1.7)	2	(0.4)	10	(1.0)
All Grades	89	(18.7)	72	(14.9)	161	(16.8)
Sodium Increased (Hypernatremia)						

Summary of Subjects with Increases from Baseline in Laboratory Test Toxicity Grade Based on Highest Post-baseline Toxicity Grade
(Overall Incidence > 0% in One or More Treatment Groups)
(APaT Population)

Laboratory Test	Pembrolizumab (N=483) n	(%)	Placebo (N=486) n	(%)	Total (N=969) n	(%)
Sodium Increased (Hypernatremia)						
Subjects with Baseline and Post-baseline Measurements	477		482		959	
Grade 1	80	(16.8)	69	(14.3)	149	(15.5)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	6	(1.3)	2	(0.4)	8	(0.8)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3-4	8	(1.7)	2	(0.4)	10	(1.0)
All Grades	89	(18.7)	72	(14.9)	161	(16.8)
Triacylglycerol Lipase Increased (Lipase increased)						
Subjects with Baseline and Post-baseline Measurements	121		135		256	
Grade 1	13	(10.7)	12	(8.9)	25	(9.8)
Grade 2	7	(5.8)	9	(6.7)	16	(6.3)
Grade 3	2	(1.7)	9	(6.7)	11	(4.3)
Grade 4	4	(3.3)	1	(0.7)	5	(2.0)
Grade 3-4	6	(5.0)	10	(7.4)	16	(6.3)
All Grades	26	(21.5)	31	(23.0)	57	(22.3)

If a subject had more than one toxicity grade for a laboratory test, only the highest grade is counted.
Number of subjects with at least one baseline and post-baseline laboratory measurement is used as the denominator in percentage calculation.
Grades are based on NCI CTCAE version 4.03.
Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-adsl; adlbgrd]

Table 14.4-3
Participants With Liver Function Laboratory Findings That Met Predetermined Criteria
(APaT Population)

Criteria	Pembrolizumab		Placebo	
	n/m	(%)	n/m	(%)
Participants in population	483		486	
Alanine Aminotransferase				
≥3 x ULN	26/482	(5.4)	7/486	(1.4)
≥5 x ULN	14/482	(2.9)	3/486	(0.6)
≥10 x ULN	3/482	(0.6)	0/486	(0.0)
≥20 x ULN	0/482	(0.0)	0/486	(0.0)
Aspartate Aminotransferase				
≥3 x ULN	21/482	(4.4)	9/486	(1.9)
≥5 x ULN	9/482	(1.9)	5/486	(1.0)
≥10 x ULN	2/482	(0.4)	0/486	(0.0)
≥20 x ULN	0/482	(0.0)	0/486	(0.0)
Aminotransferase (ALT or AST)				
≥3 x ULN	27/482	(5.6)	13/486	(2.7)
≥5 x ULN	16/482	(3.3)	7/486	(1.4)
≥10 x ULN	4/482	(0.8)	0/486	(0.0)
≥20 x ULN	0/482	(0.0)	0/486	(0.0)
Bilirubin				
≥2 x ULN	4/482	(0.8)	6/486	(1.2)
Alkaline Phosphatase				
≥1.5 x ULN	18/482	(3.7)	7/486	(1.4)
Aminotransferase (ALT or AST) and Bilirubin				
AT ≥3 x ULN and BILI ≥1.5 x ULN	3/482	(0.6)	0/486	(0.0)
AT ≥3 x ULN and BILI ≥2 x ULN	0/482	(0.0)	0/486	(0.0)
Aminotransferase (ALT or AST) and Bilirubin and Alkaline Phosphatase				
AT ≥3 x ULN and BILI ≥2 x ULN and ALP <2 x ULN	0/482	(0.0)	0/486	(0.0)

n = Number of participants with postbaseline test results (or combination of test results from the same day) that met predetermined criteria.

m = Number of participants with at least one postbaseline test result or combination of test results from the same day.

ALP = Alkaline phosphatase; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; AT = Aminotransferase (ALT or AST); BILI = Bilirubin; ULN = Upper limit of normal range.

Database Cutoff Date: 04JAN2023.

Source: [P716V04MK3475: adam-adsl; addili]

14.5 Vital Signs, Physical Examinations, and Other Observations Related to Safety

Table 14.5-1
Mean Change (SD) in Vital Sign Measurements from Baseline over Time
(APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Systolic Blood Pressure (mmHg)								
Cycle 2	Pembrolizumab	424	133.37 (15.61)	[95.00, 212.00]	132.33 (15.74)	[94.00, 183.00]	-1.04 (14.50)	[-44.00, 50.00]
	Placebo	441	130.87 (16.62)	[89.00, 215.00]	131.09 (16.05)	[84.00, 230.00]	0.22 (13.84)	[-72.00, 46.00]
Cycle 3	Pembrolizumab	400	133.12 (15.56)	[95.00, 212.00]	132.61 (15.35)	[85.00, 185.00]	-0.51 (13.61)	[-40.00, 48.00]
	Placebo	437	131.28 (16.79)	[89.00, 215.00]	130.87 (17.07)	[90.00, 207.00]	-0.41 (13.50)	[-53.00, 50.00]
Cycle 4	Pembrolizumab	401	133.36 (15.59)	[95.00, 212.00]	131.64 (15.02)	[98.00, 184.00]	-1.72 (14.39)	[-52.00, 41.00]
	Placebo	429	131.01 (16.77)	[89.00, 215.00]	130.37 (16.67)	[41.00, 210.00]	-0.64 (14.75)	[-87.00, 46.00]
Cycle 5	Pembrolizumab	391	133.36 (15.64)	[95.00, 212.00]	131.52 (15.48)	[90.00, 186.00]	-1.84 (14.79)	[-50.00, 42.00]
	Placebo	431	131.24 (16.86)	[89.00, 215.00]	130.39 (15.32)	[90.00, 199.00]	-0.86 (14.18)	[-48.00, 44.00]
Cycle 6	Pembrolizumab	381	133.35 (15.61)	[95.00, 212.00]	130.87 (15.51)	[90.00, 186.00]	-2.48 (14.85)	[-59.00, 66.00]
	Placebo	422	130.94 (16.84)	[89.00, 215.00]	129.88 (16.96)	[82.00, 206.00]	-1.05 (14.76)	[-46.00, 49.00]
Cycle 7	Pembrolizumab	368	133.36 (15.83)	[95.00, 212.00]	131.02 (14.80)	[90.00, 187.00]	-2.34 (14.93)	[-47.00, 57.00]
	Placebo	417	131.23 (16.72)	[89.00, 215.00]	130.31 (14.99)	[87.00, 189.00]	-0.92 (13.92)	[-53.00, 43.00]
Cycle 8	Pembrolizumab	356	133.23 (15.68)	[95.00, 212.00]	131.15 (15.28)	[90.00, 186.00]	-2.08 (14.97)	[-48.00, 63.00]
	Placebo	407	130.80 (16.47)	[89.00, 215.00]	129.39 (15.05)	[90.00, 181.00]	-1.41 (13.70)	[-59.00, 49.00]
Cycle 9	Pembrolizumab	340	133.35 (15.75)	[95.00, 212.00]	131.36 (15.83)	[93.00, 188.00]	-2.00 (15.13)	[-44.00, 65.00]
	Placebo	407	130.92 (16.65)	[89.00, 215.00]	130.56 (15.50)	[90.00, 207.00]	-0.36 (14.83)	[-68.00, 45.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

			Baseline		Value		Mean Change	
Visit	Treatment	N	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	337	133.46 (15.89)	[95.00, 212.00]	130.85 (14.84)	[90.00, 178.00]	-2.61 (14.30)	[-60.00, 38.00]
	Placebo	391	130.93 (16.44)	[89.00, 215.00]	130.28 (15.17)	[85.00, 179.00]	-0.64 (16.12)	[-54.00, 51.00]
Cycle 11	Pembrolizumab	326	133.36 (15.89)	[95.00, 212.00]	130.81 (15.11)	[95.00, 191.00]	-2.55 (15.18)	[-62.00, 34.00]
	Placebo	385	131.14 (16.56)	[89.00, 215.00]	129.64 (14.97)	[90.00, 194.00]	-1.49 (14.86)	[-53.00, 45.00]
Cycle 12	Pembrolizumab	319	133.26 (15.90)	[95.00, 212.00]	129.67 (14.59)	[91.00, 178.00]	-3.59 (15.88)	[-52.00, 48.00]
	Placebo	380	130.98 (16.04)	[89.00, 210.00]	129.78 (15.18)	[90.00, 198.00]	-1.20 (15.02)	[-51.00, 50.00]
Cycle 13	Pembrolizumab	316	133.35 (15.79)	[95.00, 212.00]	129.29 (15.31)	[90.00, 188.00]	-4.07 (16.40)	[-65.00, 59.00]
	Placebo	380	131.23 (16.38)	[89.00, 215.00]	129.83 (14.70)	[85.00, 191.00]	-1.40 (15.55)	[-51.00, 46.00]
Cycle 14	Pembrolizumab	310	133.01 (16.02)	[95.00, 212.00]	130.89 (15.10)	[97.00, 179.00]	-2.12 (15.43)	[-57.00, 45.00]
	Placebo	367	131.10 (15.92)	[89.00, 210.00]	129.42 (14.98)	[80.00, 191.00]	-1.68 (14.22)	[-47.00, 45.00]
Cycle 15	Pembrolizumab	306	133.00 (16.03)	[95.00, 212.00]	130.52 (14.78)	[92.00, 177.00]	-2.48 (15.57)	[-62.00, 42.00]
	Placebo	361	130.86 (16.11)	[89.00, 210.00]	130.97 (15.57)	[92.00, 202.00]	0.11 (14.62)	[-53.00, 42.00]
Cycle 16	Pembrolizumab	301	133.29 (16.00)	[95.00, 212.00]	130.05 (13.67)	[99.00, 167.00]	-3.24 (15.59)	[-59.00, 51.00]
	Placebo	354	130.77 (15.95)	[89.00, 210.00]	129.74 (14.78)	[85.00, 180.00]	-1.02 (14.57)	[-61.00, 50.00]
Cycle 17	Pembrolizumab	300	132.99 (16.03)	[95.00, 212.00]	130.11 (14.05)	[96.00, 179.00]	-2.88 (14.83)	[-63.00, 50.00]
	Placebo	345	130.86 (16.34)	[89.00, 210.00]	128.84 (15.56)	[81.00, 197.00]	-2.02 (14.18)	[-51.00, 45.00]
Follow-up	Pembrolizumab	15	133.67 (20.19)	[105.00, 179.00]	130.87 (18.88)	[100.00, 170.00]	-2.80 (10.22)	[-16.00, 24.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	13	127.15 (16.13)	[101.00, 156.00]	130.69 (11.11)	[111.00, 147.00]	3.54 (21.94)	[-31.00, 45.00]
Follow-up Day 30	Pembrolizumab	249	134.98 (16.30)	[95.00, 212.00]	132.26 (15.17)	[87.00, 167.00]	-2.72 (15.58)	[-55.00, 44.00]
	Placebo	273	131.05 (16.53)	[89.00, 210.00]	131.36 (16.08)	[90.00, 235.00]	0.30 (14.42)	[-45.00, 47.00]
Crossover Screening Visit	Pembrolizumab	6	129.50 (17.28)	[111.00, 158.00]	124.33 (15.67)	[102.00, 142.00]	-5.17 (11.44)	[-18.00, 11.00]
	Placebo	53	132.40 (15.42)	[100.00, 176.00]	131.98 (13.84)	[95.00, 169.00]	-0.42 (15.29)	[-28.00, 50.00]
Crossover Cycle 1	Pembrolizumab	1	115.00 ()	[115.00, 115.00]	108.00 ()	[108.00, 108.00]	-7.00 ()	[-7.00, -7.00]
	Placebo	2	132.50 (9.19)	[126.00, 139.00]	135.50 (4.95)	[132.00, 139.00]	3.00 (14.14)	[-7.00, 13.00]
Crossover Cycle 16	Placebo	1	120.00 ()	[120.00, 120.00]	137.00 ()	[137.00, 137.00]	17.00 ()	[17.00, 17.00]
Discontinuation Visit	Pembrolizumab	204	133.21 (15.37)	[103.00, 179.00]	130.80 (16.55)	[90.00, 177.00]	-2.40 (15.35)	[-61.00, 47.00]
	Placebo	178	130.69 (17.51)	[92.00, 215.00]	131.03 (15.54)	[96.00, 178.00]	0.34 (17.90)	[-69.00, 49.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Diastolic Blood Pressure (mmHg)								
Cycle 2	Pembrolizumab	424	78.78 (10.50)	[42.00, 115.00]	78.23 (10.28)	[50.00, 112.00]	-0.56 (9.78)	[-38.00, 30.00]
	Placebo	441	78.17 (10.26)	[48.00, 107.00]	77.95 (10.50)	[40.00, 115.00]	-0.22 (9.30)	[-32.00, 43.00]
Cycle 3	Pembrolizumab	400	78.97 (10.41)	[42.00, 115.00]	78.61 (10.27)	[48.00, 118.00]	-0.36 (10.12)	[-34.00, 28.00]
	Placebo	437	78.33 (10.26)	[48.00, 107.00]	77.75 (10.24)	[40.00, 109.00]	-0.58 (9.77)	[-42.00, 47.00]
Cycle 4	Pembrolizumab	401	78.82 (10.50)	[42.00, 115.00]	77.94 (10.30)	[39.00, 107.00]	-0.87 (10.60)	[-45.00, 34.00]
	Placebo	429	78.21 (10.22)	[48.00, 107.00]	78.12 (10.31)	[50.00, 118.00]	-0.10 (9.31)	[-30.00, 31.00]
Cycle 5	Pembrolizumab	391	78.75 (10.56)	[42.00, 115.00]	78.13 (9.90)	[54.00, 112.00]	-0.63 (10.41)	[-41.00, 33.00]
	Placebo	431	78.48 (10.26)	[48.00, 107.00]	77.53 (10.01)	[50.00, 109.00]	-0.95 (9.28)	[-29.00, 36.00]
Cycle 6	Pembrolizumab	381	78.85 (10.57)	[42.00, 115.00]	77.81 (9.89)	[53.00, 119.00]	-1.04 (10.98)	[-58.00, 36.00]
	Placebo	422	78.19 (10.25)	[48.00, 107.00]	76.90 (10.44)	[30.00, 106.00]	-1.29 (10.07)	[-48.00, 44.00]
Cycle 7	Pembrolizumab	368	78.90 (10.58)	[42.00, 115.00]	78.16 (9.32)	[48.00, 102.00]	-0.74 (10.56)	[-33.00, 31.00]
	Placebo	417	78.41 (10.32)	[48.00, 107.00]	77.43 (9.81)	[48.00, 109.00]	-0.98 (9.71)	[-27.00, 39.00]
Cycle 8	Pembrolizumab	356	78.63 (10.50)	[42.00, 114.00]	78.10 (10.31)	[47.00, 110.00]	-0.54 (10.61)	[-33.00, 39.00]
	Placebo	407	78.46 (10.27)	[48.00, 107.00]	77.10 (9.98)	[52.00, 109.00]	-1.37 (9.25)	[-27.00, 31.00]
Cycle 9	Pembrolizumab	340	78.52 (10.54)	[42.00, 114.00]	77.39 (9.71)	[50.00, 103.00]	-1.13 (10.33)	[-41.00, 29.00]
	Placebo	407	78.39 (10.32)	[48.00, 107.00]	77.40 (10.17)	[50.00, 105.00]	-0.99 (10.11)	[-41.00, 32.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

			Baseline		Value		Mean Change	
Visit	Treatment	N	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	337	78.82 (10.90)	[42.00, 115.00]	78.15 (10.09)	[51.00, 109.00]	-0.67 (10.56)	[-36.00, 28.00]
	Placebo	391	78.37 (10.34)	[48.00, 107.00]	77.66 (9.83)	[50.00, 119.00]	-0.71 (9.88)	[-34.00, 38.00]
Cycle 11	Pembrolizumab	326	78.81 (10.98)	[42.00, 115.00]	77.70 (10.12)	[43.00, 105.00]	-1.11 (10.60)	[-33.00, 33.00]
	Placebo	385	78.43 (10.40)	[48.00, 107.00]	77.59 (9.65)	[48.00, 106.00]	-0.84 (9.66)	[-33.00, 30.00]
Cycle 12	Pembrolizumab	319	78.75 (10.80)	[42.00, 114.00]	77.25 (10.38)	[45.00, 111.00]	-1.50 (11.40)	[-43.00, 39.00]
	Placebo	380	78.47 (10.13)	[48.00, 105.00]	77.69 (9.39)	[49.00, 104.00]	-0.78 (9.88)	[-40.00, 26.00]
Cycle 13	Pembrolizumab	316	78.85 (10.75)	[42.00, 114.00]	76.42 (10.12)	[53.00, 108.00]	-2.43 (10.76)	[-46.00, 32.00]
	Placebo	380	78.58 (10.29)	[48.00, 107.00]	77.84 (9.26)	[50.00, 107.00]	-0.74 (9.68)	[-26.00, 30.00]
Cycle 14	Pembrolizumab	310	78.75 (10.82)	[42.00, 114.00]	77.77 (9.62)	[52.00, 106.00]	-0.98 (9.99)	[-33.00, 32.00]
	Placebo	367	78.62 (10.27)	[48.00, 107.00]	77.77 (9.66)	[50.00, 105.00]	-0.84 (10.18)	[-33.00, 42.00]
Cycle 15	Pembrolizumab	306	78.52 (10.72)	[42.00, 103.00]	77.51 (9.81)	[50.00, 103.00]	-1.01 (10.19)	[-30.00, 31.00]
	Placebo	361	78.49 (10.30)	[48.00, 107.00]	78.09 (9.41)	[49.00, 104.00]	-0.40 (9.78)	[-33.00, 34.00]
Cycle 16	Pembrolizumab	301	78.71 (10.74)	[42.00, 103.00]	77.16 (10.33)	[48.00, 110.00]	-1.54 (10.96)	[-34.00, 35.00]
	Placebo	354	78.52 (10.20)	[48.00, 107.00]	77.35 (9.97)	[48.00, 117.00]	-1.16 (9.99)	[-36.00, 35.00]
Cycle 17	Pembrolizumab	300	78.65 (10.78)	[42.00, 103.00]	77.34 (9.66)	[51.00, 110.00]	-1.30 (10.70)	[-35.00, 42.00]
	Placebo	345	78.61 (10.42)	[48.00, 107.00]	77.66 (10.05)	[47.00, 104.00]	-0.95 (9.57)	[-27.00, 35.00]
Follow-up	Pembrolizumab	15	79.00 (8.98)	[60.00, 93.00]	74.27 (10.91)	[54.00, 91.00]	-4.73 (8.24)	[-26.00, 5.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	13	78.15 (7.58)	[67.00, 88.00]	80.15 (4.95)	[74.00, 90.00]	2.00 (10.52)	[-13.00, 21.00]
Follow-up Day 30	Pembrolizumab	249	79.29 (10.55)	[42.00, 115.00]	79.01 (10.36)	[51.00, 135.00]	-0.28 (10.98)	[-29.00, 41.00]
	Placebo	273	78.45 (10.19)	[48.00, 107.00]	78.33 (9.62)	[52.00, 111.00]	-0.11 (9.88)	[-26.00, 30.00]
Crossover Screening Visit	Pembrolizumab	6	77.50 (11.41)	[66.00, 98.00]	79.00 (8.85)	[68.00, 90.00]	1.50 (9.97)	[-8.00, 17.00]
	Placebo	53	76.26 (9.57)	[55.00, 105.00]	78.28 (10.81)	[60.00, 105.00]	2.02 (11.03)	[-18.00, 40.00]
Crossover Cycle 1	Pembrolizumab	1	78.00 ()	[78.00, 78.00]	71.00 ()	[71.00, 71.00]	-7.00 ()	[-7.00, -7.00]
	Placebo	2	82.50 (2.12)	[81.00, 84.00]	83.00 (4.24)	[80.00, 86.00]	0.50 (2.12)	[-1.00, 2.00]
Crossover Cycle 16	Placebo	1	81.00 ()	[81.00, 81.00]	92.00 ()	[92.00, 92.00]	11.00 ()	[11.00, 11.00]
Discontinuation Visit	Pembrolizumab	203	79.33 (10.35)	[54.00, 115.00]	79.06 (10.35)	[52.00, 109.00]	-0.26 (10.45)	[-34.00, 28.00]
	Placebo	178	77.93 (9.96)	[49.00, 103.00]	77.89 (10.32)	[52.00, 102.00]	-0.03 (10.53)	[-33.00, 46.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Pulse Rate (beats/min)								
Cycle 2	Pembrolizumab	425	72.71 (12.64)	[42.00, 120.00]	72.61 (12.02)	[46.00, 125.00]	-0.10 (11.01)	[-57.00, 37.00]
	Placebo	442	72.68 (11.93)	[40.00, 115.00]	72.38 (12.47)	[40.00, 130.00]	-0.30 (10.61)	[-54.00, 35.00]
Cycle 3	Pembrolizumab	399	72.69 (12.55)	[42.00, 120.00]	72.16 (11.60)	[46.00, 116.00]	-0.53 (11.03)	[-57.00, 41.00]
	Placebo	437	72.79 (11.81)	[40.00, 115.00]	71.99 (11.66)	[40.00, 109.00]	-0.80 (10.32)	[-58.00, 33.00]
Cycle 4	Pembrolizumab	401	72.44 (12.65)	[42.00, 120.00]	72.10 (12.03)	[45.00, 121.00]	-0.34 (11.28)	[-35.00, 58.00]
	Placebo	431	72.84 (11.96)	[40.00, 115.00]	72.03 (12.35)	[41.00, 128.00]	-0.82 (10.90)	[-56.00, 38.00]
Cycle 5	Pembrolizumab	391	72.38 (12.59)	[42.00, 120.00]	71.44 (11.80)	[37.00, 117.00]	-0.93 (11.69)	[-54.00, 42.00]
	Placebo	431	72.82 (11.94)	[40.00, 115.00]	72.01 (12.28)	[44.00, 115.00]	-0.81 (10.98)	[-50.00, 35.00]
Cycle 6	Pembrolizumab	381	72.65 (12.53)	[42.00, 120.00]	71.43 (11.71)	[42.00, 133.00]	-1.23 (11.24)	[-36.00, 51.00]
	Placebo	423	72.60 (11.77)	[40.00, 115.00]	71.68 (11.89)	[44.00, 116.00]	-0.91 (11.72)	[-62.00, 40.00]
Cycle 7	Pembrolizumab	368	72.57 (12.53)	[42.00, 120.00]	72.12 (11.25)	[41.00, 122.00]	-0.45 (11.62)	[-58.00, 33.00]
	Placebo	418	72.75 (11.83)	[40.00, 115.00]	71.48 (11.23)	[45.00, 106.00]	-1.27 (11.46)	[-47.00, 43.00]
Cycle 8	Pembrolizumab	356	72.70 (12.68)	[42.00, 120.00]	71.28 (11.70)	[40.00, 108.00]	-1.42 (11.69)	[-60.00, 42.00]
	Placebo	407	72.88 (11.89)	[40.00, 115.00]	72.00 (11.59)	[45.00, 107.00]	-0.89 (11.63)	[-50.00, 46.00]
Cycle 9	Pembrolizumab	341	72.71 (12.75)	[42.00, 120.00]	71.87 (11.68)	[42.00, 130.00]	-0.84 (11.79)	[-59.00, 44.00]
	Placebo	409	72.65 (11.71)	[40.00, 115.00]	71.68 (11.15)	[46.00, 120.00]	-0.97 (11.94)	[-55.00, 35.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	338	72.87 (12.62)	[42.00, 120.00]	71.70 (11.85)	[43.00, 120.00]	-1.17 (12.35)	[-60.00, 54.00]
	Placebo	392	72.71 (11.72)	[40.00, 115.00]	71.82 (11.24)	[41.00, 102.00]	-0.89 (12.07)	[-52.00, 35.00]
Cycle 11	Pembrolizumab	326	72.80 (12.55)	[42.00, 120.00]	71.31 (12.47)	[43.00, 131.00]	-1.48 (11.79)	[-60.00, 40.00]
	Placebo	385	72.81 (11.75)	[40.00, 115.00]	71.77 (11.56)	[42.00, 116.00]	-1.04 (11.74)	[-47.00, 32.00]
Cycle 12	Pembrolizumab	320	72.78 (12.43)	[42.00, 120.00]	71.62 (11.37)	[42.00, 110.00]	-1.17 (11.54)	[-60.00, 44.00]
	Placebo	380	72.96 (11.75)	[40.00, 115.00]	71.73 (10.73)	[49.00, 113.00]	-1.23 (11.79)	[-56.00, 42.00]
Cycle 13	Pembrolizumab	316	73.10 (12.33)	[47.00, 120.00]	71.65 (11.68)	[45.00, 114.00]	-1.45 (11.96)	[-60.00, 43.00]
	Placebo	381	73.02 (11.75)	[40.00, 115.00]	71.14 (11.14)	[45.00, 115.00]	-1.88 (11.19)	[-46.00, 33.00]
Cycle 14	Pembrolizumab	310	72.92 (12.42)	[47.00, 120.00]	71.28 (11.93)	[44.00, 120.00]	-1.64 (11.91)	[-60.00, 45.00]
	Placebo	368	73.03 (11.81)	[40.00, 115.00]	71.96 (11.17)	[45.00, 110.00]	-1.07 (11.90)	[-54.00, 49.00]
Cycle 15	Pembrolizumab	307	72.85 (12.59)	[42.00, 120.00]	72.15 (12.31)	[45.00, 131.00]	-0.70 (12.71)	[-59.00, 50.00]
	Placebo	361	72.87 (11.69)	[40.00, 115.00]	71.50 (11.29)	[39.00, 108.00]	-1.37 (11.78)	[-58.00, 33.00]
Cycle 16	Pembrolizumab	301	72.94 (12.67)	[42.00, 120.00]	71.97 (11.61)	[47.00, 120.00]	-0.97 (11.74)	[-60.00, 33.00]
	Placebo	355	72.95 (11.84)	[40.00, 115.00]	72.34 (11.72)	[36.00, 125.00]	-0.60 (12.16)	[-61.00, 55.00]
Cycle 17	Pembrolizumab	300	72.69 (12.56)	[42.00, 120.00]	72.93 (12.20)	[45.00, 129.00]	0.24 (12.27)	[-60.00, 37.00]
	Placebo	345	72.85 (11.62)	[40.00, 115.00]	72.45 (11.70)	[43.00, 128.00]	-0.40 (12.19)	[-55.00, 58.00]
Follow-up	Pembrolizumab	15	66.53 (12.75)	[47.00, 96.00]	68.80 (10.83)	[57.00, 85.00]	2.27 (13.97)	[-37.00, 24.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	13	76.62 (14.80)	[55.00, 101.00]	74.62 (14.19)	[49.00, 95.00]	-2.00 (14.57)	[-42.00, 15.00]
Follow-up Day 30	Pembrolizumab	249	72.52 (12.89)	[42.00, 109.00]	74.27 (12.85)	[46.00, 129.00]	1.74 (13.60)	[-35.00, 75.00]
	Placebo	274	72.57 (11.49)	[40.00, 107.00]	73.14 (12.17)	[41.00, 121.00]	0.57 (12.51)	[-38.00, 37.00]
Crossover Screening Visit	Pembrolizumab	6	68.50 (8.24)	[60.00, 82.00]	75.33 (13.81)	[59.00, 98.00]	6.83 (16.46)	[-11.00, 36.00]
	Placebo	53	72.89 (14.23)	[50.00, 115.00]	73.04 (11.85)	[50.00, 120.00]	0.15 (11.56)	[-38.00, 30.00]
Crossover Cycle 1	Pembrolizumab	1	65.00 ()	[65.00, 65.00]	82.00 ()	[82.00, 82.00]	17.00 ()	[17.00, 17.00]
	Placebo	2	69.00 (5.66)	[65.00, 73.00]	64.00 (8.49)	[58.00, 70.00]	-5.00 (2.83)	[-7.00, -3.00]
Crossover Cycle 16	Placebo	1	70.00 ()	[70.00, 70.00]	66.00 ()	[66.00, 66.00]	-4.00 ()	[-4.00, -4.00]
Discontinuation Visit	Pembrolizumab	204	71.98 (12.43)	[46.00, 120.00]	74.31 (11.30)	[48.00, 113.00]	2.33 (12.70)	[-54.00, 33.00]
	Placebo	179	72.78 (11.98)	[48.00, 115.00]	73.62 (13.39)	[47.00, 126.00]	0.84 (12.97)	[-59.00, 56.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Temperature (C)								
Cycle 2	Pembrolizumab	424	36.41 (0.44)	[35.00, 37.90]	36.37 (0.46)	[34.90, 37.67]	-0.04 (0.39)	[-1.50, 1.20]
	Placebo	442	36.41 (0.44)	[34.60, 37.60]	36.39 (0.42)	[34.60, 37.80]	-0.02 (0.42)	[-1.40, 1.30]
Cycle 3	Pembrolizumab	399	36.40 (0.44)	[35.00, 37.90]	36.38 (0.46)	[34.70, 37.60]	-0.03 (0.42)	[-1.80, 1.00]
	Placebo	436	36.41 (0.44)	[34.60, 37.60]	36.40 (0.43)	[34.50, 37.60]	-0.01 (0.45)	[-1.90, 1.60]
Cycle 4	Pembrolizumab	400	36.39 (0.44)	[35.00, 37.90]	36.35 (0.49)	[34.30, 37.70]	-0.04 (0.43)	[-1.90, 1.10]
	Placebo	430	36.41 (0.45)	[34.60, 37.60]	36.38 (0.40)	[35.00, 37.50]	-0.03 (0.47)	[-1.70, 2.00]
Cycle 5	Pembrolizumab	392	36.39 (0.45)	[35.00, 37.90]	36.35 (0.46)	[34.50, 37.60]	-0.04 (0.45)	[-1.90, 1.60]
	Placebo	427	36.40 (0.44)	[34.60, 37.70]	36.36 (0.43)	[34.80, 37.40]	-0.04 (0.46)	[-2.20, 2.00]
Cycle 6	Pembrolizumab	380	36.39 (0.45)	[35.00, 37.90]	36.32 (0.48)	[34.10, 37.70]	-0.07 (0.48)	[-2.80, 1.50]
	Placebo	422	36.40 (0.44)	[34.60, 37.70]	36.38 (0.45)	[34.90, 37.40]	-0.02 (0.45)	[-1.40, 2.00]
Cycle 7	Pembrolizumab	366	36.38 (0.44)	[35.00, 37.40]	36.32 (0.49)	[34.00, 37.70]	-0.06 (0.50)	[-2.50, 1.60]
	Placebo	417	36.41 (0.45)	[34.60, 37.70]	36.37 (0.44)	[34.50, 37.80]	-0.04 (0.45)	[-1.80, 1.90]
Cycle 8	Pembrolizumab	355	36.38 (0.44)	[35.00, 37.90]	36.33 (0.47)	[34.00, 37.40]	-0.05 (0.46)	[-1.90, 1.20]
	Placebo	408	36.40 (0.45)	[34.60, 37.50]	36.40 (0.40)	[34.70, 37.50]	-0.00 (0.44)	[-1.70, 1.80]
Cycle 9	Pembrolizumab	339	36.39 (0.44)	[35.00, 37.90]	36.33 (0.47)	[34.60, 37.50]	-0.06 (0.45)	[-1.90, 1.20]
	Placebo	408	36.40 (0.45)	[34.60, 37.50]	36.38 (0.44)	[34.50, 37.70]	-0.02 (0.47)	[-1.60, 1.80]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	337	36.37 (0.45)	[35.00, 37.90]	36.34 (0.48)	[34.50, 37.80]	-0.03 (0.44)	[-2.00, 1.30]
	Placebo	392	36.39 (0.45)	[34.60, 37.50]	36.37 (0.41)	[35.00, 37.40]	-0.02 (0.44)	[-1.60, 1.70]
Cycle 11	Pembrolizumab	326	36.37 (0.45)	[35.00, 37.40]	36.31 (0.46)	[34.90, 37.39]	-0.06 (0.44)	[-1.90, 1.00]
	Placebo	383	36.40 (0.45)	[34.60, 37.50]	36.38 (0.41)	[34.60, 37.50]	-0.02 (0.45)	[-1.40, 1.80]
Cycle 12	Pembrolizumab	318	36.38 (0.44)	[35.00, 37.40]	36.33 (0.49)	[34.30, 37.61]	-0.05 (0.47)	[-1.70, 1.40]
	Placebo	379	36.40 (0.44)	[34.60, 37.50]	36.38 (0.43)	[34.80, 37.60]	-0.02 (0.47)	[-1.40, 1.70]
Cycle 13	Pembrolizumab	315	36.37 (0.45)	[35.00, 37.40]	36.31 (0.48)	[34.70, 38.30]	-0.06 (0.46)	[-1.70, 2.30]
	Placebo	381	36.40 (0.44)	[34.60, 37.50]	36.37 (0.43)	[34.50, 37.60]	-0.03 (0.46)	[-1.50, 1.80]
Cycle 14	Pembrolizumab	309	36.36 (0.45)	[35.00, 37.40]	36.32 (0.49)	[34.60, 37.60]	-0.05 (0.46)	[-1.60, 1.30]
	Placebo	367	36.40 (0.45)	[34.60, 37.50]	36.35 (0.43)	[34.30, 37.70]	-0.05 (0.46)	[-1.70, 1.90]
Cycle 15	Pembrolizumab	304	36.36 (0.44)	[35.00, 37.40]	36.31 (0.52)	[34.00, 37.50]	-0.06 (0.49)	[-2.20, 1.20]
	Placebo	362	36.40 (0.44)	[34.60, 37.50]	36.33 (0.46)	[34.70, 37.50]	-0.07 (0.48)	[-1.60, 1.70]
Cycle 16	Pembrolizumab	299	36.36 (0.45)	[35.00, 37.40]	36.34 (0.48)	[34.60, 37.22]	-0.03 (0.48)	[-1.90, 1.20]
	Placebo	354	36.40 (0.44)	[34.60, 37.50]	36.37 (0.43)	[35.00, 38.00]	-0.03 (0.47)	[-1.60, 1.80]
Cycle 17	Pembrolizumab	298	36.37 (0.45)	[35.00, 37.40]	36.30 (0.47)	[34.30, 37.40]	-0.06 (0.47)	[-1.90, 1.20]
	Placebo	343	36.40 (0.43)	[35.00, 37.50]	36.31 (0.41)	[34.30, 37.50]	-0.08 (0.46)	[-1.40, 1.20]
Follow-up	Pembrolizumab	15	36.50 (0.37)	[35.80, 37.00]	36.47 (0.29)	[36.10, 37.00]	-0.03 (0.40)	[-0.60, 0.80]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	11	36.30 (0.49)	[35.60, 37.40]	36.53 (0.50)	[35.70, 37.44]	0.23 (0.50)	[-0.50, 1.33]
Follow-up Day 30	Pembrolizumab	249	36.44 (0.43)	[35.00, 37.40]	36.40 (0.45)	[34.40, 37.40]	-0.03 (0.47)	[-1.90, 1.50]
	Placebo	274	36.43 (0.42)	[35.10, 37.70]	36.38 (0.44)	[34.90, 37.70]	-0.05 (0.46)	[-1.80, 1.60]
Crossover Screening Visit	Pembrolizumab	6	36.49 (0.32)	[36.00, 36.90]	36.18 (0.53)	[35.20, 36.70]	-0.31 (0.70)	[-1.70, 0.10]
	Placebo	52	36.37 (0.43)	[35.00, 37.60]	36.34 (0.39)	[35.00, 37.20]	-0.02 (0.44)	[-1.40, 1.00]
Crossover Cycle 1	Pembrolizumab	1	36.40 ()	[36.40, 36.40]	36.40 ()	[36.40, 36.40]	0.00 ()	[0.00, 0.00]
	Placebo	2	36.85 (0.21)	[36.70, 37.00]	36.35 (0.21)	[36.20, 36.50]	-0.50 (0.42)	[-0.80, -0.20]
Crossover Cycle 16	Placebo	1	36.90 ()	[36.90, 36.90]	36.20 ()	[36.20, 36.20]	-0.70 ()	[-0.70, -0.70]
Discontinuation Visit	Pembrolizumab	201	36.41 (0.47)	[35.10, 37.90]	36.36 (0.51)	[33.60, 37.50]	-0.04 (0.50)	[-2.90, 1.10]
	Placebo	177	36.40 (0.49)	[35.00, 37.70]	36.33 (0.53)	[34.00, 37.80]	-0.06 (0.49)	[-1.30, 1.50]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Respiratory Rate (breaths/min)								
Cycle 2	Pembrolizumab	410	16.40 (2.09)	[10.00, 26.00]	16.50 (2.18)	[11.00, 26.00]	0.10 (1.92)	[-11.00, 9.00]
	Placebo	431	16.15 (2.09)	[8.00, 24.00]	16.10 (2.15)	[11.00, 25.00]	-0.04 (1.85)	[-6.00, 9.00]
Cycle 3	Pembrolizumab	389	16.42 (2.13)	[10.00, 26.00]	16.28 (2.07)	[10.00, 24.00]	-0.13 (2.14)	[-14.00, 9.00]
	Placebo	422	16.15 (2.09)	[8.00, 24.00]	16.28 (2.14)	[11.00, 24.00]	0.13 (1.77)	[-6.00, 8.00]
Cycle 4	Pembrolizumab	389	16.42 (2.14)	[10.00, 26.00]	16.28 (2.03)	[10.00, 24.00]	-0.14 (1.96)	[-12.00, 6.00]
	Placebo	417	16.12 (2.12)	[8.00, 24.00]	16.14 (2.20)	[11.00, 24.00]	0.03 (2.09)	[-10.00, 12.00]
Cycle 5	Pembrolizumab	379	16.37 (2.10)	[10.00, 26.00]	16.29 (2.14)	[9.00, 27.00]	-0.09 (2.14)	[-7.00, 8.00]
	Placebo	417	16.13 (2.12)	[8.00, 24.00]	16.23 (2.17)	[10.00, 24.00]	0.10 (1.87)	[-8.00, 8.00]
Cycle 6	Pembrolizumab	370	16.37 (2.12)	[10.00, 26.00]	16.44 (2.19)	[10.00, 24.00]	0.07 (2.05)	[-9.00, 6.00]
	Placebo	410	16.16 (2.12)	[8.00, 24.00]	16.16 (2.28)	[11.00, 28.00]	0.00 (2.18)	[-8.00, 12.00]
Cycle 7	Pembrolizumab	359	16.38 (2.15)	[10.00, 26.00]	16.28 (2.07)	[11.00, 24.00]	-0.11 (2.04)	[-11.00, 6.00]
	Placebo	404	16.15 (2.11)	[8.00, 24.00]	16.21 (2.15)	[10.00, 22.00]	0.06 (1.91)	[-8.00, 8.00]
Cycle 8	Pembrolizumab	341	16.33 (2.11)	[10.00, 26.00]	16.30 (2.06)	[11.00, 23.00]	-0.03 (1.98)	[-14.00, 6.00]
	Placebo	395	16.13 (2.13)	[8.00, 24.00]	16.19 (2.17)	[10.00, 22.00]	0.06 (1.92)	[-8.00, 8.00]
Cycle 9	Pembrolizumab	330	16.36 (2.16)	[10.00, 26.00]	16.25 (2.16)	[10.00, 24.00]	-0.11 (2.21)	[-12.00, 8.00]
	Placebo	393	16.17 (2.13)	[8.00, 24.00]	16.28 (2.08)	[11.00, 22.00]	0.11 (1.91)	[-8.00, 6.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

			Baseline		Value		Mean Change	
Visit	Treatment	N	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	329	16.43 (2.16)	[10.00, 26.00]	16.39 (2.12)	[10.00, 24.00]	-0.04 (2.25)	[-10.00, 10.00]
	Placebo	379	16.08 (2.15)	[8.00, 24.00]	16.19 (2.09)	[10.00, 25.00]	0.12 (1.95)	[-9.00, 7.00]
Cycle 11	Pembrolizumab	316	16.42 (2.17)	[10.00, 26.00]	16.26 (2.08)	[11.00, 24.00]	-0.16 (2.28)	[-13.00, 8.00]
	Placebo	374	16.07 (2.12)	[8.00, 24.00]	16.23 (2.25)	[10.00, 24.00]	0.16 (2.04)	[-8.00, 8.00]
Cycle 12	Pembrolizumab	311	16.38 (2.11)	[10.00, 26.00]	16.18 (2.04)	[11.00, 24.00]	-0.20 (2.21)	[-14.00, 6.00]
	Placebo	368	16.09 (2.10)	[8.00, 22.00]	16.35 (2.23)	[10.00, 24.00]	0.26 (2.06)	[-6.00, 10.00]
Cycle 13	Pembrolizumab	306	16.39 (2.14)	[10.00, 26.00]	16.32 (2.02)	[10.00, 24.00]	-0.07 (2.08)	[-14.00, 6.00]
	Placebo	372	16.08 (2.09)	[8.00, 22.00]	16.27 (2.19)	[11.00, 24.00]	0.19 (1.99)	[-6.00, 7.00]
Cycle 14	Pembrolizumab	297	16.40 (2.14)	[10.00, 26.00]	16.47 (2.07)	[10.00, 24.00]	0.06 (2.01)	[-12.00, 6.00]
	Placebo	359	16.06 (2.08)	[8.00, 22.00]	16.17 (2.17)	[11.00, 24.00]	0.10 (1.99)	[-6.00, 8.00]
Cycle 15	Pembrolizumab	295	16.44 (2.19)	[10.00, 26.00]	16.28 (1.99)	[10.00, 24.00]	-0.16 (2.03)	[-10.00, 6.00]
	Placebo	352	16.05 (2.08)	[8.00, 22.00]	16.03 (2.11)	[10.00, 21.00]	-0.02 (2.11)	[-8.00, 7.00]
Cycle 16	Pembrolizumab	291	16.45 (2.19)	[10.00, 26.00]	16.17 (1.97)	[10.00, 22.00]	-0.28 (2.18)	[-12.00, 6.00]
	Placebo	343	16.04 (2.10)	[8.00, 22.00]	16.17 (2.16)	[11.00, 24.00]	0.12 (1.95)	[-7.00, 6.00]
Cycle 17	Pembrolizumab	287	16.42 (2.15)	[10.00, 26.00]	16.35 (2.13)	[9.00, 28.00]	-0.07 (2.15)	[-10.00, 9.00]
	Placebo	335	16.09 (2.06)	[10.00, 22.00]	16.21 (2.10)	[12.00, 24.00]	0.11 (1.86)	[-7.00, 6.00]
Follow-up	Pembrolizumab	13	16.15 (1.86)	[14.00, 20.00]	16.08 (1.66)	[13.00, 19.00]	-0.08 (1.85)	[-4.00, 4.00]

Mean Change (SD) in Vital Sign Measurements from Baseline over Time (APaT Population)

Visit	Treatment	N	Baseline		Value		Mean Change	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	14	16.93 (2.23)	[12.00, 20.00]	16.71 (1.77)	[13.00, 20.00]	-0.21 (1.85)	[-4.00, 2.00]
Follow-up Day 30	Pembrolizumab	240	16.50 (1.93)	[12.00, 26.00]	16.33 (2.04)	[12.00, 24.00]	-0.17 (2.16)	[-13.00, 9.00]
	Placebo	265	16.08 (2.04)	[10.00, 22.00]	16.08 (2.06)	[10.00, 22.00]	0.00 (1.73)	[-6.00, 6.00]
Crossover Screening Visit	Pembrolizumab	6	17.83 (2.04)	[15.00, 20.00]	16.83 (1.33)	[15.00, 18.00]	-1.00 (1.67)	[-4.00, 0.00]
	Placebo	52	16.10 (2.31)	[8.00, 21.00]	16.17 (2.51)	[11.00, 24.00]	0.08 (2.71)	[-7.00, 10.00]
Crossover Cycle 1	Pembrolizumab	1	18.00 ()	[18.00, 18.00]	17.00 ()	[17.00, 17.00]	-1.00 ()	[-1.00, -1.00]
	Placebo	2	17.50 (0.71)	[17.00, 18.00]	17.50 (2.12)	[16.00, 19.00]	0.00 (1.41)	[-1.00, 1.00]
Crossover Cycle 16	Placebo	1	21.00 ()	[21.00, 21.00]	18.00 ()	[18.00, 18.00]	-3.00 ()	[-3.00, -3.00]
Discontinuation Visit	Pembrolizumab	197	16.21 (2.21)	[10.00, 24.00]	16.27 (2.24)	[8.00, 26.00]	0.06 (2.18)	[-9.00, 8.00]
	Placebo	167	16.32 (2.21)	[8.00, 24.00]	16.44 (2.26)	[12.00, 25.00]	0.11 (2.25)	[-9.00, 8.00]

Baseline is defined as last value obtained prior to the first dose of study treatment during treatment phase. A baseline and Treatment Value are required for a subject to be counted at a time point.

SD = Standard deviation, Min = Minimum, Max = Maximum.

Database Cutoff Date: 04JAN2023

Source: [P716V04MK3475: adam-advs]

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16 LIST OF APPENDICES

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16.1.1.1 Protocol

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16.1.6 Clinical Supplies Dispensed to Participants

16.1.6.1 Listing of Participants by Bulk Product and Manufacturing Lot Number Dispensed

16.1.7 Participant Intervention Assignment

16.1.8 Audit Information

16.1.9 Documentation of Statistical Methods

16.1.9.1 Supplemental Statistical Analysis Plan

16.1.10 Documentation of Interlaboratory Standardization Methods and Quality Assurance Procedures, if Used

16.1.11 Publications Based on the Study