1 TITLE PAGE

CLINICAL STUDY REPORT

Sponsor Name	Merck Sharp & Dohme Corp., a Subsidiary of Merck & Co., Inc., NJ, USA (MSD)
Compound Name	Pembrolizumab (MK-3475)
Protocol Title	Adjuvant immunotherapy with anti-PD-1 monoclonal antibody Pembrolizumab (MK-3475) versus placebo after complete resection of high-risk Stage III melanoma: A randomized, double-blind Phase 3 trial of the EORTC Melanoma Group
CSR Identification	P054V02MK3475
Indication	Adjuvant treatment of melanoma patients with lymph node involvement who have undergone complete resection
Study Design	Multicenter, efficacy, safety, randomized, double-blind, placebo-controlled
Phase	3
Study Initiation Date	22-JUN-2015
Study Completion Date	ongoing, data cut-off 03-APR-2020
Report Date	17-NOV-2020
Revised Report Date	03-DEC-2020
Previous CSR Identification	P054V01MK3475
GCP Compliance	This study was conducted in conformance with applicable country or local requirements regarding ethical committee review, informed consent, and other statutes or regulations regarding the protection of the rights and welfare 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 Corp., a Subsidiary of Merck & Co., Inc., NJ, USA (MSD)

COMPOUND NAME: Pembrolizumab

PROTOCOL TITLE: Adjuvant immunotherapy with anti-PD-1 monoclonal antibody Pembrolizumab (MK-3475) versus placebo after complete resection of high-risk Stage III melanoma: A randomized, double-blind Phase 3 trial of the EORTC Melanoma Group.

STUDY IDENTIFIERS:

IND: 110080	EudraCT: 2014-004944-37	NCT: NCT02362594	Protocol number: EORTC v7.0/ MK-3475-054-03

STUDY PHASE: 3

INDICATION: Adjuvant treatment of melanoma patients with lymph node involvement who have undergone complete resection.

STUDY CENTERS: This study was conducted at 134 centers in 23 countries.

STUDY STATUS: This study is ongoing; this report is based on the 03-APR-2020 interim analysis.

First Patient, First Visit	Last Patient, Last Visit	Data Cutoff
22-JUN-2015	03-APR-2020	03-APR-2020

NOTE: Patient = Participant

METHODOLOGY: All or part of this study was conducted during the COVID-19 pandemic. The Sponsor continued to follow its SOPs for study conduct, monitoring, and oversight during the pandemic and employed a risk-based approach to assess and mitigate impact on study conduct.
This is a multicenter, double-blinded, placebo-controlled randomized Phase 3 study of pembrolizumab adjuvant treatment in participants with Stage III melanoma following complete resection. Eligible participants were randomized into 2 equal-sized treatment groups to receive pembrolizumab or placebo. Participants were stratified by stage (IIIA [>1 mm lymph node metastasis] versus IIIB versus IIIC [1 to 3 positive lymph nodes] versus IIIC [≥4 positive lymph nodes]). The study consisted of 2 parts:
Part1: adjuvant therapy with pembrolizumab or placebo administered every 3 weeks for a total of 18 administrations (~ 1 year) or until disease recurrence or unacceptable toxicity.
Part 2: crossover or rechallenge with pembrolizumab administered every 3 weeks for up to 1 year (local recurrence) or 2 years or until disease progression.

Drug	Dose	Dose Frequency	Route of Administration	Regimen/Treatment Period	Use
Pembrolizumab	200 mg	Q3W	IV infusion	Part 1: Day 1 of each 3-week cycle for a total of 18 administrations (~1 year) Part 2: Day 1 of each 3-week cycle for up to 2 years	Experimental
Placebo	0 mg	Q3W	IV infusion	Part 1: Day 1 of each 3-week cycle for a total of 18 administrations (~1 year)	Control

IV=Intravenous; Q3W=Every 3 weeks

ELIGIBILITY CRITERIA: Male and female participants, ≥18 years of age, with Stage III melanoma after complete surgical resection were eligible.

OBJECTIVES AND ENDPOINTS:

Primary Objective(s)	Primary Endpoint(s)
• To prospectively assess whether postoperative adjuvant therapy with pembrolizumab improves recurrence-free survival (RFS), as compared to placebo in high-risk participants with complete resection of Stage IIIA (>1 mm metastasis), IIIB, and IIIC melanoma.	• RFS, defined as the time between the date of randomization and the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause).
• To prospectively assess whether in the subgroup of patients with PD-L1-positive tumor expression pembrolizumab improves RFS as compared to placebo.	• RFS in subgroup of participants with PD-L1-positive tumor expression receiving either pembrolizumab or placebo.
Secondary Objective(s)	**Secondary Endpoint(s)**
• To prospectively assess whether postoperative adjuvant therapy with pembrolizumab improves distant metastasis-free survival (DMFS) as compared to placebo.	• DMFS, defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause).

• To prospectively assess whether in the subgroup of participants with PD-L1-positive tumors expression pembrolizumab improves DMFS as compared to placebo.	• DMFS in subgroup of participants with PD-L1-positive tumor expression receiving either pembrolizumab or placebo.
• To prospectively assess whether postoperative adjuvant therapy with pembrolizumab improves overall survival (OS), as compared to placebo.	• OS, defined as the time from the date of randomization to the date of death, whatever the cause.
• To prospectively assess whether in the subgroup of subjects with PD-L1-positive tumor expression pembrolizumab improves OS as compared to placebo.	• OS in subgroup of subjects with PD-L1-positive tumor expression receiving either pembrolizumab or placebo.
• To compare adverse event (AE) and serious adverse event (SAE) profiles between participants receiving pembrolizumab versus participants in the placebo arm.	• Toxicity profile according to Common Terminology Criteria for Adverse Events v. 4.0.
• To evaluate the pharmacokinetics (PK) of pembrolizumab when pembrolizumab is administered at 200 mg every 3 weeks.	• To evaluate the PK of pembrolizumab when pembrolizumab is administered 200 mg every 3 weeks. • To assess for development of antidrug antibodies.

NUMBER OF PARTICIPANTS (planned and analyzed): A total of approximately 900 participants was planned to be randomized (approximately 450 subjects in each treatment group). As of the data cutoff date for this report, 1019 participants were randomized (514 in the pembrolizumab group, 505 in the placebo group).

STATISTICAL METHODS: A sequential approach was planned to investigate whether pembrolizumab is superior to placebo with respect to RFS, DMFS, or OS in the overall study population and in participants with PD-L1-positive tumors. Both hypotheses must be rejected to proceed to the next endpoint. The main analyses of the efficacy endpoints (RFS, DMFS) were performed on the intent-to-treat (ITT) population using the ITT principle: participants were considered in the treatment group indicated at randomization regardless of treatment duration. The Kaplan-Meier technique was used to obtain estimates of the survival-type distributions (RFS, DMFS), and the standard error of the estimates was computed using the Greenwood formula.

One interim analysis was planned for assessing whether pembrolizumab is superior to placebo with respect to the improvement of RFS in the overall population. The stopping boundaries for the interim analysis were based on the O'Brian-Fleming spending function.

Because evidence of superiority was present for pembrolizumab over placebo at that planned interim analysis, the results were considered the final RFS analysis with 351 RFS events.

The primary focus of this report is the analysis after 418 DMFS events considered final. A descriptive extended RFS analysis after 491 events is also presented. The OS analysis will be performed after reaching 380 deaths.

RESULTS:

No changes in the planned analyses of the study, and effects on participant status or efficacy and safety results were reported due to the COVID-19 pandemic. No COVID-19 related AEs were reported.

Disposition, Demographics and Baseline Characteristics:

Number of participants randomized/treated/ongoing/discontinued:

- Pembrolizumab group, 514 participants were randomized, 509 were treated, 57.8% completed study intervention, and 42.2% discontinued study intervention. A total of 19 participants were rechallenged with pembrolizumab in Part 2 of the study. A total of 97.5% are continuing in the study.
- Placebo group, 505 participants were randomized, 502 were treated, 59.4% completed study intervention, and 40.6% discontinued study intervention. A total of 151 participants crossed over to Part 2 and were treated with pembrolizumab. A total of 72.5% are continuing in the study.

Overall Median Age (range): 54.0 years (19 to 88 years)

Sex: 628 (61.6%) male, 391 (38.4%) female

Ethnicity: Not Collected

Race: Not Collected

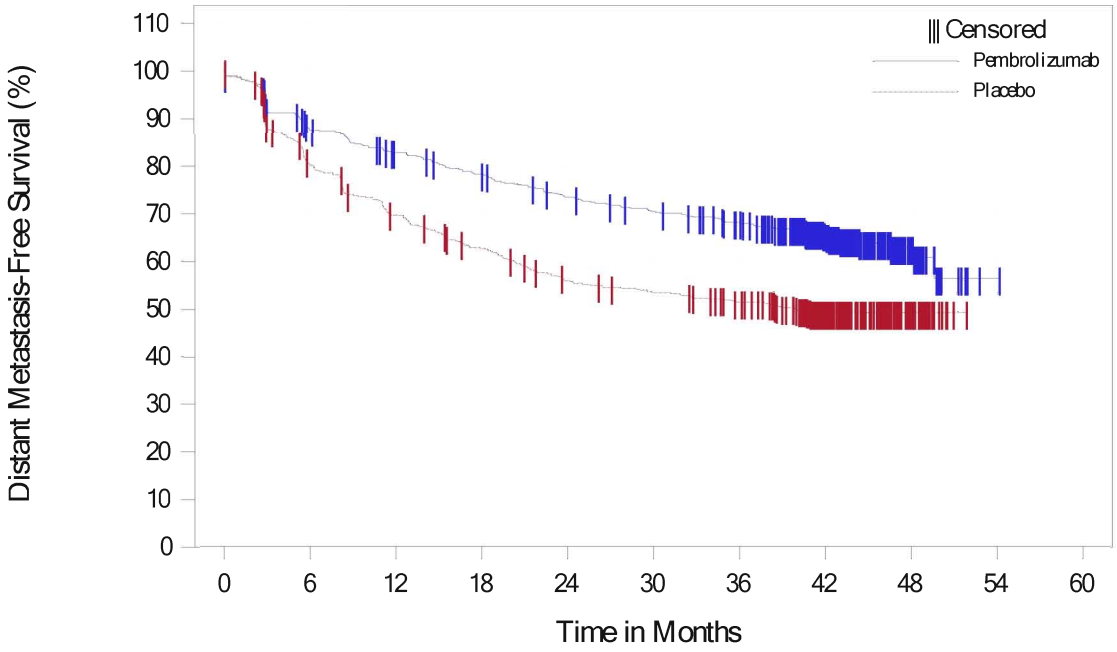
Efficacy:

- Pembrolizumab provided a statistically significant, and clinically meaningful improvement in DMFS with 45.5 months of median follow-up in the ITT population when compared with placebo. The HR was 0.60 (95% CI: 0.49, 0.73; $p<0.0001$) in favor of pembrolizumab, with a 40% reduction in the risk of distant metastases or death.
- As of the DCO, the median DMFS was not reached in the pembrolizumab group compared with 40.0 months in the placebo group for the ITT population.
- In participants with PD-L1-positive tumors, pembrolizumab provided significant and clinically meaningful improvement in DMFS with 45.5 months of median follow-up compared with placebo (HR=0.61; 95% CI: 0.49, 0.76; $p<0.0001$), with a 39% reduction in the risk of distant metastases or death in participants with PD-L1-positive tumors. The median DMFS was not yet reached in both the pembrolizumab and placebo groups.

- DMFS benefit of pembrolizumab compared with placebo that was similar to that of the ITT population was observed across all subgroups regardless of cancer stage and BRAF-mutation status.
- Pembrolizumab provided sustained RFS benefit with 45.5 months of median follow-up when compared with placebo. The HR was 0.59 (95% CI: 0.49, 0.70) in favor of pembrolizumab, with a 41% reduction in the risk of recurrence or death.

DMFS:

Kaplan-Meier Estimates of Distant Metastasis-Free Survival
ITT Population



n at risk

Pembrolizumab	514	434	404	378	352	334	314	174	32	1	0
Placebo	505	395	339	301	265	251	235	136	31	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Safety:

AE Summary for Part 1:

Adverse Event Summary
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse event	29	(5.7)	48	(9.6)	77	(7.6)
with drug-related† adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with toxicity grade 3-5 adverse events	162	(31.8)	96	(19.1)	258	(25.5)
with toxicity grade 3-5 drug-related adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with serious adverse events	127	(25.0)	83	(16.5)	210	(20.8)
with serious drug-related adverse events	62	(12.2)	6	(1.2)	68	(6.7)
who died	1	(0.2)	0	(0.0)	1	(0.1)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	71	(13.9)	18	(3.6)	89	(8.8)
discontinued drug due to a drug-related adverse event	62	(12.2)	8	(1.6)	70	(6.9)
discontinued drug due to a serious adverse event	29	(5.7)	11	(2.2)	40	(4.0)
discontinued drug due to a serious drug-related adverse event	22	(4.3)	2	(0.4)	24	(2.4)

† Determined by the investigator to be related to the drug.

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

AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

AE Summary for Part 2:

Adverse Event Summary
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	149	(87.6)
with no adverse event	21	(12.4)
with drug-related† adverse events	117	(68.8)
with toxicity grade 3-5 adverse events	46	(27.1)
with toxicity grade 3-5 drug-related adverse events	18	(10.6)
with serious adverse events	29	(17.1)
with serious drug-related adverse events	9	(5.3)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued drug due to an adverse event	19	(11.2)
discontinued drug due to a drug-related adverse event	13	(7.6)
discontinued drug due to a serious adverse event	6	(3.5)
discontinued drug due to a serious drug-related adverse event	3	(1.8)

† Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 2; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 2.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

CONCLUSIONS:

Efficacy Conclusions

- Adjuvant therapy with pembrolizumab provides a therapeutic benefit to patients with resected Stage III melanoma, who were at high risk of recurrence, as demonstrated by a statistically significant and clinical meaningful benefit in DMFS and sustained RFS benefit compared with placebo. Similar DMFS benefit and sustained RFS benefit compared with placebo was observed across all subgroups including tumor stage and BRAF-mutation status.
- The therapeutic benefit is similar for the PD-L1-positive population, demonstrated by a statistically significant and clinical meaningful DMFS benefit and sustained RFS benefit compared with placebo.

Safety Conclusions

- The safety results of this report are generally consistent with the final RFS analysis (DCO 02-OCT-2017).
- Pembrolizumab administered in the adjuvant setting for resected, Stage III melanoma continues to demonstrate a consistent and well-tolerated established safety profile.

- Safety profile in the participants that were rechallenged and crossed over in the Part 2 of the study was consistent with the established safety profile of pembrolizumab.
- The AEOSIs were similar to the established pembrolizumab safety profile and were generally manageable with dose interruption, discontinuation and/or treatment with corticosteroids.
- There were no new safety concerns for pembrolizumab in this updated analysis (or study report) of KEYNOTE-054.

PUBLICATION(S):

- Eggermont A, Blank C, Mandala M, et al. Adjuvant pembrolizumab versus placebo in resected Stage III melanoma. N Engl J Med. 2018;378: 1789-801.
- Eggermont A, Blank C, Mandala M, et al. Prognostic and predictive value of AJCC-8 staging in the Phase III EORTC1325/KEYNOTE-054 trial of pembrolizumab vs placebo in resected high-risk Stage III melanoma. Eur. J. Cancer. 2019;116: 148-157.
- Eggermont A, Kicinski M, Blank C, et al. Association between immune-related adverse events and recurrence-free survival among patients with Stage III melanoma randomized to receive pembrolizumab or placebo. A secondary analysis of a randomized clinical trial. JAMA Oncol. 2020;6(4): 519-527. January 2, 2020. DOI:10.1001/jamaoncol.2019.5570
- Eggermont A, Blank C, Mandala M, et al. Longer follow-up confirms recurrence-free survival benefit of adjuvant pembrolizumab in high-risk Stage III melanoma: Updated results from the EORTC 1325-MG/KEYNOTE-054 trial. J.Clin.Oncol. September 24, 2020. DOI:10.1200/JCO.20.02110
- Eggermont A, Blank C, Mandala M, et al. LBA46 pembrolizumab versus placebo after complete resection of high-risk Stage III melanoma: Final results regarding distant metastasis-free survival from the EORTC 1325-MG/Keynote 054 double-blinded Phase III trial. Abstract presented at: ESMO Virtual Congress 2020; September 19, 2020. Abstract LBA46.

REPORT DATE: 17-NOV-2020

REVISED REPORT DATE: 03-DEC-2020

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3.2 List of Figures

4 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

This list serves as the first appearance in text.

The following terms may be used interchangeably within the document:

- Participant and subject
- Study and trial
- Intervention, treatment, medication, and vaccine
- Sex and gender

Abbreviation/Term	Definition
ADA	Antidrug antibodies
AE	Adverse event
AEOSI	Adverse event of special interest
AJCC	American Joint Committee on Cancer
ALT	Alanine aminotransferase
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
ASaT	All subjects as treated
AST	Aspartate aminotransferase
AUC	Area under the concentration-time curve
BICR	Blinded independent central review
BMI	Body mass index
BP	Blood pressure
CFR	Code of Federal Regulations
CI	Confidence interval
CLND	Complete lymph node dissection
C_{max}	Maximum concentration
COVID-19	Coronavirus disease caused by severe acute respiratory syndrome coronavirus 2
CRF	Case report form
CSR	Clinical Study Report
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CTLA-4	Cytotoxic T lymphocyte-associated antigen-4
CV	Coefficient of variation

Abbreviation/Term	Definition
DCO	Data cutoff
DILI	Drug-induced liver injury
DMC	Data Monitoring Committee
DMFS	Distant metastasis-free survival
DRESS	Drug reaction with eosinophilia and systemic symptoms
EC	Ethics Committee
ECG	Electrocardiograms
ECI	Event of clinical interest
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
eDMC	External Data Monitoring Committee
EMA	European Medicines Agency
EORTC	European Organisation for Research and Treatment of Cancer
EQ-5D	EuroQol-5D
ERC	Ethics Review Committee
ESMO	European Society for Medical Oncology
EU	European Union
FDA	Food and Drug Administration
FPE	First participant enrolled
GCP	Good Clinical Practice
GI	Gastrointestinal
GMR	Geometric mean ratio
GPV	Global Pharmacovigilance
GPvP	Good Pharmacovigilance Practice
HA	Health Authority
HBsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
HR	Heart rate
HRQoL	Health-Related Quality of Life
ICF	Informed consent form
ICH	International Council for Harmonization (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IEC	Independent Ethics Committee
IFN-α	Interferon-alpha
IM	Intramuscular
IND	Investigational New Drug
INR	International Normalization Rate

Abbreviation/Term	Definition
IRB	Institutional Review Board
ITT	Intent-to-treat
IV	Intravenous
IVRS	Interactive Voice Response System
K-M	Kaplan-Meier
LFT	Liver function test
LN	Lymph node
LPLV	Last participant last visit
MED	Minimal effective dose
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
MRL	Merck Research Laboratories
MRP	Medical review plan
MSD	Merck Sharp & Dohme Corp., a Subsidiary of Merck & Co., Inc.
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NSAID	Nonsteroidal anti-inflammatory drug
NSCLC	Non-small cell lung carcinoma
OS	Overall survival
PD-1	Programmed cell death 1
PD-L1	Programmed cell death ligand 1
PD-L2	Programmed cell death ligand 2
Peg-IFN	Pegylated interferon-alpha
PET	Positron emission tomography
PFS	Progression-free survival
PIS/IC	Patient information sheet and informed consent
PK	Pharmacokinetic
PR	Partial response
PRFS2	Progression/recurrence-free survival 2
PT	Preferred term
Q3W	Every 3 weeks
QA	Quality Assurance
QC	Quality Control
QCI	Quality and Continuous Improvement
RECIST	Response Evaluation Criteria in Solid Tumors
RFS	Recurrence-free survival

Abbreviation/Term	Definition
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SOC	System organ class
SOP	Standard operating procedure
SPDL-1	Spindle apparatus coiled-coil protein 1
TEAE	Treatment-emergent adverse event
T_{max}	Time of maximum concentration
TTO	Time to onset
ULN	Upper limit of normal
US	United States

5 ETHICS

Part of this study was conducted during the COVID-19 pandemic. Contingency measures implemented to manage study conduct during the pandemic are described in [Sec. 9.8].

5.1 Independent Ethics Committee

The protocol and any amendments, information provided to participants and any recruitment material(s) [16.1.1] were reviewed and approved by the IEC(s) (also referred to as an IRB, ERC, or any other ethics committee) as listed in [16.1.3]. 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 conformance with the ethical principles originating from the Declaration of Helsinki, GCP requirements, and applicable country and/or local statutes and regulations regarding IEC review, informed consent and the protection of human participants in biomedical research, as stated in the MSD Code of Conduct for Interventional Clinical Trials in the study protocol [16.1.1]. The Code of Conduct includes a description of how the study was monitored to ensure compliance with GCP.

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) is available upon request. 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

This study was conducted at 134 centers, of which 124 allocated subjects to treatment. A detailed country listing and the number of centers in each country was provided in [Ref. 5.3.5.1: P054V01MK3475: 6]. A list of investigators, including study center information, is provided in [16.1.3]. Information for the administrative structure of the study (e.g., 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-054 (EORTC1325) is a multicenter, double-blind, placebo-controlled, randomized Phase 3 study evaluating adjuvant therapy with pembrolizumab (KEYTRUDA®; also known as MK-3475 in this document) versus placebo after complete resection of Stage IIIA (>1 mm lymph node metastasis), IIIB, and IIIC melanoma (AJCC seventh edition) [16.1.12.1].

The primary focus of this report is to summarize the DMFS analyses that were triggered by 418 DMFS events. This is the first and final DMFS analysis for KEYNOTE-054 to assess the effect of pembrolizumab as adjuvant therapy in high-risk patients with complete resection of Stage III melanoma. The use of DMFS as an endpoint is in alignment with other oncology clinical trials for adjuvant treatment of completely resected Stage III melanoma, and improvement in this endpoint has been reported previously with significantly prolonged OS as a confirmation of benefits observed in RFS. DMFS was defined as the time between the date of randomization and the date of first distant metastasis or the date of death (from any cause), whichever occurred first [16.1.12.2], [16.1.12.3], [16.1.12.4], [16.1.12.5],[16.1.12.6].

The analysis of 2 key secondary endpoints, as of the DCO of 03-APR-2020, are presented in this report: to investigate whether treatment with pembrolizumab provides an improvement in DMFS in the ITT and in DMFS in subjects with PD-L1-positive tumors.

The final RFS analysis, the primary endpoint of the study, was previously reported to EMA after 351 RFS events, with DCO of 02-OCT-2017 [Ref. 5.3.5.1: P054V01MK3475]. The previous report resulted in the global approval of pembrolizumab as adjuvant therapy for patients with resected Stage III melanoma. A descriptive extended RFS analysis, with data obtained since the final RFS analysis, is presented here with DCO of 03-APR-2020.

Study KEYNOTE-054 is ongoing and will continue to the next endpoint, which is OS.

7.1 Advanced Melanoma Background

Melanoma accounts for less than 2% of skin cancers [16.1.12.7]; however, 90% of cutaneous tumor deaths are associated with melanoma[16.1.12.8]. Patients with Stage III melanoma are at high-risk of relapse. According to the AJCC, relapse rates at 5 years for Stage IIIA, Stage IIIB and Stage IIIC are about 35%, 75% and 90% respectively [16.1.12.1].

The 5-year prevalence of melanoma worldwide is approximately 870,000 patients with an incidence of approximately 232,000 new cases per year and approximately 55,000 deaths annually [16.1.12.9]. The 5-year prevalence of melanoma in the EU is approximately 326,000 patients with an incidence of approximately 83,000 new cases per year and approximately 16,000 deaths annually [16.1.12.10]. In the US melanoma has an incidence of approximately 100,000 new cases per year and approximately 7,000 deaths annually. The male-to-female incidence ratio of melanoma is 1.5:1[16.1.12.11].

Surgery alone is insufficient to achieve a cure in most patients with high-risk Stage III melanoma. Patients with a metastasis of more than 1 mm in the greatest dimension have a significantly higher risk of recurrence or death than those with a metastasis of 1 mm or less in the greatest dimension [16.1.12.6], and patients with distant metastasis have a survival rate of only 5% to 10% and a median survival of 6 to 10 months, depending on the site of the metastasis. Surgery alone does not eradicate micrometastases that may show up in distant regions[16.1.12.12]. Adjuvant systemic therapy targets residual micrometastatic disease with the goal of improving RFS, DMFS, and OS [16.1.12.13], [16.1.12.14]. Improvement in DMFS, mediated by adjuvant therapy, has been reported altogether with improvement of OS [16.1.12.6].

At the time of protocol development, guidelines for adjuvant treatment were varied and included the use of IFN- α for patients with good tolerance. Other adjuvant treatments were only used in the context of clinical trials[16.1.12.15], [16.1.12.16]. The use of placebo as a comparator in KEYNOTE-054 reflected uncertainty surrounding the clinical utility of IFN-α together with a reluctance to expose patients who may be cured by surgery alone to potentially toxic regimens. Additional details are available in the study protocol [16.1.1]. A sample CRF is provided in [16.1.2]. During the conduct of the study, the adjuvant treatment landscape in melanoma changed rapidly; currently approved systemic adjuvant therapies, besides pembrolizumab are IFN-α (US and EU), pegylated IFN-α (US), ipilimumab (US), dabrafenib + trametinib (US and EU), and nivolumab (US and EU) [16.1.12.17], [16.1.12.18], [16.1.12.19], [16.1.12.20], [16.1.12.21].

Part of this study was conducted during the COVID-19 pandemic. 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]. Any effects on participant status, are described in the corresponding sections of [Sec. 10].

The study was conducted by EORTC and sponsored by Merck Sharp & Dohme Corp. (MSD), a Subsidiary of Merck & Co.

8 STUDY OBJECTIVES AND ENDPOINTS

8.1 Primary Endpoints

- To prospectively assess whether postoperative adjuvant therapy with pembrolizumab improved RFS as compared with placebo in high-risk participants with complete resection of Stage IIIA (>1 mm metastasis), IIIB, and IIIC melanoma.

- To prospectively assess whether in the subgroup of participants with PD-L1 positive tumor expression, pembrolizumab improved RFS as compared with placebo.

8.2 Secondary Endpoints

The analyses of the following secondary endpoints are the objective of this report.

- To prospectively assess whether postoperative adjuvant therapy with pembrolizumab improves DMFS as compared with placebo.
- To prospectively assess whether in the subgroup of participants with PD-L1-positive tumor expression pembrolizumab improves DMFS as compared with placebo.
- To compare adverse event profiles (AE and SAE) between participants receiving pembrolizumab versus participants in the placebo group.

8.3 Endpoints Not Analyzed

Other secondary and exploratory endpoints that were not analyzed as part of this report are listed in protocol Section 2 [16.1.1].

9 INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan

KEYNOTE-054 is a multicenter, double-blind, placebo-controlled, randomized Phase 3 study to prospectively evaluate the efficacy and safety of postoperative adjuvant therapy with pembrolizumab in high-risk participants with complete resection of Stage IIIA (>1 mm lymph node metastasis), IIIB, and IIIC melanoma (AJCC seventh edition). Additional details are available in the study protocol [16.1.1].

The planned study enrollment was approximately 900 participants randomized to either pembrolizumab 200 mg IV Q3W or placebo in 2 equally sized, double-blind study intervention groups that were stratified for cancer stage, and geographic region. Enrollment of participants with Stage IIIA melanoma (> 1 mm metastasis) was capped at a maximum of 20% of the total population.

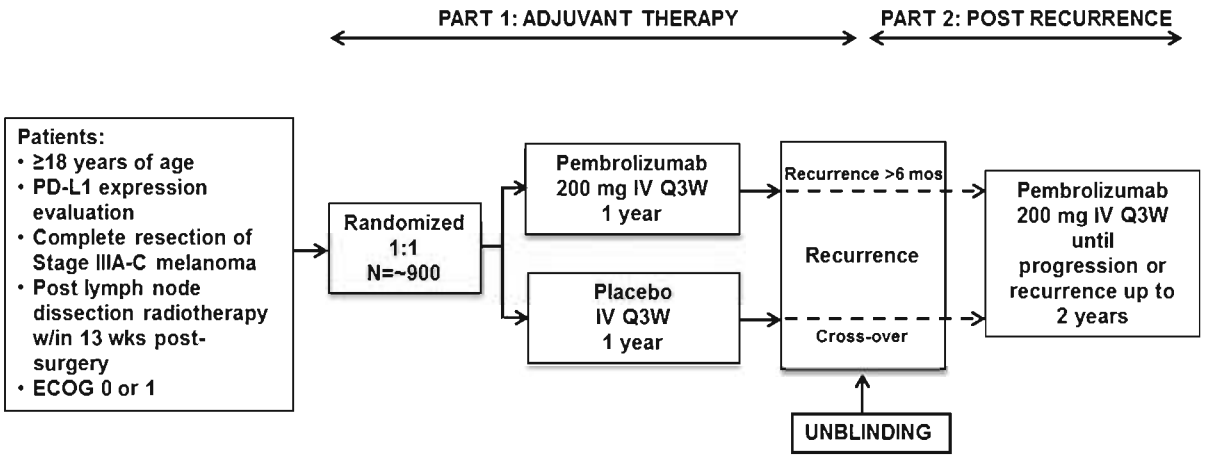
The treatment phase of the study consisted of 2 parts:

- Part 1: Adjuvant Therapy: pembrolizumab or placebo was administered IV Q3W for a total of 18 administrations (~1 year).
- Part 2: Crossover or Rechallenge: pembrolizumab was administered IV Q3W up to 1 year (local recurrence) or 2 years.

Inclusion criteria and further details are presented in [Sec. 9.3] and protocol [16.1.1]. The study design is depicted in [Figure 9-1].

The results of the planned analysis were reviewed by the EORTC IDMC as described in the protocol [16.1.1].

Figure 9-1
Study Design



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

Male and female participants, ≥18 years of age, with Stage III melanoma who met the following key inclusion and none of the exclusion criteria at screening were eligible for study enrollment. Additional clarifications and guidance on participant selection criteria are available in the protocol [16.1.1].

9.3.1 Inclusion Criteria

Key inclusion criteria included the following:

1. Had complete resection of Stage III melanoma (AJCC R0) with histologically confirmed cutaneous melanoma metastatic to lymph node, classified as (AJCC seventh edition cancer stage classification) Stage IIIA with metastasis >1 mm; any Stage IIIB or IIIC. No past or current in-transit metastases or satellitosis.
2. Had tumor sample evaluable for PD-L1 expression.
3. Resection of Stage III lymph nodes must have been performed in complete compliance with the criteria for adequate surgical procedures for CLND outlined in the protocol [16.1.1].
4. Had disease status for the postsurgery baseline assessment documented by full chest/abdomen/pelvis CT and/or MRI with neck CT and/or MRI (for head and neck primaries) and complete clinical examination after the informed consent and prior to enrollment.
5. Post lymph node dissection radiotherapy must have been completed within the 13-week postsurgery period and prior to study intervention start.

6. Had ECOG performance status of 0 or 1.
7. Had interval from surgery to first study intervention ≤13 weeks.
8. Had adequate organ function as defined by laboratory values specified in the protocol [16.1.1]. Screening laboratories should have been performed within 14 days (± 3 days) prior to study intervention initiation.

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

9.3.2 Exclusion Criteria

Key exclusion criteria included the following:

1. Had mucosal or ocular melanoma.
2. Had current disease, including loco-regional relapse, distant metastasis, or clinical evidence for brain metastases.
3. Had prior therapy for melanoma except surgery for primary melanoma lesions; participants who had previously received IFN for thick primary melanomas without evidence of lymph node involvement were eligible.
4. Had a history of another malignancy or a concurrent malignancy. Exceptions included participants who had been disease-free for 5 years, participants with a history of completely resected non-melanoma skin cancer, or participants with successfully treated in situ carcinoma.
5. Had active autoimmune disease that required systemic treatment in past 2 years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs).
6. Had a diagnosis of immunodeficiency, systemic steroid therapy, or any other form of immunosuppressive therapy within 7 days prior to the first dose of study intervention.
7. Received prior treatment with any anti-CTLA4 monoclonal antibody, anti-PD-1, anti-PD-L1, or anti-PD-L2 agent.

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 Intervention(s)

9.4.1 Intervention(s) Administered

The study interventions are presented in [Table 9-1].

Table 9-1
Study Interventions

Drug	Dose	Dose Frequency	Route of Administration	Regimen/Treatment Period	Use
Pembrolizumab	200 mg	Q3W	IV infusion	Part 1: Day 1 of each 3-week cycle for a total of 18 administrations (~1 year) Part 2: Day 1 of each 3-week cycle for up to 2 years	Experimental
Placebo	0 mg	Q3W	IV infusion	Part 1: Day 1 of each 3-week cycle for a total of 18 administrations (~1 year)	Control

IV=Intravenous; Q3W=Every 3 weeks

9.4.2 Identity of Investigational Product(s)

The manufacturing lot numbers for the investigational product(s) dispensed in this study are available in the trial master file or clinical supply database, as applicable [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 study intervention groups, including any stratification factors, if applicable, 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 Dose(s) for Each Participant

The planned dose of pembrolizumab for this study was 200 mg IV Q3W. The procedures for selecting each participant's dose(s) 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 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 Assessment(s)

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) is detailed in the AE reporting section of the study protocol [16.1.1]. The schedule for patient-reported outcome assessments is provided in the protocol [16.1.1]. Patient-reported outcome assessments are provided in a separate report.

9.5.2 Appropriateness of Measurements

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

9.5.3 Efficacy Assessments

Efficacy assessments are described in the study protocol [16.1.1].

9.5.4 Safety Assessments

Safety assessments are described in the study protocol [16.1.1]. MedDRA Version 23.0 was used in the generation of all relevant tables in this document. The MedDRA PTs 'Neoplasm Progression,' 'Malignant neoplasm progression,' and 'Disease progression' not related to the drug were excluded from the statistical safety tables.

9.5.4.1 Adverse Events of Special Interest

AEOSIs 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 AEOSIs (Version 18.0) is presented in [16.2.7.2].

9.5.5 Pharmacokinetic and Pharmacodynamic Measurements

No further assessment of the PK profile for pembrolizumab monotherapy is planned. No pharmacodynamic assessments were planned for this study.

Samples were collected for analysis of ADA at specified time points as described in the protocol [16.1.1].

Immunogenicity data and analysis from this study was reported separately along with historical data to enable interpretation [16.1.12.22].

9.6 Data Quality Assurance

QA and QC oversight activities implemented at the investigation site 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 onsite monitoring inclusive of source data verification, medical monitoring of clinical study data (including monitoring protocol deviations) and relevant reviews of regulatory submission documents. The MSD Code of Conduct for Interventional Clinical Trials (included in the protocol) describes how the study was to be monitored to ensure compliance with GCP [16.1.1]. Additional EORTC Quality Assurance and Control Unit activities are described in the protocol [16.1.1].

The Sponsor held investigator meeting(s) prior to 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.

MRL QA independently assessed quality through a comprehensive, risk-based audit program to ensure adherence with applicable GCP, GPvP regulations and applicable company policies and procedures. Audit information is provided in [16.1.8]. No occurrences of serious GCP compliance issues (including significant quality issues, unblinding events that have impacted data integrity and compliance issues reported to health authorities) were reported [16.1.8.2].

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 SAP [16.1.9] and contained in the protocol [16.1.1].

All results are described per AJCC seventh edition cancer stage classification. Results per AJCC eighth edition cancer stage classification are given.

9.8 Changes in the Conduct of the Study or Planned Analyses

9.8.1 Changes in the Conduct of the Study

Part of this study was conducted during the COVID-19 pandemic. Clinical investigator study sites were in different countries as reported in [16.1.3.1].

All changes in the conduct of the study that were implemented by protocol amendments are described in [16.1.1]. Protocol Amendment 4 was finalized (16-JAN-2020) but was not distributed to the sites in all countries at the time of DCO (03-APR-2020). No protocol amendments were made due to the COVID-19 pandemic.

The Sponsor continued to follow its SOPs for study conduct, monitoring, and oversight during the COVID-19 pandemic. A risk-based approach, consistent with recent Health Authority (FDA, EMA) guidance on conducting clinical studies during the 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. Contingency measures 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 intervention schedule, and to keep participants informed of changes to the study and other study activities. Study sites were asked to escalate any identified or emergent risk to the Sponsor. Contingency measures were constantly assessed.

Measures implemented by the Sponsor to manage key aspects of study conduct during the pandemic are summarized below (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.

Process	Measure
Study site monitoring	• Modifications to the frequency of onsite and remote monitoring were allowed due to national and local travel restrictions and/or study site restrictions to onsite monitoring (19-MAY-2020). • Remote monitoring activities were documented in a remote routine monitoring visit (19-MAY-2020). • Source data verification at 100% prior to database lock was waived for this study. Source data verification was resumed once the onsite visit was possible (19-MAY-2020).
Protocol deviations	• Study sites were queried as to the relationship of reported deviations to the COVID-19 pandemic; responses were documented (15-APR-2020).
AE reporting	• COVID-19 infection was reported in accordance with the protocol's AE and SAE reporting instructions (15-APR-2020). • If unable to visit sites, participants reported SAEs over the phone and SAEs were recorded in the clinical database per normal practice (30-MAR-2020).
Clinical supplies (including study intervention)	• If participants were unable to visit the site, alternate delivery mechanisms may have been implemented (30-MAR-2020). • Efforts were made to ensure that sites had adequate clinical supplies and ancillary supplies (30-MAR-2020).
Data management	• Study sites were queried, and responses were documented regarding the relationship of the following to the COVID-19 pandemic (19-MAY-2020): o Missing or delayed participant study visits and data: The follow-up visits were rescheduled, and when possible, conducted at the site. The visit data was entered in the clinical database regardless of whether the visit was completed in the clinic or via telephone (telemedicine). o Missing or delayed safety laboratories, scans, or doses.
Clinical laboratory and other facilities	• Alternate storage and/or shipment arrangements for study samples were allowed when required. Alternate clinical laboratory facilities were allowed for collection of samples for study participants unable to visit the study site, if endorsed by the clinical study site, local HA, and/or IRB/IEC as required per country (15-APR-2020). Alternate laboratories were accredited and followed the provided guidance for the collection, preparation, test, or shipment of samples. The procedures performed by the alternate clinical laboratory were documented (19-MAY-2020).

Process	Measure
	• The use of alternate imaging facilities and delayed scheduling at study sites were allowed for protocol-required imaging (collection outside the protocol window was reported as a protocol deviation) (15-APR-2020). Additional imaging guidance was provided to allow offsite facilities to send scans directly to the vendor (19-MAY-2020).
Informed consent	• Oral confirmation of participant consent (e.g., via telephone) was allowed when in-person discussion and signature was not possible. IRB/IEC must be notified and consulted (and agreeable) first with documentation filed (15-APR-2020).
Oncology specific survival follow-up	• If death due to COVID-19 infection occurred during the survival follow-up period, the cause of death could be captured on the eCRF used to report survival outcome data based on the protocol specified follow-up period(15-APR-2020).
HRQoL evaluation	• The HRQoL evaluation voice scripts along with instructions were provided to sites to be used to interview the participants by phone in case the onsite visit was not possible (19-MAY-2020).

Missing participant study visits and/or data were queried as per the Sponsor's standard processes. As per the Sponsor's standard process, missing procedures and study visits were to be reported as protocol deviations for that participant. Procedures and study visits conducted outside protocol-defined windows were also reported as protocol deviations. Visits obtained via telemedicine (e.g. telephone, email), were reported as a protocol deviation. Participants with protocol deviations due to the pandemic are described in [Sec. 10.2].

The missed and delayed doses due to COVID-19 were reported as requested and escalated to medical monitoring mailbox if an interruption of more than 12 weeks was anticipated. If the investigator had any safety concerns due to dose interruption, the investigator could reach out to the medical monitoring mailbox.

9.8.2 Changes in the Planned Analyses

No changes in the planned analyses of the study due to the COVID-19 pandemic or any other reason were reported through this DCO of 03-APR-2020. Changes in the planned analysis that were implemented previously by protocol amendments are described in [16.1.1] and [Ref. 5.3.5.1: P054V01MK3475: 9.8.2].

9.8.3 Changes Following Study Unblinding and Post-hoc Analyses

No changes in the planned analyses following study unblinding and no post-hoc analyses were made due to the COVID-19 pandemic or any other reason.

10 STUDY PARTICIPANTS

Data listings by participant 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].

Part 1 of the study included participants who were randomized to pembrolizumab or placebo as adjuvant therapy upon study enrollment. Participants who met prespecified criteria were allowed to enter the Part 2 of the study after the first recurrence of disease. In the Part 2, the participants had crossover or rechallenge treatment with pembrolizumab.

10.1 Disposition of Participants

The disposition of participants was comparable across study intervention groups [Table 10-1] [16.2.1]. In Part 1 of the study, 1464 participants were screened and 1019 were randomized with 514 participants randomized to pembrolizumab and 505 to placebo [Ref. 5.3.5.1: P054V01MK3475: 10.1].

The percentages of participants who completed study intervention in Part 1 of the study in the pembrolizumab and placebo groups were similar (57.8% and 59.4%, respectively). Overall, 422 participants (41.4%) discontinued. The most frequent reason for treatment discontinuation in both groups was progressive disease, with a larger percentage in the placebo arm [Table 10-1]. Progressive disease includes disease recurrence, relapse, and death due to progressive disease. The discontinuation due to other included participant or investigator's decision to stop treatment or incorrect duration of treatment due to error.

The number of subjects randomized by investigator and treatment groups is provided in [16.1.7.1], [16.1.7.2] and the characteristics of nonrandomized subjects are available in [16.2.4.1].

A total of 170 participants from Part 1 entered Part 2 of the study due to disease recurrence; 151 participants who were randomized to placebo in Part 1 crossed over to pembrolizumab in Part 2 of the study and 19 participants who were randomized to receive pembrolizumab in Part 1 were rechallenged with pembrolizumab in Part 2 of the study [Table 14.1-2], [Table 14.1-3]. The disposition of participants from Part 2 is provided in [Table 14.1-3].

The percentage of participants who completed study intervention in Part 1 of the study and entered Part 2 was 94.7% in the rechallenge group and 34.4% in the crossover group. The percentages of participants who completed Part 2 of the study in the rechallenge and crossover groups were 5.3% and 12.6%, respectively. Overall, 131 participants (77.1%) discontinued Part 2. The most frequent reason for discontinuation in both groups was progressive disease [Table 14.1-3].

At DCO, 97.5% of participants initially randomized to the pembrolizumab group and 72.5% of participants initially randomized to the placebo group were continuing in the study (Status Not Recorded) [Table 10-1].Overall, 31.6% of participants in rechallenge and 8.6% of participants in crossover continued in Part 2 (Status Not Recorded) [Table 14.1-3].

Table 10-1
Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	514		505		1019	
Status for Trial						
Completed	1	(0.2)	19	(3.8)	20	(2.0)
Discontinued	12	(2.3)	120	(23.8)	132	(13.0)
Adverse Event	1	(0.2)	19	(3.8)	20	(2.0)
Not Associated With Covid-19, No Further Information	1	(0.2)	17	(3.4)	18	(1.8)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	2	(0.4)	2	(0.2)
Lost To Follow-Up	0	(0.0)	1	(0.2)	1	(0.1)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Progressive Disease	9	(1.8)	77	(15.2)	86	(8.4)
Not Associated With Covid-19, No Further Information	6	(1.2)	33	(6.5)	39	(3.8)
Not Associated With Covid-19, Subsequently Died	3	(0.6)	44	(8.7)	47	(4.6)
Randomized By Mistake Without Study Treatment	0	(0.0)	1	(0.2)	1	(0.1)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Withdrawal By Subject	2	(0.4)	16	(3.2)	18	(1.8)
Not Associated With Covid-19, No Further Information	1	(0.2)	15	(3.0)	16	(1.6)
Not Associated With Covid-19, Subsequently Died	1	(0.2)	1	(0.2)	2	(0.2)
Other	0	(0.0)	6	(1.2)	6	(0.6)
Not Associated With Covid-19, No Further Information	0	(0.0)	5	(1.0)	5	(0.5)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Status Not Recorded	501	(97.5)	366	(72.5)	867	(85.1)

Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Status for Study Medication in Trial Segment Treatment						
Started	514		505		1019	
Completed	297	(57.8)	300	(59.4)	597	(58.6)
Discontinued	217	(42.2)	205	(40.6)	422	(41.4)
Adverse Event	73	(14.2)	11	(2.2)	84	(8.2)
Lost To Follow-Up	1	(0.2)	0	(0.0)	1	(0.1)
Non-Compliance With Study Drug	2	(0.4)	0	(0.0)	2	(0.2)
Progressive Disease	113	(22.0)	184	(36.4)	297	(29.1)
Randomized By Mistake Without Study Treatment	3	(0.6)	1	(0.2)	4	(0.4)
Screen Failure	1	(0.2)	0	(0.0)	1	(0.1)
Withdrawal By Subject	19	(3.7)	7	(1.4)	26	(2.6)
Other	5	(1.0)	2	(0.4)	7	(0.7)
Status for Study Medication in Trial Segment Crossover/Rechallenge treatment						
Started	19		151		170	
Completed	1	(5.3)	19	(12.6)	20	(11.8)
Discontinued	12	(63.2)	119	(78.8)	131	(77.1)
Adverse Event	1	(5.3)	19	(12.6)	20	(11.8)
Not Associated With Covid-19, No Further Information	1	(5.3)	17	(11.3)	18	(10.6)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	2	(1.3)	2	(1.2)
Lost To Follow-Up	0	(0.0)	1	(0.7)	1	(0.6)

Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Status for Study Medication in Trial Segment Crossover/Rechallenge treatment						
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Progressive Disease	9	(47.4)	77	(51.0)	86	(50.6)
Not Associated With Covid-19, No Further Information	6	(31.6)	33	(21.9)	39	(22.9)
Not Associated With Covid-19, Subsequently Died	3	(15.8)	44	(29.1)	47	(27.6)
Withdrawal By Subject	2	(10.5)	16	(10.6)	18	(10.6)
Not Associated With Covid-19, No Further Information	1	(5.3)	15	(9.9)	16	(9.4)
Not Associated With Covid-19, Subsequently Died	1	(5.3)	1	(0.7)	2	(1.2)
Other	0	(0.0)	6	(4.0)	6	(3.5)
Not Associated With Covid-19, No Further Information	0	(0.0)	5	(3.3)	5	(2.9)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Status Not Recorded	6	(31.6)	13	(8.6)	19	(11.2)

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

Each subject is counted once for Study Medication Disposition.

Status not Recorded for subjects that are continuing in trial or trial segment.

Database Cutoff Date: 03APR2020

Source: [P054V02MK3475: adam-adsl]

10.1.1 Premature Unblinding

A summary of participants whose treatment was prematurely unblinded was provided in the CSR for the final RFS analysis [Ref. 5.3.5.1: P054V01MK3475: 10.1]. No additional premature unblinding events were reported through this DCO of 03-APR-2020.

10.2 Protocol Deviations

EORTC reported a total of 2852 protocol deviations according to their process, which identifies any suspected deviation to assure that all protocol deviations are identified, flagged, and corrected. A clinical review of these protocol deviations, according to the MSD process and ICH E3 guidelines, determined that only 227 protocol deviations were considered important [16.2.2.1]. Of the 255 participants with protocol deviations [Table 14.1-4], only 170 participants had important protocol deviations [16.2.2.1].

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.

Of the 227 important protocol deviations, only 51 were considered to be clinically important [16.2.2.1]; and of the 170 participants that had important protocol deviations [16.2.2.1], only 43 participants had important protocol deviations that were considered to be clinically important. The clinically important protocol deviations included 2 participants who were randomized but did not meet eligibility criteria due to a different cancer than the one under study (mucosal melanoma and an adenocarcinoma), and 41 participants who had safety reporting 90 days or more after the site learned about the event[Table 10-2].

As described in [Sec. 7], part of this study was conducted during the COVID-19 pandemic. Protocol deviations associated with the pandemic were reported for 98 participants. None of these protocol deviations were considered important since they did not meet the established definitions of important deviations. These protocol deviations included 64 participants who had safety tests missed, delayed, or performed at a different laboratory facility, and 95 participants who did not comply with study procedures [Table 10-3].

No participant's data were excluded from analyses due to an important protocol deviation or a protocol deviation associated with the pandemic [Sec.10.3]. The important protocol deviations identified in this study are not expected to impact the overall safety or integrity of the study. No important protocol deviations were classified as serious GCP compliance issues [16.1.8.2].

A listing of the important protocol deviations, a listing of protocol deviations associated with the COVID-19 pandemic, and a listing of clinically important protocol deviation is presented by participant and study site in [16.2.2.1], [16.2.2.2], [16.2.2.4]. A listing of the EORTC protocol deviations by participant and study site is provided in [16.2.2.3].

Table 10-2
Summary of Important Protocol Deviations Considered to be Clinically Important

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
With one or more clinically important protocol deviations	24	(4.7)	19	(3.8)	43	(4.3)
With no clinically important protocol deviations	485	(95.3)	483	(96.2)	968	(95.7)
Inclusion/ Exclusion Criteria	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Patient had a mucosal melanoma (part 1)	1	(0.2)	0	(0.0)	1	(0.1)
Patient not disease-free at time of randomization (part 1)	0	(0.0)	1	(0.2)	1	(0.1)
Safety Reporting	**23**	**(4.5)**	**18**	**(3.6)**	**41**	**(4.1)**
Reportable safety event not reported within 24h of awareness	23	(4.5)	18	(3.6)	41	(4.1)

Every subject is counted a single time for each applicable row and column.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl] [P054V02MK3475: sdtm-dv]

Table 10-3
Summary of Protocol Deviations Associated With COVID-19

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
With one or more protocol deviations associated with COVID-19	51	(10.0)	47	(9.4)	98	(9.7)
With no protocol deviations associated with COVID-19	458	(90.0)	455	(90.6)	913	(90.3)
Safety Reporting	**37**	**(7.3)**	**27**	**(5.4)**	**64**	**(6.3)**
COVID-19: Safety lab sample got lost during processing in the lab	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were collected at an external facility and processed at on-site lab, but not all required tests were included	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were missed	32	(6.3)	25	(5.0)	57	(5.6)
COVID-19: Safety labs were performed at an external facility and not all required tests were included	2	(0.4)	0	(0.0)	2	(0.2)
COVID-19: Safety labs were performed but not all required tests were included	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Safety labs were performed out of window	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Urine analysis was missed	1	(0.2)	0	(0.0)	1	(0.1)
Trial Procedures	**49**	**(9.6)**	**46**	**(9.2)**	**95**	**(9.4)**
COVID-19: Delay in collecting patient survival information	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Imaging assessment was not performed	17	(3.3)	12	(2.4)	29	(2.9)
COVID-19: On-site visit was replaced by phone call or e-mail contact only	37	(7.3)	29	(5.8)	66	(6.5)
COVID-19: Questionnaires were completed over the phone without official transcripts	1	(0.2)	1	(0.2)	2	(0.2)
COVID-19: Questionnaires were not completed by patient	17	(3.3)	13	(2.6)	30	(3.0)
COVID-19: Skin examination was missed	39	(7.7)	33	(6.6)	72	(7.1)

Summary of Protocol Deviations Associated With COVID-19

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Trial Procedures	**49**	**(9.6)**	**46**	**(9.2)**	**95**	**(9.4)**
COVID-19: TR samples not collected	1	(0.2)	2	(0.4)	3	(0.3)

Every subject is counted a single time for each applicable row and column.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl] [P054V02MK3475: sdtm-dv]

10.3 Data Sets Analyzed

10.3.1 Efficacy Analysis Population(s)

Efficacy analyses were based on the ITT population, which included 1019 participants [Table 10-4] and [16.2.3]. Participants were analyzed according to the study intervention group allocated at randomization.

10.3.2 Safety Analysis Population

Safety analyses were based on the ASaT population, which included all 1011 randomized participants who received at least 1 dose of study treatment [Table 10-6]. A total of 8 randomized participants did not receive treatment with either pembrolizumab or placebo [Ref. 5.3.5.1: P054V01MK3475: 10.3.2].

10.4 Demographic and Other Baseline Characteristics

10.4.1 Demographic and Baseline Disease Characteristics

Demographic characteristics for Part 1 were balanced across both groups [Table 10-4]. Approximately 66% of the participants were male and from Europe. The median age was 54 years. Nearly half of the participants (45.8%) had Stage IIIB melanoma per AJCC seventh edition cancer stage classification, most had PD-L1-positive tumors (83.7%), and approximately a half (49.7%) had BRAF-mutant melanoma. A detailed presentation of participants by age category and gender is provided in [Table 14.1-8]. Baseline cancer stage per AJCC eighth edition is provided in [Table 10-4].

Demographic characteristics for Part 2 of the study are reported in [Table 14.1-9] and were consistent with Part 1.

Table 10-4
Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	514		505		1,019	
Gender						
Male	324	(63.0)	304	(60.2)	628	(61.6)
Female	190	(37.0)	201	(39.8)	391	(38.4)
Age (Years)						
< 50	193	(37.5)	186	(36.8)	379	(37.2)
50 to 64	196	(38.1)	193	(38.2)	389	(38.2)
≥ 65	125	(24.3)	126	(25.0)	251	(24.6)
Mean	53.7		53.6		53.7	
SD	13.6		14.2		13.9	
Median	54.0		54.0		54.0	
Range	19 to 88		19 to 83		19 to 88	
Region						
North America	38	(7.4)	37	(7.3)	75	(7.4)
Europe	341	(66.3)	337	(66.7)	678	(66.5)
Australia/New Zealand	111	(21.6)	111	(22.0)	222	(21.8)
Other	24	(4.7)	20	(4.0)	44	(4.3)
PD-L1 Status						
PD-L1 Positive	428	(83.3)	425	(84.2)	853	(83.7)
PD-L1 Negative	59	(11.5)	57	(11.3)	116	(11.4)
Unknown	27	(5.3)	23	(4.6)	50	(4.9)
BRAF-Mutation Status						
Mutation Detected	244	(47.5)	262	(51.9)	506	(49.7)
Mutation Not Detected	234	(45.5)	215	(42.6)	449	(44.1)
Unknown	36	(7.0)	28	(5.5)	64	(6.3)
ECOG						
0	485	(94.4)	475	(94.1)	960	(94.2)
1	29	(5.6)	30	(5.9)	59	(5.8)
Primary Cutaneous Melanoma*						
Cutaneous	455	(88.5)	460	(91.1)	915	(89.8)
Ocular	1	(0.2)	0	(0.0)	1	(0.1)

Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Unknown	58	(11.3)	45	(8.9)	103	(10.1)
Location of Primary Cutaneous Melanoma						
Head and Neck	53	(10.3)	66	(13.1)	119	(11.7)
Extremity	203	(39.5)	196	(38.8)	399	(39.2)
Trunk	196	(38.1)	189	(37.4)	385	(37.8)
Unknown	62	(12.1)	54	(10.7)	116	(11.4)
Breslow Thickness						
≤ 1.0 mm	61	(11.9)	78	(15.4)	139	(13.6)
1.01 to 2.0 mm	99	(19.3)	102	(20.2)	201	(19.7)
2.01 to 4.0 mm	156	(30.4)	151	(29.9)	307	(30.1)
> 4.0 mm	125	(24.3)	111	(22.0)	236	(23.2)
Unknown	73	(14.2)	63	(12.5)	136	(13.3)
AJCC 7 Overall Cancer Stage						
Stage IIIA (> 1 mm)	80	(15.6)	80	(15.8)	160	(15.7)
Stage IIIB	237	(46.1)	230	(45.5)	467	(45.8)
Stage IIIC (1-3 LN+)	95	(18.5)	93	(18.4)	188	(18.4)
Stage IIIC (≥ 4 LN+)	102	(19.8)	102	(20.2)	204	(20.0)
AJCC 8 Overall Cancer Stage						
Stage IIIA	42	(8.2)	40	(7.9)	82	(8.0)
Stage IIIB	163	(31.7)	190	(37.6)	353	(34.6)
Stage IIIC	267	(51.9)	235	(46.5)	502	(49.3)
Stage IIID	20	(3.9)	21	(4.2)	41	(4.0)
Unknown	22	(4.3)	19	(3.8)	41	(4.0)
Number of LN+ (pathological)						
1	226	(44.0)	238	(47.1)	464	(45.5)
2-3	176	(34.2)	164	(32.5)	340	(33.4)
≥ 4	112	(21.8)	103	(20.4)	215	(21.1)
Type of LN+ Involvement						
Microscopic	185	(36.0)	160	(31.7)	345	(33.9)
Macroscopic	329	(64.0)	345	(68.3)	674	(66.1)
Ulceration						
No	230	(44.7)	251	(49.7)	481	(47.2)

Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Yes	208	(40.5)	197	(39.0)	405	(39.7)
Unknown	76	(14.8)	57	(11.3)	133	(13.1)
Type of Surgery						
Axillary lymphadenectomy	192	(37.4)	194	(38.4)	386	(37.9)
Inguinal lymphadenectomy	137	(26.7)	130	(25.7)	267	(26.2)
Modified radical neck dissection	58	(11.3)	68	(13.5)	126	(12.4)
Other	4	(0.8)	5	(1.0)	9	(0.9)
Multiple types of surgery	123	(23.9)	108	(21.4)	231	(22.7)
Timing of First Dose of Study Therapy						
≤ 13 weeks from date of surgery	500	(97.3)	490	(97.0)	990	(97.2)
> 13 weeks from date of surgery	9	(1.8)	12	(2.4)	21	(2.1)
Unknown	5	(1.0)	3	(0.6)	8	(0.8)
*One subject with ocular primary melanoma was randomized. (Database Cutoff Date: 03APR2020).						

Source: [P054V02MK3475: adam-adsl]

10.4.2 Prior and Concomitant Treatments

The study intervention groups were comparably balanced for reported prior medications. The most frequently reported prior medications (>20% of participants overall) were analgesics (42.6%), agents acting on the renin-angiotensin system (36.3%), and lipid modifying agents (29.5%) [Ref. 5.3.5.1: P054V01MK3475: 10.4.2].

The most frequently reported concomitant medications (>20% of participants overall) were antibacterials for systemic use (52.6%), analgesics (57%), and corticosteroids for systemic use (33.7%). Concomitant medications with an incidence >0% in either study intervention group are listed in [Table 14.1-10].

10.5 Measurements of Study Intervention Compliance

Study intervention was administered in the clinic by qualified site personnel as described in the protocol [16.1.1]. There were no overdoses associated with an AE.

10.6 Extent of Exposure

As of DCO, the median duration of exposure to study intervention was 357 days and 750 participants received study intervention for ≥ 6 months, and 146 received study intervention for ≥ 12 months [Table 10-5] and [Table 10-6]. Overall, 497 participants had a duration of exposure between 11 and 12 months.

At the time of DCO, participants had a median follow-up of 45.5 months [Table 14.1-13].

Table 10-5
Summary of Drug Exposure
ASaT Population

	Pembrolizumab (N=509)	Placebo (N=502)	Total (N=1011)
Study Days On-Therapy (days)			
Mean	282.8	275.7	279.3
Median	358.0	357.0	357.0
SD	120.96	123.51	122.23
Range	1.0 to 478.0	1.0 to 424.0	1.0 to 478.0
Number of Administrations			
Mean	14.0	13.9	13.9
Median	18.0	18.0	18.0
SD	5.62	5.77	5.69
Range	1.0 to 18.0	1.0 to 19.0	1.0 to 19.0
On-Therapy is defined as receiving at least one dose of study treatment and is limited to Part 1 of the study. (Data Cutoff Date: 03APR2020).			

Source: [P054V02MK3475: adam-adsl; adexsum]

Table 10-6
Exposure by Duration
ASaT Population

	Pembrolizumab (N=509)		Placebo (N=502)		Total (N=1011)	
	n	Person-years	n	Person-years	n	Person-years
Duration of Exposure						
> 0 m	509	394	502	379	1,011	773
≥ 1 m	489	393	489	378	978	771
≥ 3 m	434	383	414	365	848	748
≥ 6 m	387	365	363	345	750	710
≥ 12 m	72	76	74	77	146	153

Each subject 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.
Exposure by Duration is given for Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adexsum]

11 EFFICACY AND OTHER EVALUATIONS

11.1 Efficacy Results

The results presented in this report are based on an analysis after 418 DMFS events and 491 RFS events at DCO of 03-APR-2020.

The "graphical approach" to test the hypotheses with respect to RFS and DMFS was adopted in this study to control the overall Type-I error rate, as described in protocol section 8.1.1 [16.1.1]. According to this multiplicity strategy, as RFS comparison was statistically significant in ITT and PD-L1-positive subgroup in the final RFS analysis (DCO 02-OCT-2017) [Ref. 5.3.5.1: P054V01MK3475], the 2.5% alpha was reallocated to the DMFS comparison.

11.1.1 Efficacy Endpoint: Distant Metastasis-Free Survival in All Participants

The results presented in this report are the first and final analysis for DMFS. DMFS events could occur during Part 1 or Part 2 of the study.

Pembrolizumab provided a statistically significant, and clinically meaningful improvement in DMFS with 45.5 months of median follow-up when compared with placebo. Fewer distant metastases developed in the pembrolizumab group, 173 (33.7%) compared with the placebo group, 245 (48.5%). The HR was 0.60 (95% CI: 0.49, 0.73; $p<0.0001$) in favor of pembrolizumab, with a 40% reduction in the risk of distant metastases or death. The median DMFS was not yet reached in the pembrolizumab group and was 40.0 months (95% CI: 27.7, -) in the placebo group [Table 11-1].

Results per AJCC eighth edition cancer stage classification are presented in [Table 14.2-2].

The K-M curves separated early at Month 3 and remained separated throughout the evaluation period in favor of pembrolizumab [Figure 11-1]. The DMFS rate was higher in the pembrolizumab group (82.8% and 65.3%) compared with the placebo group (69.8% and 49.4%) at Month 12 and Month 42, respectively [Table 14.2-5].

The sensitivity analysis 1 (HR=0.60; 95% CI: 0.50, 0.73; $p<0.0001$) and the sensitivity analysis 2 (HR=0.61; 95% CI: 0.50, 0.74; $p<0.0001$) were consistent with the primary analysis, with a reduction in the risk of distant metastases or death of 40% and 39%, respectively [Table 14.2-3], [Table 14.2-4] and [Figure 14.2-2], [Figure 14.2-3].

If a participant started new anticancer therapy prior to an event, then the date the last disease assessment prior to new anticancer therapy is the censoring date for sensitivity analysis 1 and the event date for sensitivity analysis 2. Details regarding sensitivity analyses are provided in the protocol [16.1.1].

Table 11-1
Analysis of Distant Metastasis-Free Survival
ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	514	173 (33.7)	16164.4	1.1	Not Reached (49.6, -)	65.3 (60.9, 69.5)	0.60 (0.49, 0.73)	<0.0001
Placebo	505	245 (48.5)	13310.9	1.8	40.0 (27.7, -)	49.4 (44.8, 53.8)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

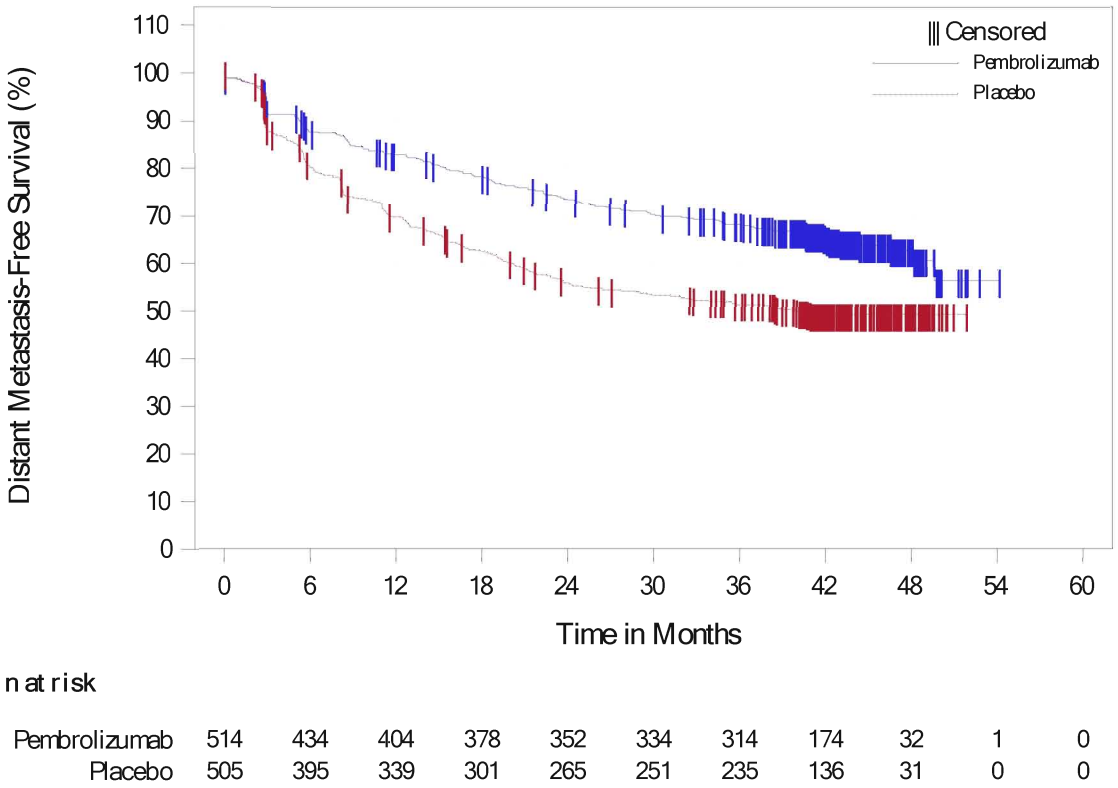
§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 11-1
Kaplan-Meier Estimates of Distant Metastasis-Free Survival

ITT Population



(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

11.1.2 Efficacy Endpoint: Distant Metastasis-Free Survival by PD-L1 Expression

Participants With PD-L1 Positive Tumors

In participants with PD-L1-positive tumors, pembrolizumab provided significant and clinically meaningful improvement in DMFS (336 events) with 45.5 months of median follow-up compared with placebo (HR=0.61; 95% CI: 0.49, 0.76; $p<0.0001$), with a 39% reduction in the risk of distant metastases or death. Benefit was similar to that of the ITT population. The median DMFS was not yet reached in the pembrolizumab and placebo groups [Table 11-2]. Results per AJCC eighth edition cancer stage classification are given in [Table 14.2-7].

The K-M curves were also similar to that of the ITT population, with an early separation at Month 3 that remained throughout the evaluation period in favor of pembrolizumab [Figure

11-2]. The DMFS rate was higher in the pembrolizumab group (66.7%) compared with the placebo group (51.6%) at Month 42 [Table 11-2].

Sensitivity analyses 1 (HR=0.61; 95% CI: 0.49, 0.76; p<0.0001) and 2 (HR=0.63; 95% CI: 0.50, 0.78; p<0.0001) were consistent with the primary analysis, with a reduction in the risk of distant metastases or death of 39% and 37%, respectively [Table 14.2-8], [Table 14.2-9] and [Figure 14.2-5], [Figure 14.2-6].

Table 11-2
Analysis of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	428	138 (32.2)	13632.1	1.0	Not Reached (49.6, -)	66.7 (61.8, 71.2)	0.61 (0.49, 0.76)	<0.0001
Placebo	425	198 (46.6)	11630.0	1.7	Not Reached (33.8, -)	51.6 (46.6, 56.4)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

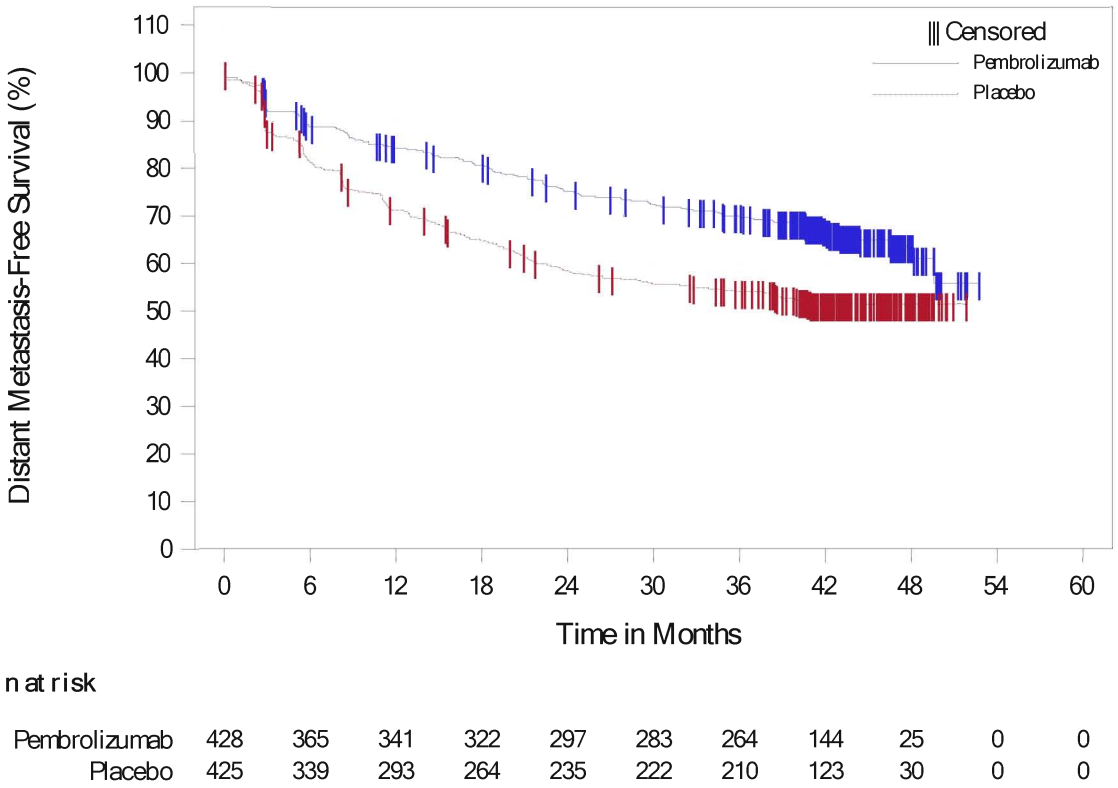
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 11-2
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population



(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Participants With PD-L1 Negative Tumors

In participants with PD-L1-negative tumors, pembrolizumab provided improvement in DMFS (56 events) with 45.5 months of median follow-up compared with placebo (HR=0.49, 95% CI: 0.28, 0.83), with a 51% of reduction in the risk of distant metastases or death. Benefit was similar to that of the ITT population and participants with PD-L1-positive tumors. The median DMFS was not yet reached in the pembrolizumab group and was 20.3 months (95% CI: 10.4, -) in the placebo group [Table 11-3]. Results per AJCC eighth edition cancer stage classification are given in [Table 14.2-11].

The K-M curves for the DMFS separated at Month 3 in favor of pembrolizumab. Although the DMFS rate was lower in pembrolizumab before Month 3, it became higher in pembrolizumab around Month 3 through Month 48 compared with placebo [Figure 11-3].

The DMFS rate was higher in the pembrolizumab group (58.0%) compared with the placebo group (40.2%) at Month 42 [Table 11-3].

Sensitivity analysis 1 (HR=0.49; 95% CI: 0.28, 0.83) and 2 (HR=0.49; 95% CI: 0.28, 0.83) were consistent with the primary analysis, with a reduction in the risk of distant metastases or death of 51% for both analyses [Table 14.2-12], [Table 14.2-13] and [Figure 14.2-8], [Figure 14.2-9].

Table 11-3
Analysis of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	24 (40.7)	1771.2	1.4	Not Reached (25.6, -)	58.0 (44.1, 69.5)	0.49 (0.28, 0.83)
Placebo	57	32 (56.1)	1252.7	2.6	20.3 (10.4, -)	40.2 (27.0, 53.0)	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

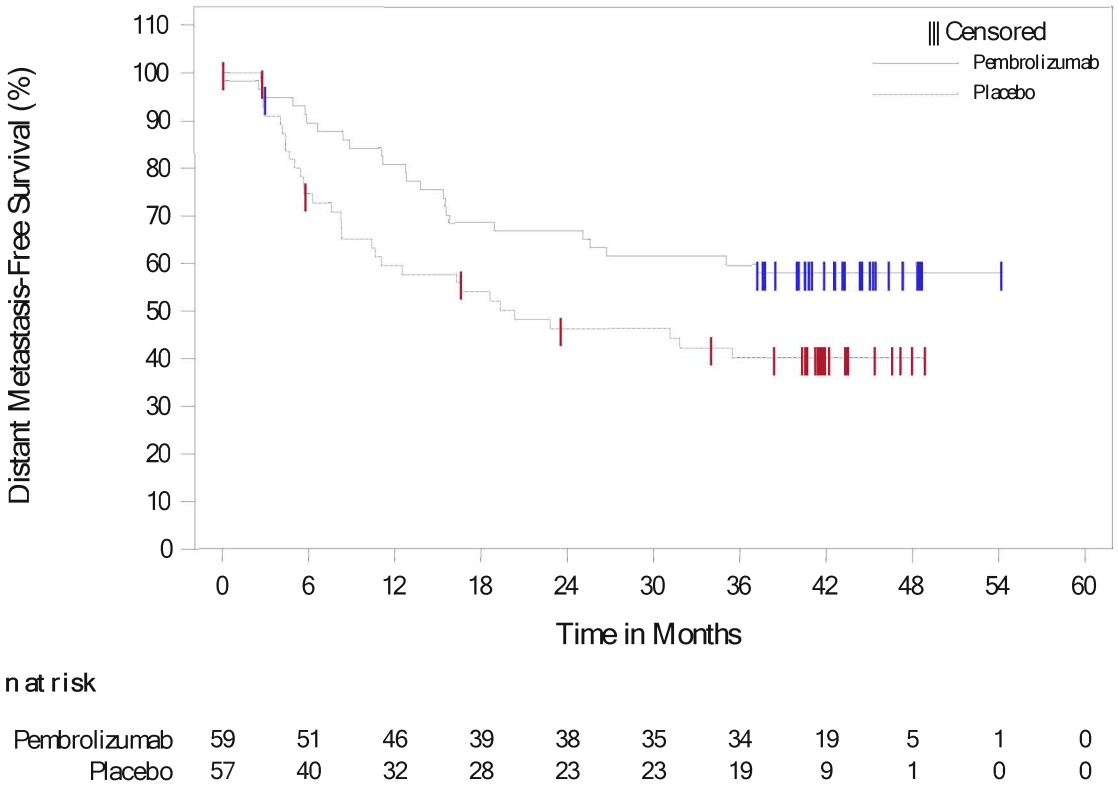
† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 11-3
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population

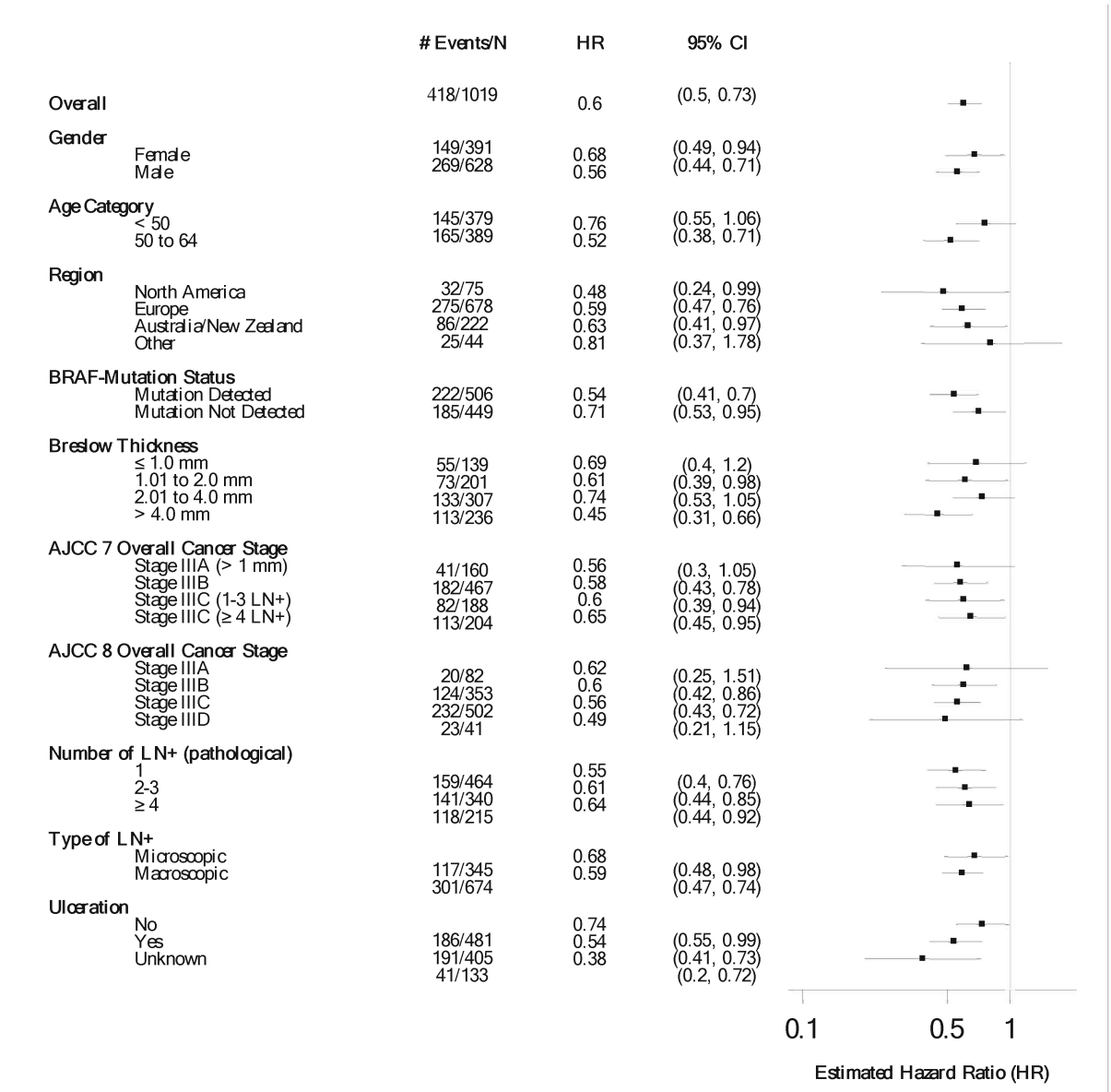


(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

11.1.3 Distant Metastasis-Free Survival by Other Subgroup

DMFS benefit of pembrolizumab compared with placebo that was similar to that of the ITT population was observed across all subgroups regardless of cancer stage (AJCC seventh and eighth edition cancer stage classification) and BRAF-mutation status [Figure 11-4].

Figure 11-4
Forest Plot of Distant Metastases-Free Survival Hazard Ratio by Subgroup Factors
ITT Population



	# Events/N	HR	95% CI
Overall	418/1019	0.6	(0.5, 0.73)
Gender			
Female	149/391	0.68	(0.49, 0.94)
Male	269/628	0.56	(0.44, 0.71)
Age Category			
< 50	145/379	0.76	(0.55, 1.06)
50 to 64	165/389	0.52	(0.38, 0.71)
Region			
North America	32/75	0.48	(0.24, 0.99)
Europe	275/678	0.59	(0.47, 0.76)
Australia/New Zealand	86/222	0.63	(0.41, 0.97)
Other	25/44	0.81	(0.37, 1.78)
BRAF-Mutation Status			
Mutation Detected	222/506	0.54	(0.41, 0.7)
Mutation Not Detected	185/449	0.71	(0.53, 0.95)
Breslow Thickness			
≤ 1.0 mm	55/139	0.69	(0.4, 1.2)
1.01 to 2.0 mm	73/201	0.61	(0.39, 0.98)
2.01 to 4.0 mm	133/307	0.74	(0.53, 1.05)
> 4.0 mm	113/236	0.45	(0.31, 0.66)
AJCC 7 Overall Cancer Stage			
Stage IIIA (> 1 mm)	41/160	0.56	(0.3, 1.05)
Stage IIIB	182/467	0.58	(0.43, 0.78)
Stage IIIC (1-3 LN+)	82/188	0.6	(0.39, 0.94)
Stage IIIC (≥ 4 LN+)	113/204	0.65	(0.45, 0.95)
AJCC 8 Overall Cancer Stage			
Stage IIIA	20/82	0.62	(0.25, 1.51)
Stage IIIB	124/353	0.6	(0.42, 0.86)
Stage IIIC	232/502	0.56	(0.43, 0.72)
Stage IIID	23/41	0.49	(0.21, 1.15)
Number of LN+ (pathological)			
1	159/464	0.55	(0.4, 0.76)
2-3	141/340	0.61	(0.44, 0.85)
≥ 4	118/215	0.64	(0.44, 0.92)
Type of LN+			
Microscopic	117/345	0.68	(0.48, 0.98)
Macroscopic	301/674	0.59	(0.47, 0.74)
Ulceration			
No	186/481	0.74	(0.55, 0.99)
Yes	191/405	0.54	(0.41, 0.73)
Unknown	41/133	0.38	(0.2, 0.72)

(Database Cutoff Date: 03APR2020).
Source: [P054V02MK3475: adam-adsl; adtte]

11.1.4 Efficacy Endpoint: Recurrence-Free Survival in All Participants

In the final RFS analysis (351 events; DCO 02-OCT-2017), treatment with pembrolizumab resulted in significantly longer RFS compared with placebo (HR=0.57; 98.4% CI: 0.43, 0.74; $p<0.0001$). Median RFS was not reached in the pembrolizumab group and was 20.4 months (95% CI: 16.2,-) in the placebo group. The 1-year RFS rate was 75.4% (95% CI: 71.3, 78.9) in the pembrolizumab group versus 61.0% (95% CI: 56.5, 65.1) in the placebo group [Ref. 5.3.5.1: P054V01MK3475].

Descriptive extended RFS analyses (491 events; DCO 03-APR-2020) with 45.5 months of median follow-up are presented in this report. The extended RFS analyses only included data from Part 1 of the study.

Pembrolizumab provided a sustained RFS benefit with 45.5 months of median follow-up when compared with placebo. The HR was 0.59 (95% CI: 0.49, 0.70) in favor of pembrolizumab, with a 41% reduction in the risk of recurrence or death. Median RFS was not yet reached in the pembrolizumab group and was 21.4 months (95% CI: 16.3, 27.0) in the placebo group [Table 11-4].

The K-M curves separated early around Month 3 and remained separated throughout the evaluation period in favor of pembrolizumab [Figure 11-5]. The RFS rate was higher in the pembrolizumab group (75.3% and 59.8%) than in the placebo group (60.0% and 41.4%) at Months 12 and 42, respectively [Table 14.2-15].

Locoregional recurrences occurred in 13.8% of the participants in the pembrolizumab group and 18.4% of the participants in the placebo group. A total of 283 events of distant metastasis contributed to the extended RFS analysis, with a higher percentage in the placebo group compared with the pembrolizumab group (32.7% vs 23.0%, respectively). Seven deaths also contributed to the extended RFS analysis [Table 14.2-16].

Table 11-4
Analysis of Recurrence-Free Survival
ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median RFS† (Months) (95% CI)	RFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	514	203 (39.5)	15278.1	1.3	Not Reached (48.1, -)	59.8 (55.3, 64.1)	0.59 (0.49, 0.70)
Placebo	505	288 (57.0)	11792.0	2.4	21.4 (16.3, 27.0)	41.4 (37.0, 45.8)	---

Recurrence-free survival is defined as time from randomization to the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

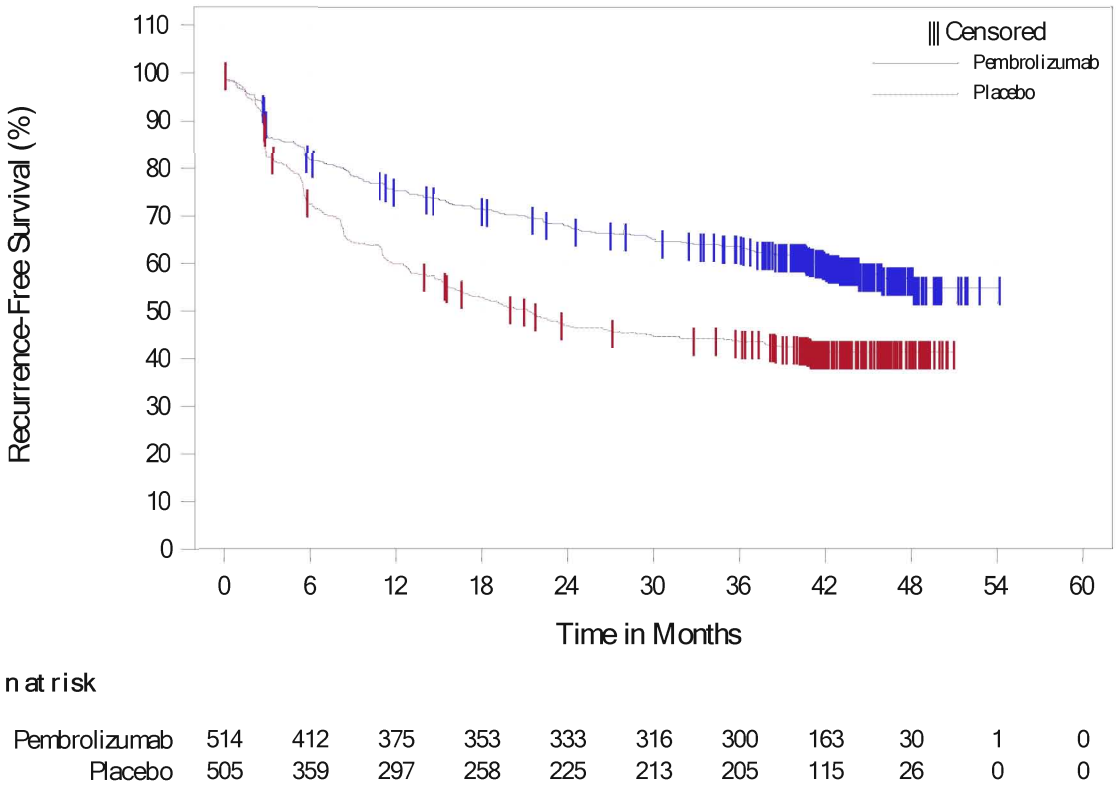
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 11-5
Kaplan-Meier Estimates of Recurrence-Free Survival

ITT Population



(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

11.1.5 Efficacy Endpoint: Recurrence-Free Survival by PD-L1 Expression

Participants With PD-L1-Positive Tumors

In participants with PD-L1 positive tumors, pembrolizumab provided continued improvement in RFS (398 events) with 45.5 months of median follow-up compared with placebo (HR=0.59; 95% CI: 0.49, 0.73), with a 41% reduction in the risk of recurrence or death. The benefit was similar to that of the ITT population. The median RFS was not yet reached in the pembrolizumab group and in the placebo group was 22.5 months (95% CI: 17.3, 37.8) [Table 14.2-17].

Participants With PD-L1-Negative Tumors

In participants with PD-L1-negative tumors, pembrolizumab provided continued improvement in RFS (64 events) with 45.5 months of median follow-up compared with placebo (HR=0.46; 95% CI: 0.27, 0.77), with a 54% reduction in the risk of recurrence or death. Benefit was similar compared with that of the ITT population and in participants with PD-L1-positive tumors. Median RFS was not yet reached in the pembrolizumab group and in the placebo group this was 16.6 months (95% CI: 5.7, 31.9) [Table 14.2-18].

11.1.6 Recurrence-Free Survival by Other Subgroups

A sustained RFS benefit of pembrolizumab compared with placebo that was similar to that of the ITT population was observed across all subgroups regardless of cancer stage (AJCC seventh and eighth edition cancer stage classification) and BRAF-mutation status [Figure 14.2-12].

11.2 Efficacy Results Summary

- Pembrolizumab provided a statistically significant, and clinically meaningful improvement in DMFS with 45.5 months of median follow-up in the ITT population when compared with placebo. The HR was 0.60 (95% CI: 0.49, 0.73; p<0.0001) in favor of pembrolizumab, with a 40% reduction in the risk of distant metastases or death.
- As of the DCO, the median DMFS was not reached in the pembrolizumab group compared with 40.0 months in the placebo group for the ITT population.
- In participants with PD-L1-positive tumors, pembrolizumab provided significant and clinically meaningful improvement in DMFS with 45.5 months of median follow-up compared with placebo (HR=0.61; 95% CI: 0.49, 0.76; p<0.0001), with a 39% reduction in the risk of distant metastases or death in participants with PD-L1-positive tumors. The median DMFS was not yet reached in both the pembrolizumab and placebo groups.
- DMFS benefit of pembrolizumab compared with placebo that was similar to that of the ITT population was observed across all subgroups regardless of cancer stage and BRAF-mutation status.
- Pembrolizumab provided sustained RFS benefit with 45.5 months of median follow-up when compared with placebo. The HR was 0.59 (95% CI: 0.49, 0.70) in favor of pembrolizumab, with a 41% reduction in the risk of recurrence or death.

12 SAFETY EVALUATION

Safety data for Parts 1 and 2 of the study are presented separately. Safety data for Part 1 of the study are the primary focus of the Safety analyses in this report; analyses presented are for Part 1 of the study unless otherwise indicated. A subset of safety tables is provided for the Part 2 of the study; those tables are presented in the corresponding section.

12.1 Adverse Events

Listing(s) of TEAEs by participant are provided in [16.2.7], [16.4].

MedDRA version 23.0 was used at the time of table generation.

12.1.1 Brief Summary of Adverse Events

The safety results of this study are generally consistent with the established safety profile for pembrolizumab and with the final RFS analysis (DCO 02-OCT-2017). As expected for the comparison of an active treatment versus placebo, the incidences of drug-related AEs, Grade 3 to 5 AEs (including those considered to be drug related), SAEs (including those considered to be drug related), and AEs leading to discontinuation were higher in the pembrolizumab group compared with the placebo group.

Of the 1011 participants in the ASaT population, 92.4% had at least 1 AE of any grade regardless of relationship to study intervention [Table 12-1]. Overall, 8.8% of participants discontinued study intervention due to an AE.

Drug-related AEs were reported for 72.3% of participants and 6.9 % had a drug-related AE leading to study intervention discontinuation. SAEs were reported for 20.8% of participants and 4.0% of participants discontinued study intervention due to a SAE.

No new deaths due to an AE occurred since the previously submitted final RFS analysis report. Additional details are provided in [Sec. 12.2.1.1].

Part 2 of the study was consistent with Part 1, 87.6% of participants had at least 1 AE of any grade regardless of relationship to study intervention. Overall, 11.2% of participants discontinued study intervention due to an AE [Table 12-2].

No COVID-19-related AEs were reported [Table 14.3-3].

Table 12-1
Adverse Event Summary
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse event	29	(5.7)	48	(9.6)	77	(7.6)
with drug-related[†] adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with toxicity grade 3-5 adverse events	162	(31.8)	96	(19.1)	258	(25.5)
with toxicity grade 3-5 drug-related adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with serious adverse events	127	(25.0)	83	(16.5)	210	(20.8)
with serious drug-related adverse events	62	(12.2)	6	(1.2)	68	(6.7)
who died	1	(0.2)	0	(0.0)	1	(0.1)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	71	(13.9)	18	(3.6)	89	(8.8)
discontinued drug due to a drug-related adverse event	62	(12.2)	8	(1.6)	70	(6.9)
discontinued drug due to a serious adverse event	29	(5.7)	11	(2.2)	40	(4.0)
discontinued drug due to a serious drug-related adverse event	22	(4.3)	2	(0.4)	24	(2.4)

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

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

AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

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

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	149	(87.6)
with no adverse event	21	(12.4)
with drug-related† adverse events	117	(68.8)
with toxicity grade 3-5 adverse events	46	(27.1)
with toxicity grade 3-5 drug-related adverse events	18	(10.6)
with serious adverse events	29	(17.1)
with serious drug-related adverse events	9	(5.3)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued drug due to an adverse event	19	(11.2)
discontinued drug due to a drug-related adverse event	13	(7.6)
discontinued drug due to a serious adverse event	6	(3.5)
discontinued drug due to a serious drug-related adverse event	3	(1.8)

† Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 2; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 2.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.1.2 Most Frequently Reported Adverse Events

Consistent with the final RFS analysis, the incidence of the most frequently reported AEs was generally similar between the 2 treatment groups [Table 12-3], and a higher proportion (≥8%) of participants in the pembrolizumab group had hypothyroidism, hyperthyroidism, and pruritus compared with placebo (14.9% vs 2.6%, 10.4% vs 1.2%, and 20.2% vs 11.8%, respectively) [Figure 14.3-1].

The most frequently reported AEs (>15% of participants) in the pembrolizumab group were fatigue, diarrhea, pruritus, headache, nausea, and arthralgia. The most frequently reported AEs (>15% of participants) in the placebo group were fatigue, diarrhea, headache, increased weight, and hypertension [Table 12-3]. Overall, AEs were mainly Grade 1 or 2 in severity [Table 14.3-5].

Part 2 of the study was consistent with Part 1 participants in pembrolizumab treatment group, the most frequently reported AEs (>15% of participants) were diarrhea, fatigue, and pruritus [Table 14.3-8].

Participants with AEs by decreasing incidence (incidence > 0%), AEs by maximum toxicity grade (incidence > 0%), and AEs by decreasing incidence by maximum toxicity grade

(incidence > 0%) are presented in [Table 14.3-7], [Table 14.3-9], [Table 14.3-10]. AEs by SOC and PT (incidence > 0%) are presented in [Table 14.3-6].

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)

Every subject 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.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.1.3 Classification of Adverse Events

12.1.3.1 Related to Study Intervention

Overall, 72.3% of participants (78.2% in the pembrolizumab group and 66.3% in the placebo group) had at least 1 drug-related AE. Consistent with the final RFS analysis, the incidence of drug-related AEs was generally similar between the 2 treatment groups [Table 12-4], and a higher proportion (≥8%) of participants in the pembrolizumab group had hypothyroidism and hyperthyroidism compared with placebo (14.5% vs 2.6% and 9.6% vs 0.6%, respectively) [Table 14.3-15] and [Figure 14.3-2].

The most frequently reported drug-related AEs (>15% of participants) in the pembrolizumab group were fatigue, diarrhea, and pruritus. The most frequently reported drug-related AEs (>15% of participants) in the placebo group were fatigue and diarrhea. Drug-related AEs were mainly Grade 1 or 2 in both treatment groups [Table 14.3-11], [Table 14.3-15].

Part 2 of the study was consistent with Part 1, 68.8% of participants had at least 1 drug-related AE. The most frequently reported drug-related AE (>15% of participants) was fatigue [Table 14.3-13].

Participants with drug-related AEs by decreasing incidence (incidence > 0%), drug-related AEs by maximum toxicity grade (incidence > 0%), and drug-related AEs by decreasing incidence by maximum toxicity grade (incidence > 0%) are presented in [Table 14.3-12], [Table 14.3-16], [Table 14.3-17]. The participants with drug-related AEs by SOC and PT (incidence > 0%) are presented in [Table 14.3-14].

A listing of all subjects with drug-related AEs is provided in [16.2.7.1.4].

Table 12-4
Subjects With Drug-related Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)

Every subject 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.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.1.3.2 Grade 3 to 5 Adverse Events

Overall, 25.5% of participants (31.8% in the pembrolizumab group and 19.1% in the placebo group) had at least 1 Grade 3 to 5 AE [Table 14.3-18]. Consistent with the final RFS analysis, Grade 3 AEs were reported for 23.3% of participants, Grade 4 for 2.1 % of participants, and Grade 5 for 0.1% of participants. The most frequently reported Grade 3 to 5 AE in both treatment groups was Grade 3 hypertension, of which the frequency was comparable between the groups [Table 14.3-5].

Participants with Grade 3-5 AEs by SOC and PT (incidence > 0%) are presented in [Table 14.3-19].

12.1.3.3 Grade 3 to 5 Adverse Events Related to Study Intervention

Overall, 9.0% of participants (14.5% in the pembrolizumab group and 3.4% in the placebo group) had at least 1 drug-related Grade 3 to 5 AE [Table 12-5]. Consistent with the final RFS analysis, drug-related Grade 3 AEs were reported for 8.3% of participants and Grade 4 for 0.7%. No drug-related Grade 5 AEs were reported. The most frequently reported drug-related, Grade 3 to 5 AEs (≥1% of participants) were Grade 3 colitis (1.4%) and Grade 3 Type 1 diabetes mellitus (1.0%) in the pembrolizumab group [Table 12-5] and [Table 14.3-15].

Participants with Grade 3-5 drug-related AEs by SOC and PT (incidence > 0%) are presented in [Table 14.3-21].

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with no adverse events	435	(85.5)	485	(96.6)	920	(91.0)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Diarrhoea	4	(0.8)	3	(0.6)	7	(0.7)
Fatigue	4	(0.8)	2	(0.4)	6	(0.6)
Lipase increased	4	(0.8)	3	(0.6)	7	(0.7)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Arthralgia	3	(0.6)	0	(0.0)	3	(0.3)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Immune-mediated enterocolitis	3	(0.6)	1	(0.2)	4	(0.4)
Pneumonitis	3	(0.6)	0	(0.0)	3	(0.3)
Blood creatine phosphokinase increased	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Hyponatraemia	2	(0.4)	1	(0.2)	3	(0.3)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypertension	1	(0.2)	2	(0.4)	3	(0.3)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypophosphataemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	1	(0.2)	1	(0.1)
Headache	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.1.3.4 Adverse Events by Demographic Subgroups

AEs summaries by demographic subgroups of age, gender, and region were consistent with the final RFS analysis and are presented in [Table 14.3-22] through [Table 14.3-25].

12.2 Serious Adverse Events and Other Clinically Meaningful Adverse Events

Listing(s) by participant of SAEs, drug-related SAE, death, study intervention discontinuations and study withdrawals due to an AE, and other clinically meaningful AEs are included in [16.2.7.1].

12.2.1 Serious Adverse Events

12.2.1.1 Deaths Due to Adverse Events

No new deaths occurred since the final RFS analysis.

As we previously reported, one AE of drug reaction with eosinophilia and systemic symptoms (DRESS) resulting in death occurred within 90 days after last administered dose. This death, initially assessed as related to pembrolizumab by the investigator, was later assessed as not related to pembrolizumab by the investigator but considered related to vemurafenib and cobimetinib, which were initiated by the participant after discontinuation of pembrolizumab [Table 12-6]; this was previously reported in [Ref. 5.3.5.1: P054V01MK3475: 12.2.1.1].

A listing of deaths due to AEs is presented in [16.2.7.1.1]. Full narratives for deaths in the pembrolizumab treatment group are provided in [16.2.7.2.1].

Table 12-6
Subjects With Adverse Events Resulting in Death by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	1	(0.2)	0	(0.0)	1	(0.1)
with no adverse events	508	(99.8)	502	(100.0)	1,010	(99.9)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.2.1.2 Other Serious Adverse Events

Overall, 20.8% of participants (25.0% in the pembrolizumab group and 16.5% in the placebo group) had at least 1 SAE. Consistent with the final RFS analysis, the most frequently reported SAEs (≥1% of participants) in the pembrolizumab group were basal cell carcinoma, colitis, pneumonitis, squamous cell carcinoma, and diarrhea. The most frequently reported SAEs (≥1% of participants) in the placebo group were basal cell carcinoma, cellulitis, and malignant melanoma in situ [Table 14.3-27]. Overall, 6.7% of participants (12.2% in the pembrolizumab group and 1.2% in the placebo group) had at least 1 drug-related SAE. The most frequently reported drug-related SAEs (≥1% of participants) were colitis and pneumonitis in the pembrolizumab treatment group [Table 12-7].

A listing of all subjects with SAEs and drug-related SAEs is provided in [16.2.7.1.2] and [16.2.7.1.3], respectively.

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	62	(12.2)	6	(1.2)	68	(6.7)
with no adverse events	447	(87.8)	496	(98.8)	943	(93.3)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Pneumonitis	7	(1.4)	0	(0.0)	7	(0.7)
Diarrhoea	4	(0.8)	1	(0.2)	5	(0.5)
Aspartate aminotransferase increased	3	(0.6)	0	(0.0)	3	(0.3)
Immune-mediated enterocolitis	3	(0.6)	0	(0.0)	3	(0.3)
Type 1 diabetes mellitus	3	(0.6)	0	(0.0)	3	(0.3)
Alanine aminotransferase increased	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Decreased appetite	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	1	(0.2)	1	(0.2)	2	(0.2)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Psoriasis	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Sarcoidosis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.2.2 Discontinuations Due to Adverse Events

12.2.2.1 Adverse Events Leading to Study Intervention Discontinuation

Overall, 8.8% of participants (13.9% in the pembrolizumab group and 3.6% in the placebo group) discontinued study intervention due to an AE [Table 12-8]. Consistent with the final RFS analysis, treatment with pembrolizumab was well tolerated as indicated by the low frequency of AEs resulting in treatment discontinuation. The most frequently reported AEs leading to study intervention discontinuation (≥1% of participants) were pneumonitis, colitis, and diarrhea in the pembrolizumab treatment group. Overall, 6.9% of participants (12.2% in the pembrolizumab group and 1.6% in the placebo group) had at least 1 drug-related AE leading to study intervention discontinuation [Table 12-9].

In Part 2 of the study, 11.8% of participants discontinued due to an AE [Table 14.1-3].

A listing of AEs and drug-related AEs leading to study intervention discontinuation is presented in [16.2.7.1.5], [16.2.7.1.7].

Table 12-8
Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	71	(13.9)	18	(3.6)	89	(8.8)
with no adverse events	438	(86.1)	484	(96.4)	922	(91.2)
Pneumonitis	8	(1.6)	1	(0.2)	9	(0.9)
Colitis	6	(1.2)	0	(0.0)	6	(0.6)
Diarrhoea	5	(1.0)	0	(0.0)	5	(0.5)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Pulmonary embolism	3	(0.6)	0	(0.0)	3	(0.3)
Sarcoidosis	3	(0.6)	0	(0.0)	3	(0.3)
Arthralgia	2	(0.4)	0	(0.0)	2	(0.2)
Aspartate aminotransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Fatigue	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Haemoglobin increased	1	(0.2)	0	(0.0)	1	(0.1)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Depression	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Immune-mediated enterocolitis	0	(0.0)	1	(0.2)	1	(0.1)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Malignant melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Secondary adrenocortical insufficiency	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 12-9
Subjects With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	62	(12.2)	8	(1.6)	70	(6.9)
with no adverse events	447	(87.8)	494	(98.4)	941	(93.1)
Pneumonitis	8	(1.6)	1	(0.2)	9	(0.9)
Colitis	6	(1.2)	0	(0.0)	6	(0.6)
Diarrhoea	5	(1.0)	0	(0.0)	5	(0.5)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Sarcoidosis	3	(0.6)	0	(0.0)	3	(0.3)
Arthralgia	2	(0.4)	0	(0.0)	2	(0.2)
Aspartate aminotransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Fatigue	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	1	(0.2)	0	(0.0)	1	(0.1)
Depression	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	0	(0.0)	1	(0.2)	1	(0.1)
Immune-mediated enterocolitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Secondary adrenocortical insufficiency	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.2.2.2 Adverse Events Leading to Study Intervention Interruption

Overall, 14.2% of participants (19.3% in the pembrolizumab group and 9.2% in the placebo group) had at least 1 AE resulting in dose interruption. The most frequently reported AEs resulting in dose interruption (≥1% of participants) were diarrhea, pneumonitis, increased ALT, arthralgia, increased AST, colitis, and fatigue in the pembrolizumab treatment group [Table 14.3-31]. Overall, 9.1% of participants (14.5% in the pembrolizumab group and 3.6% in the placebo group) had at least 1 drug-related AE resulting in dose interruption [Table 12-10].

A listing of AEs and drug-related AEs leading to study intervention interruption is presented in [16.2.7.1.6], [16.2.7.1.8].

Table 12-10
Subjects With Drug-Related Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	74	(14.5)	18	(3.6)	92	(9.1)
with no adverse events	435	(85.5)	484	(96.4)	919	(90.9)
Diarrhoea	10	(2.0)	3	(0.6)	13	(1.3)
Pneumonitis	10	(2.0)	2	(0.4)	12	(1.2)
Arthralgia	7	(1.4)	0	(0.0)	7	(0.7)
Alanine aminotransferase increased	5	(1.0)	1	(0.2)	6	(0.6)
Aspartate aminotransferase increased	5	(1.0)	1	(0.2)	6	(0.6)
Colitis	5	(1.0)	1	(0.2)	6	(0.6)
Fatigue	4	(0.8)	0	(0.0)	4	(0.4)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Cough	2	(0.4)	1	(0.2)	3	(0.3)
Dyspnoea	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Hyperthyroidism	2	(0.4)	0	(0.0)	2	(0.2)
Hypopituitarism	2	(0.4)	0	(0.0)	2	(0.2)
Lipase increased	2	(0.4)	2	(0.4)	4	(0.4)
Nausea	2	(0.4)	0	(0.0)	2	(0.2)
Oral lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Vomiting	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	1	(0.2)	0	(0.0)	1	(0.1)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	1	(0.2)	2	(0.2)
Blood creatinine increased	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Headache	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Influenza like illness	1	(0.2)	1	(0.2)	2	(0.2)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Sinusitis	1	(0.2)	0	(0.0)	1	(0.1)
Asthenia	0	(0.0)	1	(0.2)	1	(0.1)
Hypothyroidism	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia	0	(0.0)	1	(0.2)	1	(0.1)
Rash maculo-papular	0	(0.0)	1	(0.2)	1	(0.1)
Thrombocytopenia	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.2.3 Adverse Events of Special Interest

12.2.3.1 Summary of AEOSI

Overall, 21.6% of participants (35.2% in the pembrolizumab group and 7.8% in the placebo group) had at least 1 AEOSI [Table 12-11]. Consistent with the final RFS analysis, participants in the pembrolizumab group had more AEOSIs compared with the placebo group. The most frequently reported AEOSIs (>5% of participants) were hypothyroidism and hyperthyroidism [Table 14.3-36], with a higher proportion (≥8%) in the pembrolizumab group compared with placebo (14.9% vs 2.6 and 10.4% vs 1.2%, respectively) [Figure 14.3-1]. The majority of the AEOSIs were Grade 1 or 2 in both treatment groups [Table 12-12]. Overall, 4.0% of participants (6.7% in the pembrolizumab group and 1.2% in the placebo group) discontinued study intervention due to an AEOSI [Table 12-11].

Drug-related AEOSIs were reported for 19.3% of participants (32.4% in the pembrolizumab group and 6.0% in the placebo group) and 3.9% of participants (6.7% in the pembrolizumab group and 1.0% in the placebo group) had a drug-related AEOSI leading to study intervention discontinuation. Serious AEOSIs were reported for 4.3% of participants (7.9% in the pembrolizumab group and 0.6% in the placebo group) and 1.5% of participants (2.4% in the pembrolizumab group and 0.6% in the placebo group) discontinued study intervention due to a serious AEOSI [Table 12-11].

The mean TTO of the first AEOSI was 127 days (standard deviation: 101.3) [Table 14.3-40].

AEOSI results for Part 2 of the study were consistent with Part 1: 26.5% of participants had at least 1 AEOSI. [Table 14.3-35], and the most frequently reported (≥10% of participants) were Grade 1 and 2 hypothyroidism and hyperthyroidism [Table 14.3-38]. Overall, 4.1% of participants discontinued study intervention due to an AEOSI in Part 2 of the study [Table 14.3-35].

In Part 2, drug-related AEOSIs were reported for 25.3% of participants and 4.1% had a drug-related AEOSI leading to study intervention discontinuation. Serious AEOSIs were reported for 4.7% of participants and 1.8% discontinued study intervention due to a serious AEOSI [Table 14.3-35].

Participants with AEOSIs by maximum toxicity grade (incidence > 0%) are presented in [Table 14.3-37], AEOSIs summaries by AEOSI category are provided in [Table 14.3-41] through [Table 14.3-58]. A summary of concomitant corticosteroid use for AEOSIs is provided in [Table 14.3-39] and a listing of concomitant systemic corticosteroid use for AEOSIs is provided in [16.2.7.1.10].

A listing of AEOSIs is presented in [16.2.7.1.9].

Table 12-11
Adverse Event Summary
AEOSI
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
with no adverse event	330	(64.8)	463	(92.2)	793	(78.4)
with drug-related† adverse events	165	(32.4)	30	(6.0)	195	(19.3)
with toxicity grade 3-5 adverse events	39	(7.7)	3	(0.6)	42	(4.2)
with toxicity grade 3-5 drug-related adverse events	34	(6.7)	3	(0.6)	37	(3.7)
with serious adverse events	40	(7.9)	3	(0.6)	43	(4.3)
with serious drug-related adverse events	36	(7.1)	2	(0.4)	38	(3.8)
who died	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)
discontinued drug due to an adverse event	34	(6.7)	6	(1.2)	40	(4.0)
discontinued drug due to a drug-related adverse event	34	(6.7)	5	(1.0)	39	(3.9)
discontinued drug due to a serious adverse event	12	(2.4)	3	(0.6)	15	(1.5)
discontinued drug due to a serious drug-related adverse event	12	(2.4)	2	(0.4)	14	(1.4)

† Determined by the investigator to be related to the drug.

AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

AEs of special interest per ECI guidance.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 12-12
Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
Grade 1	43	(8.4)	21	(4.2)	64	(6.3)
Grade 2	97	(19.1)	15	(3.0)	112	(11.1)
Grade 3	34	(6.7)	3	(0.6)	37	(3.7)
Grade 4	5	(1.0)	0	(0.0)	5	(0.5)
with no adverse events	330	(64.8)	463	(92.2)	793	(78.4)
Hyperthyroidism	**53**	**(10.4)**	**6**	**(1.2)**	**59**	**(5.8)**
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypothyroidism	**76**	**(14.9)**	**13**	**(2.6)**	**89**	**(8.8)**
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.
Grades are based on NCI CTCAE version 4.03.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

12.2.3.2 Pregnancies

As of the DCO, there were 2 pregnancies reported during KEYNOTE-054. [redacted]

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 are presented in [16.2.7.2.1].

Participant narratives may have used data from the safety database CIOMS reports in [16.2.7.2.2], which was independently maintained and may have minor differences in content that do not impact the key narrative information.

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

The mean changes in laboratory values from baseline over time are generally consistent with the established safety profile for pembrolizumab and do not reveal any new safety concerns [Table 14.4-1]. Shifts in toxicity grade from baseline to worst postbaseline values were mainly Grades ≤ 2. Notable shifts to Grade 3 or 4 in the pembrolizumab group included increased ALT (2.8% of participants), increased AST (2.0% of participants), and hyponatremia (2.4% of participants) [Table 14.4-3].

A summary of increases in highest laboratory test toxicity grade from baseline is provided in [Table 14.4-2].

12.3.2.2 Individual Participant Changes in Laboratory Values

Listing of laboratory measurements by participant are provided in [16.2.8].

12.3.2.3 Specific Clinically Meaningful Laboratory Abnormalities

No new specific clinically meaningful laboratory abnormalities were reported since the final RFS analysis.

One participant met the predetermined criteria for potential DILI (aminotransaminase [ALT and AST] ≥ 3X ULN, bilirubin ≥ 2X ULN, and alkaline phosphatase <2X ULN). As reported in [Ref. 5.3.5.1: P054V01MK3475: 12.3.2.3], the investigator determined that the laboratory abnormalities were a result of a concurrent pancreatitis and not DILI.

Participants with LFTs results that met predetermined criteria are in [Table 12-13].

Table 12-13
Subjects With Liver Function Laboratory Findings That Met Predetermined Criteria
Treatment and Follow-Up Phases
ASaT Population

Criteria	Pembrolizumab		Placebo	
	n/m	(%)	n/m	(%)
Subjects in population	509		502	
Alanine Aminotransferase				
≥3 x ULN	25/507	(4.9)	10/498	(2.0)
≥5 x ULN	14/507	(2.8)	2/498	(0.4)
≥10 x ULN	4/507	(0.8)	1/498	(0.2)
≥20 x ULN	1/507	(0.2)	0/498	(0.0)
Aspartate Aminotransferase				
≥3 x ULN	26/507	(5.1)	8/496	(1.6)
≥5 x ULN	10/507	(2.0)	2/496	(0.4)
≥10 x ULN	1/507	(0.2)	0/496	(0.0)
≥20 x ULN	1/507	(0.2)	0/496	(0.0)
Aminotransferase (ALT or AST)				
≥3 x ULN	33/507	(6.5)	14/496	(2.8)
≥5 x ULN	16/507	(3.2)	3/496	(0.6)
≥10 x ULN	4/507	(0.8)	1/496	(0.2)
≥20 x ULN	1/507	(0.2)	0/496	(0.0)

Subjects With Liver Function Laboratory Findings That Met Predetermined Criteria
Treatment and Follow-Up Phases
ASaT Population

Criteria	Pembrolizumab		Placebo	
	n/m	(%)	n/m	(%)
Bilirubin				
≥2 x ULN	10/507	(2.0)	10/498	(2.0)
Alkaline Phosphatase				
≥1.5 x ULN	26/506	(5.1)	9/494	(1.8)
Aminotransferase (ALT or AST) and Bilirubin				
AT ≥3 x ULN and BILI ≥1.5 x ULN	3/507	(0.6)	0/498	(0.0)
AT ≥3 x ULN and BILI ≥2 x ULN	1/507	(0.2)	0/498	(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	1/507	(0.2)	0/498	(0.0)

n = Number of Subjects with postbaseline test results (or combination of test results from the same day) that met predetermined criteria.
m = Number of Subjects 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.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-addili]

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

Vital signs and physical examinations were not part of the analysis plan.

12.5 Safety Results Summary

- The safety results of this report are generally consistent with the established safety profile for pembrolizumab. The majority of subjects (>90%) in both treatment groups had at least 1 AE.
- As expected, a higher proportion of subjects in the pembrolizumab group had drug-related AEs, Grade 3 to 5 AEs, SAEs, and AEOSIs compared with placebo.
- The overall severity and nature of the AEOSIs were similar to the established pembrolizumab safety profile and the AEOSIs were generally manageable with dose interruption, discontinuation, and/or treatment with corticosteroids.
- No new safety concerns were identified for pembrolizumab.

13 CONCLUSIONS

Efficacy Conclusions

- Adjuvant therapy with pembrolizumab provides a therapeutic benefit to patients with resected Stage III melanoma, who were at high risk of recurrence, as demonstrated by a statistically significant and clinical meaningful benefit in DMFS and sustained RFS benefit compared with placebo. Similar DMFS benefit and sustained RFS benefit compared with placebo was observed across all subgroups including tumor stage and BRAF-mutation status.
- The therapeutic benefit is similar for the PD-L1-positive population, demonstrated by a statistically significant and clinical meaningful DMFS benefit and sustained RFS benefit compared with placebo.

Safety Conclusions

- The safety results of this report are generally consistent with the final RFS analysis (DCO 02-OCT-2017).
- Pembrolizumab administered in the adjuvant setting for resected, Stage III melanoma continues to demonstrate a consistent and well-tolerated established safety profile.
- Safety profile in the participants that were rechallenged and crossed over in the Part 2 of the study was consistent with the established safety profile of pembrolizumab.
- The AEOSIs were similar to the established pembrolizumab safety profile and were generally manageable with dose interruption, discontinuation, and/or treatment with corticosteroids.
- There were no new safety concerns for pembrolizumab in this updated analysis (or study report) of KEYNOTE-054.

14 SUPPLEMENTAL TABLES AND/OR FIGURES

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

14.1.1 Participant Disposition, Exposure, Protocol Deviations, Demographics, Baseline Characteristics, and Medical History

14.1.1.1 Participant Disposition

Table 14.1-1

Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	514		505		1019	
Status for Trial						
Completed	1	(0.2)	19	(3.8)	20	(2.0)
Discontinued	12	(2.3)	120	(23.8)	132	(13.0)
Adverse Event	1	(0.2)	19	(3.8)	20	(2.0)
Not Associated With Covid-19, No Further Information	1	(0.2)	17	(3.4)	18	(1.8)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	2	(0.4)	2	(0.2)
Lost To Follow-Up	0	(0.0)	1	(0.2)	1	(0.1)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Progressive Disease	9	(1.8)	77	(15.2)	86	(8.4)
Not Associated With Covid-19, No Further Information	6	(1.2)	33	(6.5)	39	(3.8)
Not Associated With Covid-19, Subsequently Died	3	(0.6)	44	(8.7)	47	(4.6)
Randomized By Mistake Without Study Treatment	0	(0.0)	1	(0.2)	1	(0.1)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Withdrawal By Subject	2	(0.4)	16	(3.2)	18	(1.8)
Not Associated With Covid-19, No Further Information	1	(0.2)	15	(3.0)	16	(1.6)
Not Associated With Covid-19, Subsequently Died	1	(0.2)	1	(0.2)	2	(0.2)
Other	0	(0.0)	6	(1.2)	6	(0.6)
Not Associated With Covid-19, No Further Information	0	(0.0)	5	(1.0)	5	(0.5)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.2)	1	(0.1)
Status Not Recorded	501	(97.5)	366	(72.5)	867	(85.1)

Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Status for Study Medication in Trial Segment Treatment						
Started	514		505		1019	
Completed	297	(57.8)	300	(59.4)	597	(58.6)
Discontinued	217	(42.2)	205	(40.6)	422	(41.4)
Adverse Event	73	(14.2)	11	(2.2)	84	(8.2)
Lost To Follow-Up	1	(0.2)	0	(0.0)	1	(0.1)
Non-Compliance With Study Drug	2	(0.4)	0	(0.0)	2	(0.2)
Progressive Disease	113	(22.0)	184	(36.4)	297	(29.1)
Randomized By Mistake Without Study Treatment	3	(0.6)	1	(0.2)	4	(0.4)
Screen Failure	1	(0.2)	0	(0.0)	1	(0.1)
Withdrawal By Subject	19	(3.7)	7	(1.4)	26	(2.6)
Other	5	(1.0)	2	(0.4)	7	(0.7)
Status for Study Medication in Trial Segment Crossover/Rechallenge treatment						
Started	19		151		170	
Completed	1	(5.3)	19	(12.6)	20	(11.8)
Discontinued	12	(63.2)	119	(78.8)	131	(77.1)
Adverse Event	1	(5.3)	19	(12.6)	20	(11.8)
Not Associated With Covid-19, No Further Information	1	(5.3)	17	(11.3)	18	(10.6)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	2	(1.3)	2	(1.2)
Lost To Follow-Up	0	(0.0)	1	(0.7)	1	(0.6)

Disposition of Subjects
ITT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Status for Study Medication in Trial Segment Crossover/Rechallenge treatment						
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Progressive Disease	9	(47.4)	77	(51.0)	86	(50.6)
Not Associated With Covid-19, No Further Information	6	(31.6)	33	(21.9)	39	(22.9)
Not Associated With Covid-19, Subsequently Died	3	(15.8)	44	(29.1)	47	(27.6)
Withdrawal By Subject	2	(10.5)	16	(10.6)	18	(10.6)
Not Associated With Covid-19, No Further Information	1	(5.3)	15	(9.9)	16	(9.4)
Not Associated With Covid-19, Subsequently Died	1	(5.3)	1	(0.7)	2	(1.2)
Other	0	(0.0)	6	(4.0)	6	(3.5)
Not Associated With Covid-19, No Further Information	0	(0.0)	5	(3.3)	5	(2.9)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Status Not Recorded	6	(31.6)	13	(8.6)	19	(11.2)

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

Each subject is counted once for Study Medication Disposition.

Status not Recorded for subjects that are continuing in trial or trial segment.

Database Cutoff Date: 03APR2020

Source: [P054V02MK3475: adam-adsl]

Table 14.1-2

Summary of Status for Part 2 of Trial
ITT Population

Status for Part 2 of Trial	Pembrolizumab (N=514)	Placebo (N=505)
Crossed over to pembrolizumab	0 (0.0%)	151 (29.9%)
Rechallenged with pembrolizumab	19 (3.7%)	0 (0.0%)

Source: [P054V02MK3475: adam-adsl]

Table 14.1-3

Disposition of Subjects
ASaT Population - Part 2

	Rechallenged with Pembrolizumab		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	19		151		170	
Status for Trial						
Completed	1	(5.3)	19	(12.6)	20	(11.8)
Discontinued	12	(63.2)	119	(78.8)	131	(77.1)
Adverse Event	1	(5.3)	19	(12.6)	20	(11.8)
Not Associated With Covid-19, No Further Information	1	(5.3)	17	(11.3)	18	(10.6)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	2	(1.3)	2	(1.2)
Lost To Follow-Up	0	(0.0)	1	(0.7)	1	(0.6)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Progressive Disease	9	(47.4)	77	(51.0)	86	(50.6)
Not Associated With Covid-19, No Further Information	6	(31.6)	33	(21.9)	39	(22.9)
Not Associated With Covid-19, Subsequently Died	3	(15.8)	44	(29.1)	47	(27.6)
Withdrawal By Subject	2	(10.5)	16	(10.6)	18	(10.6)
Not Associated With Covid-19, No Further Information	1	(5.3)	15	(9.9)	16	(9.4)
Not Associated With Covid-19, Subsequently Died	1	(5.3)	1	(0.7)	2	(1.2)
Other	0	(0.0)	6	(4.0)	6	(3.5)
Not Associated With Covid-19, No Further Information	0	(0.0)	5	(3.3)	5	(2.9)
Not Associated With Covid-19, Subsequently Died	0	(0.0)	1	(0.7)	1	(0.6)
Status Not Recorded	6	(31.6)	13	(8.6)	19	(11.2)

Disposition of Subjects
ASaT Population - Part 2

	Rechallenged with Pembrolizumab		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
Status for Study Medication in Trial Segment Treatment						
Started	19		151		170	
Completed	18	(94.7)	52	(34.4)	70	(41.2)
Discontinued	1	(5.3)	99	(65.6)	100	(58.8)
Adverse Event	1	(5.3)	0	(0.0)	1	(0.6)
Progressive Disease	0	(0.0)	99	(65.6)	99	(58.2)

If the overall count of subjects is calculated and displayed within a section in the first row, then it is used as the denominator for the percentage calculation. Otherwise, subjects in population is used as the denominator for the percentage calculation.
Each subject is counted once for Study Medication Disposition.
Status not Recorded for subjects that are continuing in trial or trial segment.
Database Cutoff Date: 03APR2020

Source: [P054V02MK3475: adam-adsl]

14.1.1.2 Protocol Deviations

Table 14.1-4
Summary of Protocol Deviations

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
With one or more protocol deviations	115	(22.6)	140	(27.9)	255	(25.2)
With no protocol deviations	394	(77.4)	362	(72.1)	756	(74.8)
Discontinuation Criteria	**3**	**(0.6)**	**29**	**(5.8)**	**32**	**(3.2)**
Participants assigned to pembrolizumab/placebo who develop an adverse event for which the protocol instructs study treatment discontinuation but were not discontinued from pembrolizumab/placebo	0	(0.0)	8	(1.6)	8	(0.8)
Withdrawal criteria not followed per protocol: study treatment not discontinued in time despite disease progression or occurrence of new malignancy	3	(0.6)	23	(4.6)	26	(2.6)
Inclusion/ Exclusion Criteria	**5**	**(1.0)**	**9**	**(1.8)**	**14**	**(1.4)**
In transit metastasis or satellitosis (part 1)	2	(0.4)	7	(1.4)	9	(0.9)
Lab test required per protocol was not done or out of the allowed window at baseline (part 1)	0	(0.0)	1	(0.2)	1	(0.1)
Patient had a mucosal melanoma (part 1)	1	(0.2)	0	(0.0)	1	(0.1)
Patient had uncontrolled thyroid disorder at baseline (part 1)	1	(0.2)	0	(0.0)	1	(0.1)
Patient not disease-free at time of randomization (part 1)	0	(0.0)	1	(0.2)	1	(0.1)
Prior treatment with IFN with known lymph node involvement (part 1)	1	(0.2)	0	(0.0)	1	(0.1)
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)

Summary of Protocol Deviations

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Safety Reporting	**92**	**(18.1)**	**82**	**(16.3)**	**174**	**(17.2)**
COVID-19: Safety lab sample got lost during processing in the lab	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were collected at an external facility and processed at on-site lab, but not all required tests were included	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were missed	32	(6.3)	25	(5.0)	57	(5.6)
COVID-19: Safety labs were performed at an external facility and not all required tests were included	2	(0.4)	0	(0.0)	2	(0.2)
COVID-19: Safety labs were performed but not all required tests were included	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Safety labs were performed out of window	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Urine analysis was missed	1	(0.2)	0	(0.0)	1	(0.1)
Reportable safety event not reported within 24h of awareness	58	(11.4)	57	(11.4)	115	(11.4)
Study Intervention	**3**	**(0.6)**	**4**	**(0.8)**	**7**	**(0.7)**
Participants who received incorrect study treatment and/or were administered improperly stored study treatment if deemed unacceptable for treatment	3	(0.6)	4	(0.8)	7	(0.7)
Trial Procedures	**49**	**(9.6)**	**62**	**(12.4)**	**111**	**(11.0)**
COVID-19: Delay in collecting patient survival information	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Imaging assessment was not performed	17	(3.3)	12	(2.4)	29	(2.9)
COVID-19: On-site visit was replaced by phone call or e-mail contact only	37	(7.3)	29	(5.8)	66	(6.5)
COVID-19: Questionnaires were completed over the phone without official transcripts	1	(0.2)	1	(0.2)	2	(0.2)
COVID-19: Questionnaires were not completed by patient	17	(3.3)	13	(2.6)	30	(3.0)

Summary of Protocol Deviations

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Trial Procedures	**49**	**(9.6)**	**62**	**(12.4)**	**111**	**(11.0)**
COVID-19: Skin examination was missed	39	(7.7)	33	(6.6)	72	(7.1)
COVID-19: TR samples not collected	1	(0.2)	2	(0.4)	3	(0.3)
Imaging work up repeatedly not done or not performed per protocol	0	(0.0)	2	(0.4)	2	(0.2)
Incomplete or missing source documentation	0	(0.0)	13	(2.6)	13	(1.3)
No patient data entered in clinical database in a significant period of time	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl] [P054V02MK3475: sdtm-dv]

Table 14.1-5
Summary of Protocol Deviations Associated With COVID-19

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
With one or more protocol deviations associated with COVID-19	51	(10.0)	47	(9.4)	98	(9.7)
With no protocol deviations associated with COVID-19	458	(90.0)	455	(90.6)	913	(90.3)
Safety Reporting	**37**	**(7.3)**	**27**	**(5.4)**	**64**	**(6.3)**
COVID-19: Safety lab sample got lost during processing in the lab	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were collected at an external facility and processed at on-site lab, but not all required tests were included	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Safety labs were missed	32	(6.3)	25	(5.0)	57	(5.6)
COVID-19: Safety labs were performed at an external facility and not all required tests were included	2	(0.4)	0	(0.0)	2	(0.2)
COVID-19: Safety labs were performed but not all required tests were included	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Safety labs were performed out of window	1	(0.2)	0	(0.0)	1	(0.1)
COVID-19: Urine analysis was missed	1	(0.2)	0	(0.0)	1	(0.1)
Trial Procedures	**49**	**(9.6)**	**46**	**(9.2)**	**95**	**(9.4)**
COVID-19: Delay in collecting patient survival information	0	(0.0)	1	(0.2)	1	(0.1)
COVID-19: Imaging assessment was not performed	17	(3.3)	12	(2.4)	29	(2.9)
COVID-19: On-site visit was replaced by phone call or e-mail contact only	37	(7.3)	29	(5.8)	66	(6.5)
COVID-19: Questionnaires were completed over the phone without official transcripts	1	(0.2)	1	(0.2)	2	(0.2)
COVID-19: Questionnaires were not completed by patient	17	(3.3)	13	(2.6)	30	(3.0)
COVID-19: Skin examination was missed	39	(7.7)	33	(6.6)	72	(7.1)

Summary of Protocol Deviations Associated With COVID-19

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Trial Procedures	**49**	**(9.6)**	**46**	**(9.2)**	**95**	**(9.4)**
COVID-19: TR samples not collected	1	(0.2)	2	(0.4)	3	(0.3)

Every subject is counted a single time for each applicable row and column.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl] [P054V02MK3475: sdtm-dv]

Table 14.1-6
Summary of Important Protocol Deviations Considered to be Clinically Important

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
With one or more clinically important protocol deviations	24	(4.7)	19	(3.8)	43	(4.3)
With no clinically important protocol deviations	485	(95.3)	483	(96.2)	968	(95.7)
Inclusion/ Exclusion Criteria	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Patient had a mucosal melanoma (part 1)	1	(0.2)	0	(0.0)	1	(0.1)
Patient not disease-free at time of randomization (part 1)	0	(0.0)	1	(0.2)	1	(0.1)
Safety Reporting	**23**	**(4.5)**	**18**	**(3.6)**	**41**	**(4.1)**
Reportable safety event not reported within 24h of awareness	23	(4.5)	18	(3.6)	41	(4.1)

Every subject is counted a single time for each applicable row and column.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl] [P054V02MK3475: sdtm-dv]

14.1.1.3 Demographic and Other Baseline Characteristics

14.1.1.3.1 Demographic and Baseline Disease Characteristics

Table 14.1-7
Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	514		505		1,019	
Gender						
Male	324	(63.0)	304	(60.2)	628	(61.6)
Female	190	(37.0)	201	(39.8)	391	(38.4)
Age (Years)						
< 50	193	(37.5)	186	(36.8)	379	(37.2)
50 to 64	196	(38.1)	193	(38.2)	389	(38.2)
≥ 65	125	(24.3)	126	(25.0)	251	(24.6)
Mean	53.7		53.6		53.7	
SD	13.6		14.2		13.9	
Median	54.0		54.0		54.0	
Range	19 to 88		19 to 83		19 to 88	
Region						
North America	38	(7.4)	37	(7.3)	75	(7.4)
Europe	341	(66.3)	337	(66.7)	678	(66.5)
Australia/New Zealand	111	(21.6)	111	(22.0)	222	(21.8)
Other	24	(4.7)	20	(4.0)	44	(4.3)
PD-L1 Status						
PD-L1 Positive	428	(83.3)	425	(84.2)	853	(83.7)
PD-L1 Negative	59	(11.5)	57	(11.3)	116	(11.4)
Unknown	27	(5.3)	23	(4.6)	50	(4.9)
BRAF-Mutation Status						
Mutation Detected	244	(47.5)	262	(51.9)	506	(49.7)
Mutation Not Detected	234	(45.5)	215	(42.6)	449	(44.1)
Unknown	36	(7.0)	28	(5.5)	64	(6.3)
ECOG						
0	485	(94.4)	475	(94.1)	960	(94.2)
1	29	(5.6)	30	(5.9)	59	(5.8)
Primary Cutaneous Melanoma*						
Cutaneous	455	(88.5)	460	(91.1)	915	(89.8)
Ocular	1	(0.2)	0	(0.0)	1	(0.1)

Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Unknown	58	(11.3)	45	(8.9)	103	(10.1)
Location of Primary Cutaneous Melanoma						
Head and Neck	53	(10.3)	66	(13.1)	119	(11.7)
Extremity	203	(39.5)	196	(38.8)	399	(39.2)
Trunk	196	(38.1)	189	(37.4)	385	(37.8)
Unknown	62	(12.1)	54	(10.7)	116	(11.4)
Breslow Thickness						
≤ 1.0 mm	61	(11.9)	78	(15.4)	139	(13.6)
1.01 to 2.0 mm	99	(19.3)	102	(20.2)	201	(19.7)
2.01 to 4.0 mm	156	(30.4)	151	(29.9)	307	(30.1)
> 4.0 mm	125	(24.3)	111	(22.0)	236	(23.2)
Unknown	73	(14.2)	63	(12.5)	136	(13.3)
AJCC 7 Overall Cancer Stage						
Stage IIIA (> 1 mm)	80	(15.6)	80	(15.8)	160	(15.7)
Stage IIIB	237	(46.1)	230	(45.5)	467	(45.8)
Stage IIIC (1-3 LN+)	95	(18.5)	93	(18.4)	188	(18.4)
Stage IIIC (≥ 4 LN+)	102	(19.8)	102	(20.2)	204	(20.0)
AJCC 8 Overall Cancer Stage						
Stage IIIA	42	(8.2)	40	(7.9)	82	(8.0)
Stage IIIB	163	(31.7)	190	(37.6)	353	(34.6)
Stage IIIC	267	(51.9)	235	(46.5)	502	(49.3)
Stage IIID	20	(3.9)	21	(4.2)	41	(4.0)
Unknown	22	(4.3)	19	(3.8)	41	(4.0)
Number of LN+ (pathological)						
1	226	(44.0)	238	(47.1)	464	(45.5)
2-3	176	(34.2)	164	(32.5)	340	(33.4)
≥ 4	112	(21.8)	103	(20.4)	215	(21.1)
Type of LN+ Involvement						
Microscopic	185	(36.0)	160	(31.7)	345	(33.9)
Macroscopic	329	(64.0)	345	(68.3)	674	(66.1)
Ulceration						
No	230	(44.7)	251	(49.7)	481	(47.2)

Subject Characteristics
(ITT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Yes	208	(40.5)	197	(39.0)	405	(39.7)
Unknown	76	(14.8)	57	(11.3)	133	(13.1)
Type of Surgery						
Axillary lymphadenectomy	192	(37.4)	194	(38.4)	386	(37.9)
Inguinal lymphadenectomy	137	(26.7)	130	(25.7)	267	(26.2)
Modified radical neck dissection	58	(11.3)	68	(13.5)	126	(12.4)
Other	4	(0.8)	5	(1.0)	9	(0.9)
Multiple types of surgery	123	(23.9)	108	(21.4)	231	(22.7)
Timing of First Dose of Study Therapy						
≤ 13 weeks from date of surgery	500	(97.3)	490	(97.0)	990	(97.2)
> 13 weeks from date of surgery	9	(1.8)	12	(2.4)	21	(2.1)
Unknown	5	(1.0)	3	(0.6)	8	(0.8)

*One subject with ocular primary melanoma was randomized.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl]

Table 14.1-8

Subjects by Age Category and Gender
ITT Population

	Pembrolizumab			Placebo			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Subjects in population	324	190	514	304	201	505	628	391	1,019
Age (Years)									
<50	113	80	193	108	78	186	221	158	379
50 to 64	125	71	196	114	79	193	239	150	389
65 to 74	67	30	97	62	36	98	129	66	195
≥75	19	9	28	20	8	28	39	17	56
Mean	54.7	52.1	53.7	54.0	52.9	53.6	54.4	52.5	53.7
SD	13.3	14.1	13.6	14.7	13.3	14.2	13.9	13.7	13.9
Median	55.0	53.0	54.0	54.0	54.0	54.0	55.0	53.0	54.0
Range	19 to 85	19 to 88	19 to 88	19 to 83	19 to 82	19 to 83	19 to 85	19 to 88	19 to 88
(Data Cutoff Date: 03APR2020).									

Source: [P054V02MK3475: adam-adsl]

Table 14.1-9

Subject Characteristics
ITT Population- Part 2

	Rechallenged with Pembrolizumab		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	19		151		170	
Gender						
Male	12	(63.2)	94	(62.3)	106	(62.4)
Female	7	(36.8)	57	(37.7)	64	(37.6)
Age (Years)						
< 50	8	(42.1)	49	(32.5)	57	(33.5)
50 to 64	9	(47.4)	58	(38.4)	67	(39.4)
≥ 65	2	(10.5)	44	(29.1)	46	(27.1)
Mean	49.9		54.8		54.3	
SD	12.6		13.5		13.5	
Median	51.0		56.0		55.5	
Range	25 to 67		24 to 78		24 to 78	
Region						
North America	0	(0.0)	8	(5.3)	8	(4.7)
Europe	13	(68.4)	102	(67.5)	115	(67.6)
Australia/New Zealand	6	(31.6)	36	(23.8)	42	(24.7)
Other	0	(0.0)	5	(3.3)	5	(2.9)
PD-L1 Status						
PD-L1 Positive	17	(89.5)	116	(76.8)	133	(78.2)
PD-L1 Negative	2	(10.5)	24	(15.9)	26	(15.3)
Unknown	0	(0.0)	11	(7.3)	11	(6.5)
BRAF-Mutation Status						
Mutation Detected	10	(52.6)	86	(57.0)	96	(56.5)
Mutation Not Detected	8	(42.1)	62	(41.1)	70	(41.2)
Unknown	1	(5.3)	3	(2.0)	4	(2.4)
ECOG						
0	19	(100.0)	140	(92.7)	159	(93.5)
1	0	(0.0)	11	(7.3)	11	(6.5)
Primary Cutaneous Melanoma						
Cutaneous	16	(84.2)	142	(94.0)	158	(92.9)

Subject Characteristics
ITT Population- Part 2

	Rechallenged with Pembrolizumab		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
Unknown	3	(15.8)	9	(6.0)	12	(7.1)
Location of Primary Cutaneous Melanoma						
Head and Neck	0	(0.0)	25	(16.6)	25	(14.7)
Extremity	8	(42.1)	54	(35.8)	62	(36.5)
Trunk	8	(42.1)	63	(41.7)	71	(41.8)
Unknown	3	(15.8)	9	(6.0)	12	(7.1)
Breslow Thickness						
≤ 1.0 mm	1	(5.3)	24	(15.9)	25	(14.7)
1.01 to 2.0 mm	4	(21.1)	25	(16.6)	29	(17.1)
2.01 to 4.0 mm	7	(36.8)	48	(31.8)	55	(32.4)
> 4.0 mm	4	(21.1)	42	(27.8)	46	(27.1)
Unknown	3	(15.8)	12	(7.9)	15	(8.8)
AJCC 7 Overall Cancer Stage						
Stage IIIA (> 1 mm)	3	(15.8)	22	(14.6)	25	(14.7)
Stage IIIB	9	(47.4)	57	(37.7)	66	(38.8)
Stage IIIC (1-3 LN+)	4	(21.1)	32	(21.2)	36	(21.2)
Stage IIIC (≥ 4 LN+)	3	(15.8)	40	(26.5)	43	(25.3)
AJCC 8 Overall Cancer Stage						
Stage IIIA	2	(10.5)	10	(6.6)	12	(7.1)
Stage IIIB	6	(31.6)	43	(28.5)	49	(28.8)
Stage IIIC	10	(52.6)	84	(55.6)	94	(55.3)
Stage IIID	0	(0.0)	11	(7.3)	11	(6.5)
Unknown	1	(5.3)	3	(2.0)	4	(2.4)
Number of LN+ (pathological)						
1	13	(68.4)	61	(40.4)	74	(43.5)
2-3	3	(15.8)	49	(32.5)	52	(30.6)
≥ 4	3	(15.8)	41	(27.2)	44	(25.9)
Type of LN+ Involvement						
Microscopic	8	(42.1)	45	(29.8)	53	(31.2)
Macroscopic	11	(57.9)	106	(70.2)	117	(68.8)
Ulceration						

Subject Characteristics
ITT Population- Part 2

	Rechallenged with Pembrolizumab		Crossover to Pembrolizumab		Total	
	n	(%)	n	(%)	n	(%)
No	6	(31.6)	67	(44.4)	73	(42.9)
Yes	9	(47.4)	71	(47.0)	80	(47.1)
Unknown	4	(21.1)	13	(8.6)	17	(10.0)
Type of Surgery						
Axillary lymphadenectomy	8	(42.1)	51	(33.8)	59	(34.7)
Inguinal lymphadenectomy	8	(42.1)	47	(31.1)	55	(32.4)
Modified radical neck dissection	2	(10.5)	26	(17.2)	28	(16.5)
Multiple types of surgery	1	(5.3)	27	(17.9)	28	(16.5)
Timing of First Dose of Study Therapy						
≤ 13 weeks from date of surgery	19	(100.0)	149	(98.7)	168	(98.8)
> 13 weeks from date of surgery	0	(0.0)	2	(1.3)	2	(1.2)
(Database Cutoff Date: 03APR2020).						

Source: [P054V02MK3475: adam-adsl]

14.1.1.3.2 Prior and Concomitant Treatments

Table 14.1-10
Subjects With Specific Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
ITT Population

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
Subjects in population	514		505	
With one or more concomitant medications	401	(78.0)	339	(67.1)
With no concomitant medications	113	(22.0)	166	(32.9)
alimentary tract and metabolism				
antidiarrheals, intestinal antiinflammatory/antiinfective agents	**55**	**(10.7)**	**28**	**(5.5)**
Bifidobacterium (unspecified)	1	(0.2)	0	(0.0)
Enterococcus faecium	1	(0.2)	0	(0.0)
Lactobacillus acidophilus	1	(0.2)	1	(0.2)
Lactobacillus plantarum	1	(0.2)	0	(0.0)
Saccharomyces boulardii	4	(0.8)	0	(0.0)
albumin tannate	1	(0.2)	0	(0.0)
aluminum silicate	1	(0.2)	0	(0.0)
berberine	1	(0.2)	0	(0.0)
charcoal, activated	1	(0.2)	0	(0.0)
dextrose (+) potassium chloride (+) sodium chloride (+) sodium citrate	1	(0.2)	0	(0.0)
loperamide	14	(2.7)	5	(1.0)
loperamide hydrochloride	30	(5.8)	13	(2.6)
mesalamine	1	(0.2)	0	(0.0)
nifuroxazide	3	(0.6)	0	(0.0)
paromomycin	1	(0.2)	0	(0.0)
probiotics (unspecified)	2	(0.4)	1	(0.2)
racecadotril	1	(0.2)	5	(1.0)
rifaximin	1	(0.2)	0	(0.0)
smectite	4	(0.8)	7	(1.4)
sulfasalazine	1	(0.2)	0	(0.0)
antiemetics and antinauseants	**11**	**(2.1)**	**14**	**(2.8)**
dronabinol	1	(0.2)	0	(0.0)
granisetron	1	(0.2)	0	(0.0)
granisetron hydrochloride	1	(0.2)	1	(0.2)
metopimazine	1	(0.2)	1	(0.2)
ondansetron	5	(1.0)	2	(0.4)
ondansetron hydrochloride	3	(0.6)	10	(2.0)
digestives, incl. enzymes	**1**	**(0.2)**	**2**	**(0.4)**
alpha amylase	0	(0.0)	1	(0.2)
digestive enzymes	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
alimentary tract and metabolism				
digestives, incl. enzymes	**1**	**(0.2)**	**2**	**(0.4)**
protease	0	(0.0)	1	(0.2)
drugs for acid related disorders	**79**	**(15.4)**	**44**	**(8.7)**
aluminum hydroxide (+) magnesium hydroxide	1	(0.2)	0	(0.0)
aluminum hydroxide (+) magnesium hydroxide (+) magnesium trisilicate	1	(0.2)	0	(0.0)
aluminum hydroxide (+) magnesium hydroxide (+) simethicone	1	(0.2)	1	(0.2)
calcium carbonate	2	(0.4)	0	(0.0)
calcium carbonate (+) magnesium carbonate	2	(0.4)	0	(0.0)
calcium carbonate (+) sodium alginate (+) sodium bicarbonate	1	(0.2)	0	(0.0)
cimetidine	1	(0.2)	0	(0.0)
esomeprazole	14	(2.7)	6	(1.2)
famotidine	2	(0.4)	1	(0.2)
lansoprazole	4	(0.8)	4	(0.8)
magnesium oxide	1	(0.2)	1	(0.2)
omeprazole	20	(3.9)	12	(2.4)
pantoprazole	21	(4.1)	6	(1.2)
pantoprazole sodium	15	(2.9)	8	(1.6)
potassium bicarbonate (+) sodium alginate	0	(0.0)	1	(0.2)
rabeprazole sodium	0	(0.0)	1	(0.2)
ranitidine	4	(0.8)	5	(1.0)
ranitidine hydrochloride	2	(0.4)	1	(0.2)
sodium alginate (+) sodium bicarbonate	0	(0.0)	1	(0.2)
sucralfate	2	(0.4)	0	(0.0)
teprenone	1	(0.2)	1	(0.2)
drugs for constipation	**23**	**(4.5)**	**22**	**(4.4)**
ascorbic acid (+) electrolytes (unspecified) (+) polyethylene glycol 3350	1	(0.2)	0	(0.0)
bisacodyl	0	(0.0)	4	(0.8)
citric acid (+) magnesium oxide (+) sodium picosulfate	1	(0.2)	0	(0.0)
docusate sodium	4	(0.8)	1	(0.2)
docusate sodium (+) sennosides	3	(0.6)	3	(0.6)
electrolytes (unspecified) (+) polyethylene glycol	0	(0.0)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
alimentary tract and metabolism				
drugs for constipation	**23**	**(4.5)**	**22**	**(4.4)**
electrolytes (unspecified) (+) polyethylene glycol 3350	1	(0.2)	2	(0.4)
electrolytes (unspecified) (+) polyethylene glycol 4000	0	(0.0)	2	(0.4)
lactulose	1	(0.2)	3	(0.6)
mineral oil	1	(0.2)	0	(0.0)
polyethylene glycol	3	(0.6)	3	(0.6)
polyethylene glycol 3350	2	(0.4)	0	(0.0)
polyethylene glycol 3350 (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride	8	(1.6)	1	(0.2)
polyethylene glycol 3350 (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride (+) sodium sulfate	0	(0.0)	1	(0.2)
polyethylene glycol 4000	0	(0.0)	2	(0.4)
psyllium husk	0	(0.0)	1	(0.2)
senna	1	(0.2)	2	(0.4)
sennosides	1	(0.2)	0	(0.0)
sodium citrate (+) sodium lauryl sulfoacetate (+) sorbitol	1	(0.2)	1	(0.2)
sodium lauryl sulfoacetate (+) sorbitol	0	(0.0)	1	(0.2)
sodium phosphate, dibasic (+) sodium phosphate, monobasic	3	(0.6)	1	(0.2)
sodium picosulfate	0	(0.0)	1	(0.2)
drugs for functional gastrointestinal disorders	**27**	**(5.3)**	**22**	**(4.4)**
alizapride	1	(0.2)	0	(0.0)
alizapride hydrochloride	2	(0.4)	0	(0.0)
atropine sulfate	0	(0.0)	1	(0.2)
butylscopolamine bromide	3	(0.6)	0	(0.0)
domperidone	3	(0.6)	1	(0.2)
drotaverine hydrochloride	0	(0.0)	1	(0.2)
metoclopramide	9	(1.8)	9	(1.8)
metoclopramide hydrochloride	10	(1.9)	6	(1.2)
phloroglucinol (+) trimethylphloroglucinol	3	(0.6)	5	(1.0)
tiquizium bromide	2	(0.4)	0	(0.0)
drugs used in diabetes	**9**	**(1.8)**	**7**	**(1.4)**

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
alimentary tract and metabolism				
drugs used in diabetes	**9**	**(1.8)**	**7**	**(1.4)**
empagliflozin	1	(0.2)	1	(0.2)
empagliflozin (+) metformin hydrochloride	1	(0.2)	0	(0.0)
gliclazide	2	(0.4)	0	(0.0)
glimepiride	1	(0.2)	0	(0.0)
insulin	1	(0.2)	0	(0.0)
insulin aspart	1	(0.2)	0	(0.0)
insulin degludec	1	(0.2)	0	(0.0)
insulin glargine	3	(0.6)	1	(0.2)
insulin glulisine	2	(0.4)	0	(0.0)
insulin human	3	(0.6)	0	(0.0)
insulin lispro	1	(0.2)	0	(0.0)
linagliptin	0	(0.0)	1	(0.2)
liraglutide	1	(0.2)	0	(0.0)
metformin	4	(0.8)	2	(0.4)
metformin hydrochloride	1	(0.2)	0	(0.0)
metformin hydrochloride (+) sitagliptin phosphate	1	(0.2)	1	(0.2)
sitagliptin phosphate	3	(0.6)	0	(0.0)
trelagliptin succinate	0	(0.0)	1	(0.2)
mineral supplements	**19**	**(3.7)**	**8**	**(1.6)**
calcium (unspecified) (+) magnesium (unspecified) (+) zinc (unspecified)	1	(0.2)	0	(0.0)
calcium carbonate (+) cholecalciferol	6	(1.2)	2	(0.4)
copper (unspecified)	1	(0.2)	0	(0.0)
magnesium (unspecified)	3	(0.6)	2	(0.4)
magnesium chloride	1	(0.2)	1	(0.2)
magnesium citrate	1	(0.2)	1	(0.2)
magnesium gluconate	1	(0.2)	0	(0.0)
magnesium sulfate	1	(0.2)	1	(0.2)
potassium (unspecified)	1	(0.2)	1	(0.2)
potassium bicarbonate (+) potassium citrate	0	(0.0)	1	(0.2)
potassium chloride	8	(1.6)	1	(0.2)
zinc gluconate	0	(0.0)	1	(0.2)
other alimentary tract and metabolism products	**12**	**(2.3)**	**3**	**(0.6)**
anethole trithione	1	(0.2)	0	(0.0)
gastrointestinal preparations (unspecified)	11	(2.1)	3	(0.6)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
alimentary tract and metabolism				
stomatological preparations	**9**	**(1.8)**	**2**	**(0.4)**
Chinese rhubarb (+) salicylic acid	1	(0.2)	0	(0.0)
carboxymethylcellulose sodium (+) electrolytes (unspecified) (+) sorbitol	1	(0.2)	0	(0.0)
chlorhexidine gluconate (+) polyethylene glycol 1500 (+) polyethylene glycol 300	1	(0.2)	0	(0.0)
enoxolone (+) hyaluronate sodium (+) povidone	1	(0.2)	0	(0.0)
glucose oxidase (as drug) (+) lactoferrin (as drug) (+) lysozyme chloride (+) peroxidase (as drug)	3	(0.6)	1	(0.2)
glycerin (+) hydrocortisone (+) lidocaine hydrochloride (+) nystatin (+) sodium chloride	2	(0.4)	0	(0.0)
glycerin (+) marshmallow (+) potassium chloride (+) potassium phosphate, monobasic (+) povidone (+) sodium phosphate, dibasic (+) xylitol	1	(0.2)	0	(0.0)
hexetidine	0	(0.0)	1	(0.2)
lipids (unspecified) (+) silicon dioxide	1	(0.2)	0	(0.0)
other agents for local oral treatement (unspecified)	1	(0.2)	0	(0.0)
vitamins	**17**	**(3.3)**	**16**	**(3.2)**
aloe vera (+) betaine (+) bilberry (+) bioflavonoids (+) black currant seed oil (+) cranberry (+) choline (+) grape seeds (+) inositol (+) maitake (+) minerals (+) papain (+) reishi (+) rosemary (+) shiitake (+) turmeric (+) vitamins (+) xanthophyll	1	(0.2)	0	(0.0)
ascorbic acid	4	(0.8)	1	(0.2)
ascorbic acid (+) chromium (unspecified) (+) folic acid (+) magnesium (unspecified) (+) manganese (unspecified) (+) selenium (unspecified) (+) vitamin B complex (+) vitamin D (unspecified) (+) vitaminE (+) zinc (unspecified)	1	(0.2)	0	(0.0)
astaxanthin (+) broccoli (+) cranberry (+) minerals (unspecified) (+) thioctic acid (+) vitamins (unspecified)	0	(0.0)	1	(0.2)
biotin (+) cystine (+) evening primrose oil (+) ferrous sulfate (+) gelatin (+) methionine (+) niacinamide (+) pyridoxine hydrochloride (+) vitamin E acetate	0	(0.0)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
alimentary tract and metabolism				
vitamins	**17**	**(3.3)**	**16**	**(3.2)**
black currant seed oil (+) borage oil (+) grape seeds (+) lycopene (+) minerals (unspecified) (+) omega-3 marine triglycerides (+) ubidecarenone (+) vitamins (unspecified) (+) xanthophyll	0	(0.0)	1	(0.2)
calcitriol	0	(0.0)	1	(0.2)
calcium ascorbate	1	(0.2)	0	(0.0)
cholecalciferol	6	(1.2)	4	(0.8)
cholecalciferol (+) menatetrenone	0	(0.0)	1	(0.2)
dexpanthenol	0	(0.0)	1	(0.2)
magnesium glycinate (+) pyridoxine hydrochloride	2	(0.4)	0	(0.0)
minerals (unspecified) (+) red clover (+) soy isoflavones (+) vitamins (unspecified)	0	(0.0)	1	(0.2)
niacinamide	1	(0.2)	0	(0.0)
vitamin B complex	1	(0.2)	0	(0.0)
vitamin D (unspecified)	3	(0.6)	1	(0.2)
vitamins (unspecified)	2	(0.4)	3	(0.6)
antiinfectives for systemic use				
antibacterials for systemic use	**150**	**(29.2)**	**118**	**(23.4)**
amoxicillin	37	(7.2)	25	(5.0)
amoxicillin (+) clavulanate potassium	36	(7.0)	27	(5.3)
amoxicillin sodium	0	(0.0)	1	(0.2)
ampicillin	1	(0.2)	0	(0.0)
ampicillin sodium (+) sulbactam sodium	1	(0.2)	0	(0.0)
antimicrobial (unspecified)	4	(0.8)	4	(0.8)
azithromycin	10	(1.9)	3	(0.6)
cefaclor	0	(0.0)	1	(0.2)
cefadroxil	0	(0.0)	2	(0.4)
cefazolin	6	(1.2)	2	(0.4)
cefazolin sodium	2	(0.4)	0	(0.0)
cefcapene pivoxil hydrochloride	1	(0.2)	1	(0.2)
cefditoren pivoxil	0	(0.0)	1	(0.2)
cefixime	1	(0.2)	1	(0.2)
ceftazidime	0	(0.0)	1	(0.2)
ceftibuten	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
antiinfectives for systemic use				
antibacterials for systemic use	**150**	**(29.2)**	**118**	**(23.4)**
ceftriaxone	2	(0.4)	2	(0.4)
ceftriaxone sodium	2	(0.4)	2	(0.4)
cefuroxime	4	(0.8)	2	(0.4)
cefuroxime axetil	1	(0.2)	2	(0.4)
cephalexin	14	(2.7)	16	(3.2)
cephalothin sodium	1	(0.2)	0	(0.0)
chloramphenicol	2	(0.4)	4	(0.8)
ciprofloxacin	12	(2.3)	5	(1.0)
ciprofloxacin hydrochloride	1	(0.2)	1	(0.2)
clarithromycin	7	(1.4)	5	(1.0)
clarithromycin lactobionate	3	(0.6)	1	(0.2)
clindamycin	4	(0.8)	4	(0.8)
clindamycin hydrochloride	2	(0.4)	3	(0.6)
dicloxacillin	1	(0.2)	0	(0.0)
dicloxacillin sodium	0	(0.0)	1	(0.2)
doxycycline	10	(1.9)	11	(2.2)
erythromycin	1	(0.2)	2	(0.4)
floxacillin	12	(2.3)	5	(1.0)
floxacillin sodium	2	(0.4)	1	(0.2)
fosfomycin	2	(0.4)	0	(0.0)
fosfomycin tromethamine	1	(0.2)	2	(0.4)
furazidine	0	(0.0)	1	(0.2)
fusidic acid	2	(0.4)	3	(0.6)
garenoxacin mesylate	1	(0.2)	0	(0.0)
gentamicin	1	(0.2)	2	(0.4)
gentamicin sulfate	0	(0.0)	1	(0.2)
levofloxacin	6	(1.2)	8	(1.6)
lincomycin	1	(0.2)	0	(0.0)
meropenem	1	(0.2)	0	(0.0)
methenamine hippurate	1	(0.2)	0	(0.0)
metronidazole	5	(1.0)	7	(1.4)
metronidazole (+) spiramycin	3	(0.6)	0	(0.0)
moxifloxacin	1	(0.2)	0	(0.0)
moxifloxacin hydrochloride	1	(0.2)	0	(0.0)
nitrofurantoin	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
antiinfectives for systemic use				
antibacterials for systemic use	**150**	**(29.2)**	**118**	**(23.4)**
norfloxacin	0	(0.0)	2	(0.4)
ofloxacin	2	(0.4)	1	(0.2)
penicillin (unspecified)	1	(0.2)	2	(0.4)
penicillin G	2	(0.4)	1	(0.2)
penicillin G sodium	0	(0.0)	1	(0.2)
penicillin V	1	(0.2)	0	(0.0)
penicillin V potassium	0	(0.0)	1	(0.2)
piperacillin sodium (+) tazobactam sodium	3	(0.6)	3	(0.6)
pristinamycin	1	(0.2)	3	(0.6)
roxithromycin	2	(0.4)	1	(0.2)
spiramycin	1	(0.2)	1	(0.2)
sulfamethizole	1	(0.2)	0	(0.0)
sulfamethoxazole (+) trimethoprim	4	(0.8)	1	(0.2)
sultamicillin tosylate	0	(0.0)	1	(0.2)
tetracycline	1	(0.2)	0	(0.0)
trimethoprim	4	(0.8)	4	(0.8)
vancomycin	3	(0.6)	0	(0.0)
antimycobacterials	**0**	**(0.0)**	**1**	**(0.2)**
rifamycin sodium	0	(0.0)	1	(0.2)
antimycotics for systemic use	**1**	**(0.2)**	**3**	**(0.6)**
amphotericin B	0	(0.0)	1	(0.2)
fluconazole	0	(0.0)	2	(0.4)
itraconazole	1	(0.2)	0	(0.0)
antivirals for systemic use	**8**	**(1.6)**	**7**	**(1.4)**
acyclovir	5	(1.0)	5	(1.0)
famciclovir	0	(0.0)	1	(0.2)
oseltamivir phosphate	1	(0.2)	1	(0.2)
valacyclovir hydrochloride	3	(0.6)	1	(0.2)
immune sera and immunoglobulins	**0**	**(0.0)**	**1**	**(0.2)**
globulin, immune	0	(0.0)	1	(0.2)
vaccines	**9**	**(1.8)**	**6**	**(1.2)**
diphtheria toxoid (+) pertussis acellular vaccine (unspecified) (+) tetanus toxoid	0	(0.0)	1	(0.2)
influenza virus sAg 3v vaccine inactivated	1	(0.2)	1	(0.2)
influenza virus split virion 3v vaccine inactivated	1	(0.2)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
antiinfectives for systemic use				
vaccines	**9**	**(1.8)**	**6**	**(1.2)**
influenza virus split virion 4v vaccine inactivated	1	(0.2)	1	(0.2)
influenza virus vaccine (unspecified)	3	(0.6)	1	(0.2)
influenza virus vaccine inactivated (unspecified)	2	(0.4)	1	(0.2)
pneumococcal 4 6B 9V 14 18C 19F 23F conj vaccine (CRM197)	0	(0.0)	1	(0.2)
tetanus toxoid	1	(0.2)	0	(0.0)
antineoplastic and immunomodulating agents				
antineoplastic agents	**3**	**(0.6)**	**1**	**(0.2)**
fluorouracil	3	(0.6)	1	(0.2)
immunostimulants	**1**	**(0.2)**	**0**	**(0.0)**
andrographis (+) Echinacea purpurea (+) eleuthero (+) turmeric (+) vitamin A acetate (+) zinc sulfate	1	(0.2)	0	(0.0)
immunosuppressants	**2**	**(0.4)**	**0**	**(0.0)**
tacrolimus	2	(0.4)	0	(0.0)
antiparasitic products, insecticides, and repellents				
anthelmintics	**4**	**(0.8)**	**1**	**(0.2)**
ivermectin	4	(0.8)	1	(0.2)
antiprotozoals	**1**	**(0.2)**	**0**	**(0.0)**
atovaquone (+) chlorguanide hydrochloride	1	(0.2)	0	(0.0)
blood and blood forming organs				
antianemic preparations	**5**	**(1.0)**	**3**	**(0.6)**
ascorbic acid (+) ferric pyrophosphate	1	(0.2)	0	(0.0)
cyanocobalamin	1	(0.2)	0	(0.0)
cyanocobalamin (+) ferrous glycine sulfate (+) folic acid	1	(0.2)	0	(0.0)
ferrous glycine sulfate	1	(0.2)	0	(0.0)
ferrous sulfate	2	(0.4)	2	(0.4)
hydroxocobalamin	0	(0.0)	1	(0.2)
iron (unspecified)	1	(0.2)	0	(0.0)
antihemorrhagics	**2**	**(0.4)**	**2**	**(0.4)**
tranexamic acid	2	(0.4)	2	(0.4)
antithrombotic agents	**26**	**(5.1)**	**15**	**(3.0)**

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
blood and blood forming organs				
antithrombotic agents	**26**	**(5.1)**	**15**	**(3.0)**
acenocoumarol	0	(0.0)	1	(0.2)
apixaban	1	(0.2)	0	(0.0)
aspirin (+) magnesium hydroxide	0	(0.0)	1	(0.2)
certoparin sodium	0	(0.0)	1	(0.2)
clopidogrel	1	(0.2)	0	(0.0)
dabigatran	0	(0.0)	1	(0.2)
dabigatran etexilate mesylate	0	(0.0)	1	(0.2)
dalteparin sodium	2	(0.4)	3	(0.6)
enoxaparin sodium	13	(2.5)	5	(1.0)
fondaparinux sodium	1	(0.2)	0	(0.0)
heparin	1	(0.2)	1	(0.2)
heparin sodium	0	(0.0)	1	(0.2)
nadroparin calcium	2	(0.4)	1	(0.2)
rivaroxaban	3	(0.6)	1	(0.2)
ticagrelor	1	(0.2)	0	(0.0)
tinzaparin sodium	3	(0.6)	1	(0.2)
blood substitutes and perfusion solutions	**18**	**(3.5)**	**8**	**(1.6)**
dextrose (+) potassium citrate (+) sodium chloride	2	(0.4)	0	(0.0)
electrolytes (unspecified) (+) sodium lactate	3	(0.6)	0	(0.0)
glycine	0	(0.0)	1	(0.2)
phosphate (unspecified)	1	(0.2)	2	(0.4)
potassium (unspecified) (+) sodium chloride	1	(0.2)	0	(0.0)
sodium bicarbonate	2	(0.4)	0	(0.0)
sodium bicarbonate (+) sodium chloride	1	(0.2)	0	(0.0)
sodium chloride	13	(2.5)	6	(1.2)
cardiovascular system				
agents acting on the renin-angiotensin system	**27**	**(5.3)**	**21**	**(4.2)**
amlodipine besylate (+) hydrochlorothiazide (+) valsartan	1	(0.2)	0	(0.0)
amlodipine besylate (+) lisinopril	0	(0.0)	1	(0.2)
amlodipine besylate (+) perindopril arginine	2	(0.4)	0	(0.0)
amlodipine besylate (+) telmisartan	1	(0.2)	0	(0.0)
candesartan	1	(0.2)	0	(0.0)
candesartan cilexetil	0	(0.0)	2	(0.4)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
cardiovascular system				
agents acting on the renin-angiotensin system	**27**	**(5.3)**	**21**	**(4.2)**
candesartan cilexetil (+) hydrochlorothiazide	0	(0.0)	1	(0.2)
captopril	1	(0.2)	0	(0.0)
cilazapril	1	(0.2)	1	(0.2)
delapril hydrochloride (+) indapamide	0	(0.0)	1	(0.2)
enalapril	0	(0.0)	1	(0.2)
enalapril maleate (+) hydrochlorothiazide	1	(0.2)	0	(0.0)
hydrochlorothiazide (+) losartan potassium	0	(0.0)	1	(0.2)
hydrochlorothiazide (+) valsartan	0	(0.0)	2	(0.4)
indapamide (+) perindopril arginine	1	(0.2)	0	(0.0)
indapamide (+) perindopril erbumine	1	(0.2)	0	(0.0)
irbesartan	2	(0.4)	2	(0.4)
lisinopril	1	(0.2)	2	(0.4)
losartan	2	(0.4)	1	(0.2)
losartan potassium	0	(0.0)	1	(0.2)
olmesartan medoxomil	1	(0.2)	0	(0.0)
perindopril	1	(0.2)	2	(0.4)
ramipril	7	(1.4)	5	(1.0)
telmisartan	3	(0.6)	0	(0.0)
valsartan	1	(0.2)	1	(0.2)
antihypertensives	**3**	**(0.6)**	**0**	**(0.0)**
clonidine hydrochloride	1	(0.2)	0	(0.0)
doxazosin	1	(0.2)	0	(0.0)
prazosin	1	(0.2)	0	(0.0)
beta blocking agents	**13**	**(2.5)**	**10**	**(2.0)**
atenolol	0	(0.0)	1	(0.2)
bisoprolol	3	(0.6)	6	(1.2)
bisoprolol fumarate	1	(0.2)	1	(0.2)
bisoprolol fumarate (+) hydrochlorothiazide	0	(0.0)	1	(0.2)
metoprolol	2	(0.4)	0	(0.0)
nebivolol	1	(0.2)	0	(0.0)
nebivolol hydrochloride	0	(0.0)	1	(0.2)
propranolol	5	(1.0)	1	(0.2)
propranolol hydrochloride	3	(0.6)	0	(0.0)
calcium channel blockers	**19**	**(3.7)**	**4**	**(0.8)**
amlodipine	5	(1.0)	2	(0.4)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
cardiovascular system				
calcium channel blockers	**19**	**(3.7)**	**4**	**(0.8)**
amlodipine besylate	3	(0.6)	0	(0.0)
lacidipine	1	(0.2)	0	(0.0)
lercanidipine	1	(0.2)	0	(0.0)
lercanidipine hydrochloride	1	(0.2)	0	(0.0)
nicardipine hydrochloride	2	(0.4)	0	(0.0)
nifedipine	5	(1.0)	0	(0.0)
nitrendipine	0	(0.0)	1	(0.2)
verapamil hydrochloride	2	(0.4)	1	(0.2)
cardiac therapy	**9**	**(1.8)**	**1**	**(0.2)**
adenosine	1	(0.2)	0	(0.0)
bucladesine sodium	1	(0.2)	0	(0.0)
flecainide	1	(0.2)	0	(0.0)
flecainide acetate	1	(0.2)	0	(0.0)
lappaconitine hydrobromide	1	(0.2)	0	(0.0)
metaraminol	0	(0.0)	1	(0.2)
nitroglycerin	3	(0.6)	0	(0.0)
ubidecarenone	1	(0.2)	0	(0.0)
diuretics	**12**	**(2.3)**	**8**	**(1.6)**
bendroflumethiazide	0	(0.0)	1	(0.2)
furosemide	6	(1.2)	2	(0.4)
hydrochlorothiazide	6	(1.2)	4	(0.8)
indapamide	0	(0.0)	1	(0.2)
lipid modifying agents	**9**	**(1.8)**	**12**	**(2.4)**
atorvastatin	2	(0.4)	2	(0.4)
atorvastatin calcium	1	(0.2)	1	(0.2)
cholestyramine resin	0	(0.0)	1	(0.2)
ezetimibe (+) simvastatin	0	(0.0)	1	(0.2)
fenofibrate	2	(0.4)	0	(0.0)
fish oil	0	(0.0)	3	(0.6)
omega-3 marine triglycerides	0	(0.0)	1	(0.2)
pravastatin	0	(0.0)	1	(0.2)
pravastatin sodium	1	(0.2)	1	(0.2)
rosuvastatin	2	(0.4)	0	(0.0)
rosuvastatin calcium	1	(0.2)	0	(0.0)
simvastatin	2	(0.4)	2	(0.4)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
cardiovascular system				
vasoprotectives	**6**	**(1.2)**	**8**	**(1.6)**
aluminum acetate (+) hydrocortisone acetate (+) lidocaine (+) zinc oxide	1	(0.2)	0	(0.0)
bioflavonoids	1	(0.2)	0	(0.0)
dibucaine hydrochloride (+) hydrocortisone	1	(0.2)	0	(0.0)
diosmin (+) hesperidin	1	(0.2)	2	(0.4)
heparinoid	2	(0.4)	4	(0.8)
pentosan polysulfate sodium	0	(0.0)	1	(0.2)
polidocanol	0	(0.0)	1	(0.2)
dermatologicals				
anti-acne preparations	**0**	**(0.0)**	**2**	**(0.4)**
sulfur (+) zinc oxide	0	(0.0)	1	(0.2)
tretinoin	0	(0.0)	1	(0.2)
antibiotics and chemotherapeutics for dermatological use	**7**	**(1.4)**	**2**	**(0.4)**
antibacterial dermatologic (unspecified)	2	(0.4)	0	(0.0)
benzalkonium chloride (+) idoxuridine (+) lidocaine hydrochloride	0	(0.0)	1	(0.2)
imiquimod	1	(0.2)	0	(0.0)
mupirocin	4	(0.8)	1	(0.2)
antifungals for dermatological use	**34**	**(6.6)**	**30**	**(5.9)**
amorolfine hydrochloride	1	(0.2)	0	(0.0)
antifungal dermatologic (unspecified)	0	(0.0)	1	(0.2)
betamethasone dipropionate (+) clotrimazole	1	(0.2)	0	(0.0)
bifonazole	4	(0.8)	5	(1.0)
bifonazole (+) urea	0	(0.0)	3	(0.6)
ciclopirox	2	(0.4)	0	(0.0)
ciclopirox olamine	5	(1.0)	6	(1.2)
ciclopirox olamine (+) keluamid (+) pyrithione zinc	1	(0.2)	0	(0.0)
clotrimazole	5	(1.0)	1	(0.2)
clotrimazole (+) hydrocortisone	1	(0.2)	0	(0.0)
econazole	3	(0.6)	3	(0.6)
econazole nitrate	1	(0.2)	0	(0.0)
hydrocortisone (+) miconazole nitrate	1	(0.2)	1	(0.2)
ketoconazole	7	(1.4)	3	(0.6)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
dermatologicals				
antifungals for dermatological use	**34**	**(6.6)**	**30**	**(5.9)**
miconazole	1	(0.2)	3	(0.6)
miconazole nitrate	1	(0.2)	1	(0.2)
nystatin	4	(0.8)	2	(0.4)
oxiconazole nitrate	2	(0.4)	1	(0.2)
terbinafine	0	(0.0)	3	(0.6)
terbinafine hydrochloride	1	(0.2)	0	(0.0)
tioconazole	0	(0.0)	2	(0.4)
antipruritics, incl. antihistamines, anesthetics, etc.	**3**	**(0.6)**	**2**	**(0.4)**
calamine (+) zinc oxide	0	(0.0)	1	(0.2)
crotamiton	1	(0.2)	0	(0.0)
menthol (+) mineral oil (+) petrolatum, white	1	(0.2)	1	(0.2)
papain (+) sodium pidolate (+) witch hazel	1	(0.2)	0	(0.0)
antipsoriatics	**2**	**(0.4)**	**0**	**(0.0)**
calcipotriene	1	(0.2)	0	(0.0)
pine tar	1	(0.2)	0	(0.0)
antiseptics and disinfectants	**15**	**(2.9)**	**7**	**(1.4)**
alcohol (+) chlorhexidine gluconate	1	(0.2)	0	(0.0)
benzalkonium chloride	1	(0.2)	0	(0.0)
benzalkonium chloride (+) benzyl alcohol (+) chlorhexidine gluconate	0	(0.0)	2	(0.4)
benzalkonium chloride (+) chlorhexidine hydrochloride (+) isopropyl myristate (+) mineral oil	1	(0.2)	0	(0.0)
calcium chloride (+) polihexanide (+) polyethylene glycol 4000 (+) potassium chloride (+) sodium chloride	0	(0.0)	1	(0.2)
cethexonium bromide	1	(0.2)	0	(0.0)
cetostearyl alcohol (+) phenoxyethanol (+) sodium lauryl sulfate	1	(0.2)	0	(0.0)
chlorhexidine	2	(0.4)	1	(0.2)
chlorhexidine gluconate	1	(0.2)	0	(0.0)
entsufon sodium (+) hexachlorophene	1	(0.2)	0	(0.0)
hexamidine isethionate	0	(0.0)	1	(0.2)
ichthammol	1	(0.2)	0	(0.0)
iodine	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
dermatologicals				
antiseptics and disinfectants	**15**	**(2.9)**	**7**	**(1.4)**
octenidine hydrochloride	2	(0.4)	0	(0.0)
povidone-iodine	2	(0.4)	0	(0.0)
silver nitrate	2	(0.4)	0	(0.0)
topical antiseptic (unspecified)	0	(0.0)	1	(0.2)
triclosan	0	(0.0)	1	(0.2)
witch hazel	1	(0.2)	0	(0.0)
corticosteroids, dermatological preparations	**83**	**(16.1)**	**39**	**(7.7)**
alclometasone dipropionate	1	(0.2)	0	(0.0)
betamethasone butyrate propionate	0	(0.0)	2	(0.4)
betamethasone dipropionate	13	(2.5)	1	(0.2)
betamethasone dipropionate (+) calcipotriene	3	(0.6)	0	(0.0)
betamethasone dipropionate (+) gentamicin sulfate	1	(0.2)	0	(0.0)
betamethasone dipropionate (+) salicylic acid	0	(0.0)	1	(0.2)
betamethasone valerate	6	(1.2)	5	(1.0)
betamethasone valerate (+) fusidic acid	6	(1.2)	1	(0.2)
betamethasone valerate (+) ichthammol (+) salicylic acid	1	(0.2)	0	(0.0)
chlorquinaldol (+) diflucortolone valerate	0	(0.0)	1	(0.2)
clobetasol propionate	7	(1.4)	3	(0.6)
desonide	1	(0.2)	1	(0.2)
desoximetasone	0	(0.0)	1	(0.2)
diflucortolone valerate	2	(0.4)	3	(0.6)
difluprednate	2	(0.4)	0	(0.0)
flumethasone pivalate	1	(0.2)	0	(0.0)
flumethasone pivalate (+) triclosan	0	(0.0)	1	(0.2)
fluocinolone acetonide	1	(0.2)	0	(0.0)
fluorometholone	1	(0.2)	0	(0.0)
fluprednidene acetate (+) miconazole nitrate	0	(0.0)	1	(0.2)
flurandrenolide	1	(0.2)	0	(0.0)
fusidic acid (+) hydrocortisone acetate	1	(0.2)	1	(0.2)
gramicidin (+) neomycin sulfate (+) nystatin (+) triamcinolone acetonide	3	(0.6)	0	(0.0)
hydrocortisone (+) urea	1	(0.2)	0	(0.0)
hydrocortisone acetate	13	(2.5)	12	(2.4)
hydrocortisone butyrate	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
dermatologicals				
corticosteroids, dermatological preparations	**83**	**(16.1)**	**39**	**(7.7)**
lanolin (+) triamcinolone acetonide	1	(0.2)	0	(0.0)
methylprednisolone aceponate	9	(1.8)	2	(0.4)
mometasone furoate	24	(4.7)	4	(0.8)
salicylic acid (+) triamcinolone acetonide	0	(0.0)	1	(0.2)
emollients and protectives	**30**	**(5.8)**	**11**	**(2.2)**
allantoin (+) almond oil (+) aloe vera (+) coconut oil (+) hops (+) lavender oil (+) melaleuca oil (+) olive oil (+) rosemary oil (+) vitamin E acetate	1	(0.2)	0	(0.0)
allantoin (+) glycerin (+) hydrolyzed wheat protein (+) shea butter	1	(0.2)	0	(0.0)
almond oil (+) borage oil (+) calendula (+) caprylyl glycol (+) dextrin (+) dimethicone (+) glycerin (+) licorice (+) marshmallow (+) okra (+) panthenol (+) phenyl trimethicone (+) vitamin E	1	(0.2)	0	(0.0)
almond oil (+) cabbage rose (+) sodium borate (+) wax, white	0	(0.0)	1	(0.2)
almond oil (+) cetyl alcohol (+) glyceryl monooleate (+) lanolin (+) mineral oil (+) panthenol (+) petrolatum (+) stearyl alcohol (+) wax, white (+) wax, yellow	1	(0.2)	1	(0.2)
almond oil (+) collagen (+) dimethicone (+) glycerin (+) goat milk (+) sunflower oil	1	(0.2)	0	(0.0)
aloe vera	1	(0.2)	0	(0.0)
aloe vera (+) ethylhexyl stearate (+) shea butter	0	(0.0)	1	(0.2)
aminobenzoic acid	1	(0.2)	0	(0.0)
caprylyl glycol (+) chlorphenesin (+) dimethicone (+) glycerin (+) sodium polyacrylate (+) vitamin E acetate	1	(0.2)	0	(0.0)
cetomacrogol 1000 (+) cetostearyl alcohol (+) mineral oil (+) petrolatum, white	1	(0.2)	0	(0.0)
cetomacrogol 1000 (+) cetostearyl alcohol (+) mineral oil (+) petrolatum, white (+) propylene glycol	1	(0.2)	0	(0.0)
cetyl palmitate (+) mineral oil (+) wax, white	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
dermatologicals				
emollients and protectives	**30**	**(5.8)**	**11**	**(2.2)**
copper gluconate (+) dimethicone (+) glycerin (+) madecassoside (+) magnesium sulfate (+) manganese gluconate (+) panthenol (+) shea butter (+) zinc gluconate	0	(0.0)	1	(0.2)
cupric sulfate (+) oat (+) zinc oxide (+) zinc sulfate	0	(0.0)	1	(0.2)
dimethicone (+) glycerin (+) isopropyl myristate (+) lanolin	0	(0.0)	1	(0.2)
dimethicone (+) isopropyl myristate (+) mineral oil (+) petrolatum (+) polyethylene glycol	1	(0.2)	0	(0.0)
glycerin (+) isopropyl palmitate (+) oat (+) petrolatum, white (+) sodium pidolate	1	(0.2)	0	(0.0)
glycerin (+) mineral oil (+) petrolatum, white	7	(1.4)	0	(0.0)
isopropyl myristate (+) mineral oil	0	(0.0)	1	(0.2)
lanolin (+) mineral oil (+) petrolatum	2	(0.4)	0	(0.0)
mineral oil (+) petrolatum	0	(0.0)	1	(0.2)
mineral oil (+) petrolatum, white (+) wax, emulsifying	1	(0.2)	0	(0.0)
petrolatum, white	2	(0.4)	2	(0.4)
polidocanol (+) urea	3	(0.6)	0	(0.0)
silicone	1	(0.2)	0	(0.0)
urea	2	(0.4)	2	(0.4)
other dermatological preparations	**27**	**(5.3)**	**13**	**(2.6)**
caprylyl glycol (+) carbomer (+) chlorphenesin (+) piroctone olamine	1	(0.2)	0	(0.0)
cetomacrogol 1000 (+) salicylic acid	1	(0.2)	0	(0.0)
dermatologic (unspecified)	22	(4.3)	7	(1.4)
dimethyl sulfoxide (+) fluorouracil (+) salicylic acid	0	(0.0)	1	(0.2)
minoxidil	2	(0.4)	3	(0.6)
pimecrolimus	0	(0.0)	2	(0.4)
sodium phenolsulfonic acid phenol formaldehyde urea condensate	1	(0.2)	0	(0.0)
preparations for the treatment of wounds and ulcers	**2**	**(0.4)**	**0**	**(0.0)**

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
dermatologicals				
preparations for the treatment of wounds and ulcers	**2**	**(0.4)**	**0**	**(0.0)**
Enterococcus faecalis (+) Escherichia coli (+) Pseudomonas aeruginosa (+) salicylic acid (+) Staphylococcus aureus (+) Streptococcus pyogenes lysate (+) zinc oxide	1	(0.2)	0	(0.0)
chlorhexidine hydrochloride (+) dexpanthenol	1	(0.2)	0	(0.0)
genitourinary system and sex hormones				
gynecological antiinfectives and antiseptics	**0**	**(0.0)**	**1**	**(0.2)**
lactic acid (+) sodium lactate	0	(0.0)	1	(0.2)
other gynecologicals	**2**	**(0.4)**	**0**	**(0.0)**
copper intrauterine device	1	(0.2)	0	(0.0)
ethinyl estradiol (+) etonogestrel	1	(0.2)	0	(0.0)
sex hormones and modulators of the genital system	**3**	**(0.6)**	**7**	**(1.4)**
desogestrel	1	(0.2)	1	(0.2)
estriol	0	(0.0)	2	(0.4)
ethinyl estradiol (+) levonorgestrel	1	(0.2)	0	(0.0)
ethinyl estradiol (+) norethindrone	0	(0.0)	1	(0.2)
ethinyl estradiol (+) norgestimate	1	(0.2)	0	(0.0)
levonorgestrel	0	(0.0)	1	(0.2)
medroxyprogesterone acetate	0	(0.0)	1	(0.2)
norethindrone	0	(0.0)	1	(0.2)
urologicals	**4**	**(0.8)**	**11**	**(2.2)**
alfuzosin hydrochloride	0	(0.0)	2	(0.4)
citric acid (+) sodium bicarbonate (+) sodium citrate (+) tartaric acid	0	(0.0)	1	(0.2)
dutasteride (+) tamsulosin hydrochloride	1	(0.2)	2	(0.4)
phenazopyridine hydrochloride	0	(0.0)	2	(0.4)
sildenafil citrate	0	(0.0)	2	(0.4)
solifenacin succinate	0	(0.0)	1	(0.2)
tadalafil	0	(0.0)	1	(0.2)
tamsulosin hydrochloride	3	(0.6)	1	(0.2)
musculoskeletal system				
antigout preparations	**4**	**(0.8)**	**1**	**(0.2)**

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
musculoskeletal system				
antigout preparations	**4**	**(0.8)**	**1**	**(0.2)**
allopurinol	3	(0.6)	0	(0.0)
colchicine	1	(0.2)	1	(0.2)
antiinflammatory and antirheumatic products	**96**	**(18.7)**	**90**	**(17.8)**
aceclofenac	0	(0.0)	1	(0.2)
apronalide (+) caffeine (+) ibuprofen	0	(0.0)	1	(0.2)
benzydamine hydrochloride	1	(0.2)	0	(0.0)
celecoxib	3	(0.6)	6	(1.2)
dexketoprofen tromethamine	3	(0.6)	0	(0.0)
diclofenac	11	(2.1)	12	(2.4)
diclofenac diethylamine	3	(0.6)	4	(0.8)
diclofenac epolamine	0	(0.0)	1	(0.2)
diclofenac potassium	0	(0.0)	1	(0.2)
diclofenac resinate	1	(0.2)	0	(0.0)
diclofenac sodium	5	(1.0)	8	(1.6)
diclofenac sodium (+) misoprostol	0	(0.0)	1	(0.2)
etodolac	0	(0.0)	1	(0.2)
etoricoxib	3	(0.6)	1	(0.2)
ibuprofen	50	(9.7)	46	(9.1)
ibuprofen lysine	1	(0.2)	0	(0.0)
indomethacin	0	(0.0)	1	(0.2)
ketoprofen	4	(0.8)	8	(1.6)
ketoprofen lysine	0	(0.0)	1	(0.2)
ketorolac tromethamine	2	(0.4)	3	(0.6)
lornoxicam	1	(0.2)	0	(0.0)
loxoprofen	0	(0.0)	2	(0.4)
loxoprofen sodium	0	(0.0)	1	(0.2)
mefenamic acid	0	(0.0)	2	(0.4)
meloxicam	4	(0.8)	0	(0.0)
mucopolysaccharide polysulfate	1	(0.2)	1	(0.2)
nabumetone	0	(0.0)	1	(0.2)
naproxen	13	(2.5)	8	(1.6)
naproxen sodium	0	(0.0)	1	(0.2)
nimesulide	1	(0.2)	2	(0.4)
nonsteroidal anti-inflammatory drug (unspecified)	1	(0.2)	0	(0.0)
parecoxib	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
musculoskeletal system				
antiinflammatory and antirheumatic products	**96**	**(18.7)**	**90**	**(17.8)**
parecoxib sodium	1	(0.2)	0	(0.0)
piroxicam	0	(0.0)	1	(0.2)
drugs for treatment of bone diseases	**2**	**(0.4)**	**2**	**(0.4)**
alendronate sodium	1	(0.2)	0	(0.0)
denosumab	0	(0.0)	1	(0.2)
risedronate sodium	1	(0.2)	1	(0.2)
muscle relaxants	**4**	**(0.8)**	**2**	**(0.4)**
cyclobenzaprine hydrochloride	1	(0.2)	1	(0.2)
succinylcholine chloride	0	(0.0)	1	(0.2)
thiocolchicoside	2	(0.4)	0	(0.0)
vecuronium bromide	1	(0.2)	0	(0.0)
other drugs for disorders of musculo-skeletal system	**2**	**(0.4)**	**2**	**(0.4)**
hyaluronate sodium	2	(0.4)	1	(0.2)
hyaluronic acid	0	(0.0)	1	(0.2)
topical products for joint and muscular pain	**1**	**(0.2)**	**1**	**(0.2)**
Cajuput oil (+) camphor (+) clove oil (+) menthol (+) peppermint oil	0	(0.0)	1	(0.2)
arnica (+) capsicum oleoresin	1	(0.2)	0	(0.0)
nervous system				
analgesics	**159**	**(30.9)**	**132**	**(26.1)**
acetaminophen	116	(22.6)	89	(17.6)
acetaminophen (+) Asian ginseng (+) benfotiamine (+) caffeine (+) cassia (+) Chinese licorice (+) clemastine fumarate (+) dextromethorphan hydrobromide (+) ephedra (+) guaifenesin	1	(0.2)	0	(0.0)
acetaminophen (+) ascorbic acid (+) caffeine (+) chlorpheniramine maleate	2	(0.4)	2	(0.4)
acetaminophen (+) ascorbic acid (+) pheniramine maleate	2	(0.4)	1	(0.2)
acetaminophen (+) ascorbic acid (+) phenylephrine hydrochloride	0	(0.0)	1	(0.2)
acetaminophen (+) aspirin (+) caffeine	1	(0.2)	1	(0.2)
acetaminophen (+) caffeine	0	(0.0)	1	(0.2)
acetaminophen (+) caffeine (+) opium	4	(0.8)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
nervous system				
analgesics	**159**	**(30.9)**	**132**	**(26.1)**
acetaminophen (+) caffeine (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)
acetaminophen (+) caffeine (+) promethazine methylenedisalicylate (+) salicylamide	2	(0.4)	2	(0.4)
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	0	(0.0)	1	(0.2)
acetaminophen (+) codeine	3	(0.6)	1	(0.2)
acetaminophen (+) codeine phosphate	10	(1.9)	9	(1.8)
acetaminophen (+) codeine phosphate (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)
acetaminophen (+) codeine phosphate (+) pseudoephedrine hydrochloride	1	(0.2)	2	(0.4)
acetaminophen (+) codeine phosphate (+) pseudoephedrine hydrochloride (+) triprolidine hydrochloride	1	(0.2)	1	(0.2)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)
acetaminophen (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	0	(0.0)	1	(0.2)
acetaminophen (+) dextromethorphan hydrobromide (+) pholcodine (+) promethazine hydrochloride (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)
acetaminophen (+) dichloralphenazone (+) isometheptene mucate	0	(0.0)	1	(0.2)
acetaminophen (+) guaifenesin (+) phenylephrine hydrochloride	0	(0.0)	1	(0.2)
acetaminophen (+) ibuprofen	2	(0.4)	0	(0.0)
acetaminophen (+) opium	0	(0.0)	1	(0.2)
acetaminophen (+) oxycodone hydrochloride	0	(0.0)	1	(0.2)
acetaminophen (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)
acetaminophen (+) pseudoephedrine hydrochloride (+) triprolidine hydrochloride	1	(0.2)	1	(0.2)
acetaminophen (+) sobrerol	0	(0.0)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
nervous system				
analgesics	**159**	**(30.9)**	**132**	**(26.1)**
acetaminophen (+) tramadol hydrochloride	2	(0.4)	7	(1.4)
analgesic (unspecified)	1	(0.2)	0	(0.0)
aspirin	12	(2.3)	7	(1.4)
aspirin (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)
aspirin lysine	1	(0.2)	1	(0.2)
bupivacaine hydrochloride (+) morphine sulfate	1	(0.2)	0	(0.0)
buprenorphine	1	(0.2)	0	(0.0)
carbaspirin calcium	1	(0.2)	0	(0.0)
codeine phosphate (+) ibuprofen	0	(0.0)	2	(0.4)
dihydrocodeine	1	(0.2)	0	(0.0)
dihydrocodeine bitartrate	0	(0.0)	1	(0.2)
dipyrone	7	(1.4)	4	(0.8)
eletriptan hydrobromide	0	(0.0)	1	(0.2)
fentanyl	6	(1.2)	1	(0.2)
hydromorphone hydrochloride	3	(0.6)	0	(0.0)
meperidine hydrochloride	0	(0.0)	1	(0.2)
morphine	6	(1.2)	1	(0.2)
morphine sulfate	2	(0.4)	2	(0.4)
naloxone hydrochloride (+) oxycodone hydrochloride	2	(0.4)	3	(0.6)
nefopam hydrochloride	0	(0.0)	1	(0.2)
oxycodone	2	(0.4)	3	(0.6)
oxycodone hydrochloride	7	(1.4)	9	(1.8)
piritramide	2	(0.4)	0	(0.0)
rizatriptan benzoate	1	(0.2)	1	(0.2)
tapentadol	1	(0.2)	1	(0.2)
tramadol hydrochloride	12	(2.3)	8	(1.6)
zolmitriptan	1	(0.2)	1	(0.2)
anesthetics	**19**	**(3.7)**	**26**	**(5.1)**
alfentanil hydrochloride	1	(0.2)	0	(0.0)
anesthetic (unspecified)	1	(0.2)	1	(0.2)
bupivacaine	1	(0.2)	0	(0.0)
bupivacaine hydrochloride	0	(0.0)	3	(0.6)
capsaicin	1	(0.2)	0	(0.0)
epinephrine (+) lidocaine (+) ropivacaine	0	(0.0)	2	(0.4)
epinephrine (+) lidocaine hydrochloride	2	(0.4)	6	(1.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
nervous system				
anesthetics	**19**	**(3.7)**	**26**	**(5.1)**
ketamine	1	(0.2)	0	(0.0)
ketamine hydrochloride	1	(0.2)	0	(0.0)
lidocaine	5	(1.0)	13	(2.6)
lidocaine hydrochloride	1	(0.2)	0	(0.0)
mepivacaine hydrochloride	0	(0.0)	3	(0.6)
prilocaine hydrochloride	0	(0.0)	1	(0.2)
propofol	6	(1.2)	1	(0.2)
ropivacaine	0	(0.0)	1	(0.2)
ropivacaine hydrochloride	3	(0.6)	0	(0.0)
tetracaine	1	(0.2)	0	(0.0)
anti-Parkinson drugs	**0**	**(0.0)**	**1**	**(0.2)**
pramipexole	0	(0.0)	1	(0.2)
antiepileptics	**10**	**(1.9)**	**14**	**(2.8)**
carbamazepine	1	(0.2)	0	(0.0)
gabapentin	3	(0.6)	7	(1.4)
lamotrigine	0	(0.0)	1	(0.2)
pregabalin	6	(1.2)	9	(1.8)
other nervous system drugs	**2**	**(0.4)**	**2**	**(0.4)**
betahistine	0	(0.0)	1	(0.2)
betahistine hydrochloride	1	(0.2)	0	(0.0)
cinnarizine	1	(0.2)	0	(0.0)
varenicline tartrate	0	(0.0)	1	(0.2)
psychoanaleptics	**23**	**(4.5)**	**24**	**(4.8)**
amitriptyline hydrochloride	5	(1.0)	4	(0.8)
citalopram	2	(0.4)	2	(0.4)
citalopram hydrobromide	2	(0.4)	1	(0.2)
desvenlafaxine succinate	0	(0.0)	1	(0.2)
doxepin hydrochloride	1	(0.2)	0	(0.0)
duloxetine hydrochloride	0	(0.0)	2	(0.4)
escitalopram	0	(0.0)	4	(0.8)
escitalopram oxalate	3	(0.6)	2	(0.4)
fluoxetine	2	(0.4)	0	(0.0)
methylphenidate hydrochloride	0	(0.0)	1	(0.2)
mianserin hydrochloride	1	(0.2)	0	(0.0)
mirtazapine	1	(0.2)	3	(0.6)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
nervous system				
psychoanaleptics	**23**	**(4.5)**	**24**	**(4.8)**
nortriptyline	1	(0.2)	1	(0.2)
nortriptyline hydrochloride	0	(0.0)	1	(0.2)
paroxetine	1	(0.2)	0	(0.0)
rivastigmine	0	(0.0)	1	(0.2)
sertraline hydrochloride	2	(0.4)	0	(0.0)
trazodone hydrochloride	1	(0.2)	1	(0.2)
venlafaxine hydrochloride	1	(0.2)	1	(0.2)
psycholeptics	**42**	**(8.2)**	**37**	**(7.3)**
California poppy (+) hops (+) lemon balm (+) melatonin (+) passionflower (+) pyridoxine (+) valerian	1	(0.2)	0	(0.0)
alprazolam	3	(0.6)	4	(0.8)
aripiprazole	0	(0.0)	1	(0.2)
bromazepam	2	(0.4)	2	(0.4)
buspirone hydrochloride	0	(0.0)	1	(0.2)
calcium phosphate, dibasic (+) chamomile (+) hops (+) magnesium phosphate (+) passionflower (+) valerian	1	(0.2)	0	(0.0)
diazepam	3	(0.6)	6	(1.2)
doxylamine succinate (+) valerian	0	(0.0)	1	(0.2)
hydroxyzine	2	(0.4)	2	(0.4)
hydroxyzine hydrochloride	4	(0.8)	3	(0.6)
lorazepam	5	(1.0)	5	(1.0)
melatonin	1	(0.2)	0	(0.0)
midazolam	8	(1.6)	3	(0.6)
midazolam hydrochloride	1	(0.2)	0	(0.0)
oxazepam	0	(0.0)	3	(0.6)
prochlorperazine	3	(0.6)	5	(1.0)
prochlorperazine maleate	1	(0.2)	0	(0.0)
temazepam	4	(0.8)	2	(0.4)
zolpidem	2	(0.4)	1	(0.2)
zolpidem tartrate	1	(0.2)	4	(0.8)
zopiclone	3	(0.6)	7	(1.4)
respiratory system				

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
respiratory system				
antihistamines for systemic use	**101**	**(19.6)**	**51**	**(10.1)**
bepotastine besylate	2	(0.4)	0	(0.0)
bilastine	2	(0.4)	1	(0.2)
brompheniramine maleate	1	(0.2)	0	(0.0)
cetirizine hydrochloride	33	(6.4)	11	(2.2)
chlorpheniramine maleate	2	(0.4)	1	(0.2)
clemastine	2	(0.4)	0	(0.0)
clemastine fumarate	2	(0.4)	1	(0.2)
cyclizine	0	(0.0)	2	(0.4)
desloratadine	10	(1.9)	3	(0.6)
dexchlorpheniramine maleate	23	(4.5)	13	(2.6)
dimenhydrinate	0	(0.0)	1	(0.2)
dimethindene maleate	1	(0.2)	1	(0.2)
diphenhydramine	0	(0.0)	1	(0.2)
diphenhydramine hydrochloride	7	(1.4)	4	(0.8)
ebastine	4	(0.8)	2	(0.4)
fexofenadine hydrochloride	8	(1.6)	1	(0.2)
levocetirizine	1	(0.2)	1	(0.2)
levocetirizine dihydrochloride	2	(0.4)	2	(0.4)
loratadine	18	(3.5)	9	(1.8)
mebhydroline	0	(0.0)	1	(0.2)
meclizine hydrochloride	1	(0.2)	0	(0.0)
oxatomide	1	(0.2)	0	(0.0)
oxomemazine	1	(0.2)	0	(0.0)
promethazine	1	(0.2)	0	(0.0)
promethazine hydrochloride	2	(0.4)	1	(0.2)
rupatadine fumarate	1	(0.2)	0	(0.0)
cough and cold preparations	**27**	**(5.3)**	**30**	**(5.9)**
acetylcysteine	4	(0.8)	3	(0.6)
ambroxol hydrochloride	0	(0.0)	2	(0.4)
bromhexine hydrochloride	1	(0.2)	1	(0.2)
bromhexine hydrochloride (+) guaifenesin (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)
bromhexine hydrochloride (+) pholcodine	0	(0.0)	1	(0.2)
carbocysteine	3	(0.6)	4	(0.8)
codeine	1	(0.2)	6	(1.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
respiratory system				
cough and cold preparations	**27**	**(5.3)**	**30**	**(5.9)**
codeine phosphate	0	(0.0)	1	(0.2)
codeine phosphate (+) guaifenesin	0	(0.0)	1	(0.2)
codeine phosphate (+) potassium guaiacolsulfonate	0	(0.0)	1	(0.2)
cough, cold, and flu therapies (unspecified)	13	(2.5)	8	(1.6)
dextromethorphan	0	(0.0)	1	(0.2)
dextromethorphan hydrobromide	3	(0.6)	1	(0.2)
dimemorfan phosphate	1	(0.2)	0	(0.0)
guaifenesin	4	(0.8)	1	(0.2)
guaifenesin (+) hydrocodone bitartrate	0	(0.0)	1	(0.2)
guaifenesin (+) menthol	1	(0.2)	1	(0.2)
hydrocodone	0	(0.0)	1	(0.2)
meglumine benzoate (+) polysorbate 20 (+) promethazine hydrochloride	0	(0.0)	1	(0.2)
noscapine polistirex	0	(0.0)	1	(0.2)
drugs for obstructive airway diseases	**34**	**(6.6)**	**19**	**(3.8)**
albuterol	8	(1.6)	5	(1.0)
albuterol (+) ipratropium bromide	1	(0.2)	0	(0.0)
albuterol sulfate	2	(0.4)	0	(0.0)
albuterol sulfate (+) ipratropium bromide	1	(0.2)	0	(0.0)
aminophylline	0	(0.0)	1	(0.2)
beclomethasone dipropionate	1	(0.2)	2	(0.4)
beclomethasone dipropionate (+) formoterol fumarate	5	(1.0)	0	(0.0)
budesonide	4	(0.8)	1	(0.2)
budesonide (+) formoterol fumarate	4	(0.8)	1	(0.2)
cromolyn sodium	4	(0.8)	0	(0.0)
epinephrine	3	(0.6)	2	(0.4)
fenoterol hydrobromide (+) ipratropium bromide	0	(0.0)	1	(0.2)
fenspiride hydrochloride	0	(0.0)	1	(0.2)
flunisolide	0	(0.0)	1	(0.2)
fluticasone	1	(0.2)	0	(0.0)
fluticasone furoate	3	(0.6)	1	(0.2)
fluticasone furoate (+) vilanterol	1	(0.2)	0	(0.0)
fluticasone propionate	3	(0.6)	4	(0.8)
fluticasone propionate (+) salmeterol xinafoate	2	(0.4)	0	(0.0)
formoterol fumarate	0	(0.0)	2	(0.4)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
respiratory system				
drugs for obstructive airway diseases	**34**	**(6.6)**	**19**	**(3.8)**
ipratropium bromide	2	(0.4)	1	(0.2)
montelukast sodium	1	(0.2)	0	(0.0)
terbutaline sulfate	1	(0.2)	0	(0.0)
theophylline	0	(0.0)	1	(0.2)
nasal preparations	**21**	**(4.1)**	**14**	**(2.8)**
acetylcysteine (+) benzalkonium chloride (+) tuaminoheptane sulfate	1	(0.2)	0	(0.0)
azelastine hydrochloride (+) fluticasone propionate	1	(0.2)	0	(0.0)
benzododecinium bromide (+) polysorbate 80	1	(0.2)	0	(0.0)
cetirizine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.2)
dimethindene maleate (+) phenylephrine	1	(0.2)	1	(0.2)
framycetin sulfate (+) thenoate olamine	1	(0.2)	1	(0.2)
levocabastine hydrochloride	0	(0.0)	1	(0.2)
lysozyme chloride (+) phenolpropamine iodide (+) thonzylamine hydrochloride	1	(0.2)	0	(0.0)
phenylephrine hydrochloride	2	(0.4)	1	(0.2)
pseudoephedrine	1	(0.2)	0	(0.0)
pseudoephedrine hydrochloride	3	(0.6)	1	(0.2)
sea water	1	(0.2)	1	(0.2)
tetrahydrozoline hydrochloride	0	(0.0)	1	(0.2)
tixocortol pivalate	1	(0.2)	2	(0.4)
xylometazoline hydrochloride	8	(1.6)	4	(0.8)
throat preparations	**3**	**(0.6)**	**5**	**(1.0)**
amylmetacresol (+) dichlorobenzyl alcohol	2	(0.4)	1	(0.2)
benzalkonium chloride (+) benzocaine (+) tyrothricin	0	(0.0)	1	(0.2)
benzocaine (+) cetylpyridinium chloride	1	(0.2)	0	(0.0)
biclotymol	0	(0.0)	1	(0.2)
cetylpyridinium chloride	0	(0.0)	1	(0.2)
chlorhexidine gluconate (+) tetracaine hydrochloride	0	(0.0)	1	(0.2)
sensory organs				
ophthalmological and otological preparations	**0**	**(0.0)**	**1**	**(0.2)**
dexamethasone (+) framycetin sulfate (+) gramicidin	0	(0.0)	1	(0.2)
ophthalmologicals	**12**	**(2.3)**	**17**	**(3.4)**

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
sensory organs				
ophthalmologicals	**12**	**(2.3)**	**17**	**(3.4)**
boric acid (+) sodium borate (+) sodium chloride	0	(0.0)	2	(0.4)
brinzolamide	0	(0.0)	1	(0.2)
carboxymethylcellulose sodium	0	(0.0)	1	(0.2)
carboxymethylcellulose sodium (+) glycerin (+) polysorbate 80	1	(0.2)	0	(0.0)
dexamethasone (+) tobramycin	1	(0.2)	1	(0.2)
dexamethasone sodium phosphate (+) gentamicin sulfate	0	(0.0)	1	(0.2)
fluorescein	1	(0.2)	0	(0.0)
hyaluronate sodium (+) sodium chloride	0	(0.0)	1	(0.2)
hypromellose	1	(0.2)	0	(0.0)
latanoprost	0	(0.0)	1	(0.2)
latanoprost (+) timolol maleate	0	(0.0)	1	(0.2)
methylcellulose	1	(0.2)	0	(0.0)
mineral oil (+) petrolatum, white	2	(0.4)	0	(0.0)
olopatadine hydrochloride	1	(0.2)	0	(0.0)
ophthalmic preparations (unspecified)	2	(0.4)	2	(0.4)
phenylephrine hydrochloride (+) prednisolone acetate	0	(0.0)	3	(0.6)
picloxydine hydrochloride	0	(0.0)	2	(0.4)
polyethylene glycol (+) propylene glycol	1	(0.2)	0	(0.0)
timolol	0	(0.0)	2	(0.4)
tropicamide	1	(0.2)	0	(0.0)
otologicals	**0**	**(0.0)**	**1**	**(0.2)**
fludrocortisone acetate (+) lidocaine hydrochloride (+) neomycin sulfate (+) polymyxin B sulfate	0	(0.0)	1	(0.2)
systemic hormonal preparations, excl. sex hormones and insulins				
corticosteroids for systemic use	**118**	**(23.0)**	**54**	**(10.7)**
betamethasone	8	(1.6)	1	(0.2)
betamethasone (+) dexchlorpheniramine maleate	0	(0.0)	1	(0.2)
betamethasone acetate	0	(0.0)	1	(0.2)
betamethasone sodium phosphate	2	(0.4)	1	(0.2)
corticosteroids (unspecified)	12	(2.3)	1	(0.2)
cortisone	1	(0.2)	1	(0.2)
cortisone acetate	4	(0.8)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
systemic hormonal preparations, excl. sex hormones and insulins				
corticosteroids for systemic use	**118**	**(23.0)**	**54**	**(10.7)**
deflazacort	0	(0.0)	1	(0.2)
dexamethasone	7	(1.4)	2	(0.4)
dexamethasone phosphate	0	(0.0)	1	(0.2)
dexamethasone sodium phosphate	0	(0.0)	4	(0.8)
hydrocortisone	9	(1.8)	8	(1.6)
hydrocortisone sodium succinate	1	(0.2)	0	(0.0)
methylprednisolone	9	(1.8)	2	(0.4)
methylprednisolone acetate	1	(0.2)	0	(0.0)
methylprednisolone sodium succinate	2	(0.4)	1	(0.2)
prednisolone	31	(6.0)	7	(1.4)
prednisolone sodium metazoate	2	(0.4)	5	(1.0)
prednisone	42	(8.2)	15	(3.0)
triamcinolone	4	(0.8)	5	(1.0)
triamcinolone acetonide	8	(1.6)	4	(0.8)
thyroid therapy	**75**	**(14.6)**	**17**	**(3.4)**
carbimazole	3	(0.6)	0	(0.0)
levothyroxine sodium	72	(14.0)	17	(3.4)
liothyronine sodium	1	(0.2)	0	(0.0)
methimazole	4	(0.8)	1	(0.2)
various				
all other non-therapeutic products	**3**	**(0.6)**	**1**	**(0.2)**
carbomer 940	1	(0.2)	1	(0.2)
carbomer 980	1	(0.2)	0	(0.0)
paraffin	1	(0.2)	0	(0.0)
all other therapeutic products	**47**	**(9.1)**	**40**	**(7.9)**
American ginseng	1	(0.2)	0	(0.0)
English ivy	1	(0.2)	0	(0.0)
English ivy (+) thyme oil	1	(0.2)	0	(0.0)
Gentiana lutea (+) Primula (+) Rumex acetosa (+) Sambucus nigra (+) Verbena officinalis	2	(0.4)	1	(0.2)
Luffa operculata (+) mercuric iodide (+) porcine nasal mucous membrane (+) pulsatilla (+) resin spurge (+) silver nitrate (+) sinusitis nosode (+) sulfurated lime	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
various				
all other therapeutic products	**47**	**(9.1)**	**40**	**(7.9)**
Pelargonium sidoides	0	(0.0)	1	(0.2)
[composition unspecified]	24	(4.7)	14	(2.8)
aconite (+) atropine sulfate (+) mercuric cyanide	0	(0.0)	1	(0.2)
allantoin (+) almond oil (+) aloe vera (+) chamomile (+) gotu kola (+) hops (+) olive oil (+) sage oil (+) vitamin E	1	(0.2)	0	(0.0)
ambergris (+) Anamirta paniculata (+) Conium maculatum (+) kerosene	0	(0.0)	1	(0.2)
antimony potassium tartrate (+) coccus cacti (+) ipecac (+) lungwort (+) Spongia officinalis (+) sundew (+) white bryony (+) yellow dock	0	(0.0)	1	(0.2)
antioxidants (+) astragalus (+) buchu (+) damiana (+) ginkgo (+) ginseng (+) gotu kola (+) hawthorn (+) herbs (+) inositol (+) licorice (+) milk thistle (+) minerals (+) sarsaparilla (+) saw palmetto (+) tea (+) ubidecarenone (+) uva ursi (+) vitamins	1	(0.2)	0	(0.0)
arnica (+) butchers broom (+) horse chestnut	0	(0.0)	1	(0.2)
arsenic triiodide (+) arsenic trioxide (+) black mustard (+) eyebright (+) lungwort lichen (+) naphthalene (+) onion (+) potassium iodate (+) ragweed (+) sabadilla	0	(0.0)	1	(0.2)
arsenic trioxide (+) bloodroot (+) calendula (+) celandine (+) clubmoss (+) condurango (+) Culvers root (+) dandelion (+) echinacea (unspecified) (+) goldenseal (+) milk thistle (+) poke	1	(0.2)	0	(0.0)
ascorbic acid (+) Echinacea purpurea (+) garlic (+) zinc gluconate	0	(0.0)	1	(0.2)
boneset (+) Echinacea angustifolia (+) elecampane (+) European elder (+) licorice (+) plantain (+) thyme (+) yarrow	0	(0.0)	1	(0.2)
camphor oil (+) peppermint oil	0	(0.0)	1	(0.2)
cannabidiol	1	(0.2)	0	(0.0)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
various				
all other therapeutic products	**47**	**(9.1)**	**40**	**(7.9)**
cholecalciferol (+) chondroitin sulfate sodium (+) dimethyl sulfone (+) collagen (+) glucosamine sulfate potassium (+) hyaluronic acid (+) mecobalamin (+) menatetrenone (+) minerals (unspecified) (+) thioctic acid (+) white willow	1	(0.2)	0	(0.0)
chondroitin (+) glucosamine	1	(0.2)	0	(0.0)
chondroitin sulfate sodium	0	(0.0)	1	(0.2)
coltsfoot (+) thyme	1	(0.2)	0	(0.0)
cowslip (+) thyme	1	(0.2)	0	(0.0)
cranberry	0	(0.0)	1	(0.2)
cranberry (+) D-mannose	0	(0.0)	1	(0.2)
cyperus	1	(0.2)	0	(0.0)
ectoine	0	(0.0)	1	(0.2)
emoxypine succinate	0	(0.0)	1	(0.2)
ginger (+) Indian frankincense (+) pepper (+) turmeric	1	(0.2)	0	(0.0)
ginkgo	0	(0.0)	1	(0.2)
ginseng (unspecified)	1	(0.2)	0	(0.0)
glucosamine	2	(0.4)	1	(0.2)
gold (+) iron (unspecified) (+) potassium phosphate, dibasic	1	(0.2)	0	(0.0)
grape seed oil (+) sweet wormwood	0	(0.0)	1	(0.2)
helicidine	0	(0.0)	1	(0.2)
honey (+) rose (unspecified)	1	(0.2)	0	(0.0)
jujube (+) protein hydrolysate	1	(0.2)	0	(0.0)
lemon	1	(0.2)	0	(0.0)
milk thistle	1	(0.2)	0	(0.0)
mushroom (unspecified)	2	(0.4)	0	(0.0)
myrtle oil	2	(0.4)	1	(0.2)
nitrogen	2	(0.4)	0	(0.0)
oat	0	(0.0)	1	(0.2)
povidone	0	(0.0)	1	(0.2)
propolis	1	(0.2)	1	(0.2)
silicon dioxide, colloidal	0	(0.0)	1	(0.2)
sodium polystyrene sulfonate	1	(0.2)	4	(0.8)
tea tree	1	(0.2)	1	(0.2)

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

	Pembrolizumab		Placebo	
	n	(%)	n	(%)
various				
all other therapeutic products	**47**	**(9.1)**	**40**	**(7.9)**
turmeric	2	(0.4)	0	(0.0)
general nutrients	**1**	**(0.2)**	**0**	**(0.0)**
dextrose	1	(0.2)	0	(0.0)

Every subject is counted a single time for each applicable specific concomitant medication. A subject with multiple concomitant medications within a medication category is counted a single time for that category.

A medication class or specific medication 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.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adcm]

14.1.1.4 Extent of Exposure

Table 14.1-11

Summary of Drug Exposure
ASaT Population

	Pembrolizumab (N=509)	Placebo (N=502)	Total (N=1011)
Study Days On-Therapy (days)			
Mean	282.8	275.7	279.3
Median	358.0	357.0	357.0
SD	120.96	123.51	122.23
Range	1.0 to 478.0	1.0 to 424.0	1.0 to 478.0
Number of Administrations			
Mean	14.0	13.9	13.9
Median	18.0	18.0	18.0
SD	5.62	5.77	5.69
Range	1.0 to 18.0	1.0 to 19.0	1.0 to 19.0
On-Therapy is defined as receiving at least one dose of study treatment and is limited to Part 1 of the study. (Data Cutoff Date: 03APR2020).			

Source: [P054V02MK3475: adam-adsl; adexsum]

Table 14.1-12

Exposure by Duration
ASaT Population

	Pembrolizumab (N=509)		Placebo (N=502)		Total (N=1011)	
	n	Person-years	n	Person-years	n	Person-years
Duration of Exposure						
> 0 m	509	394	502	379	1,011	773
≥ 1 m	489	393	489	378	978	771
≥ 3 m	434	383	414	365	848	748
≥ 6 m	387	365	363	345	750	710
≥ 12 m	72	76	74	77	146	153

Each subject 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.
Exposure by Duration is given for Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adexsum]

Table 14.1-13

Summary of Follow-up Duration
ITT Population

	Pembrolizumab N=514	Placebo N=505	Total N=1019
Follow-up duration (months)†			
Median (Range)	45.4 (4.4-55.3)	45.6 (2.5-54.8)	45.5 (2.5-55.3)
Mean (SD)	42.3 (10.6)	41.8 (11.4)	42.1 (11.0)
†Follow-up duration is defined as the time from randomization to the date of death or the database cutoff date if the subject was still alive. (Data Cutoff Date: 03APR2020).			

Source: [P054V02MK3475: adam-adsl]

14.2 Efficacy and Other Evaluations

14.2.1 Efficacy Endpoint: Distant Metastasis-free Survival in All Participants

Table 14.2-1
Analysis of Distant Metastasis-Free Survival
ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	514	173 (33.7)	16164.4	1.1	Not Reached (49.6, -)	65.3 (60.9, 69.5)	0.60 (0.49, 0.73)	<0.0001
Placebo	505	245 (48.5)	13310.9	1.8	40.0 (27.7, -)	49.4 (44.8, 53.8)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-2
Analysis of Distant Metastasis-Free Survival
(8th Edition Cancer Stage)
ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	514	173 (33.7)	16164.4	1.1	Not Reached (49.6, -)	65.3 (60.9, 69.5)	0.58 (0.48, 0.71)	<0.0001
Placebo	505	245 (48.5)	13310.9	1.8	40.0 (27.7, -)	49.4 (44.8, 53.8)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by AJCC 8th Edition cancer stage as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-3
Analysis of Distant Metastasis-Free Survival
ITT Population – Sensitivity Analysis 1

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	514	173 (33.7)	16087.8	1.1	Not Reached (49.6, -)	65.2 (60.7, 69.3)	0.60 (0.50, 0.73)	<0.0001
Placebo	505	245 (48.5)	13307.7	1.8	40.0 (26.4, -)	49.4 (44.8, 53.8)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-4
Analysis of Distant Metastasis-Free Survival
ITT Population – Sensitivity Analysis 2

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	514	176 (34.2)	16087.8	1.1	Not Reached (49.6, -)	64.8 (60.3, 68.9)	0.61 (0.50, 0.74)	<0.0001
Placebo	505	246 (48.7)	13307.7	1.8	40.0 (26.4, -)	49.2 (44.7, 53.6)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

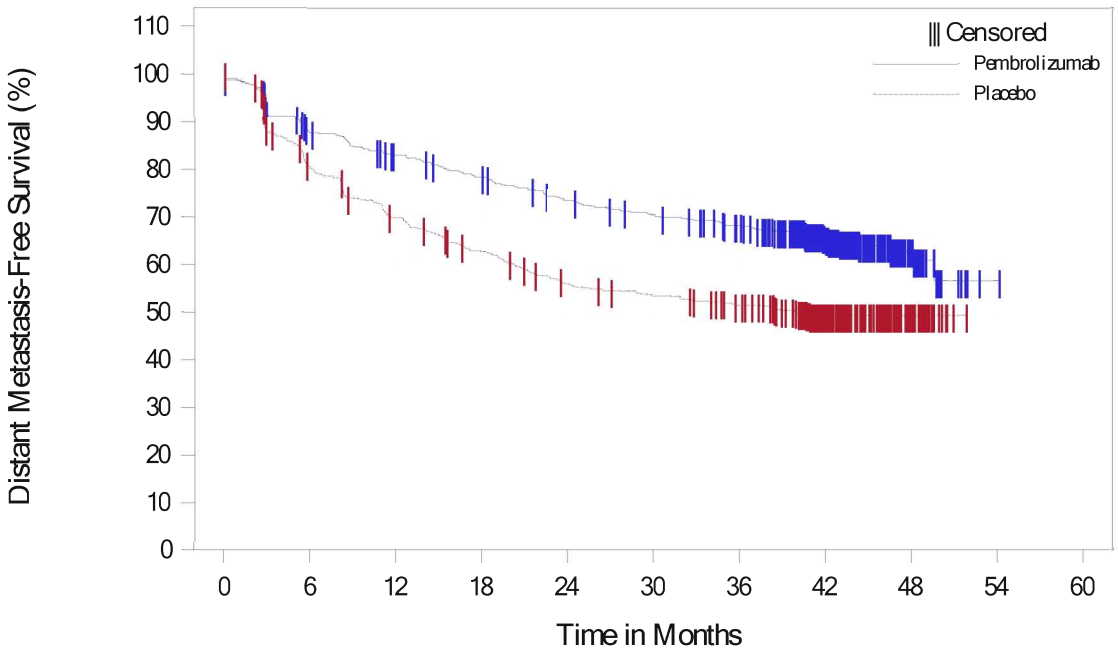
§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-1
Kaplan-Meier Estimates of Distant Metastasis-Free Survival

ITT Population



n at risk

Pembrolizumab	514	434	404	378	352	334	314	174	32	1	0
Placebo	505	395	339	301	265	251	235	136	31	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-5
Distant Metastasis-Free Survival Rate Over Time
(ITT Population)

	Pembrolizumab (N=514)	Placebo (N=505)
DMFS rate at 6 Months in % (95% CI)†	87.7 (84.5, 90.3)	80.6 (76.8, 83.8)
DMFS rate at 12 Months in % (95% CI)†	82.8 (79.2, 85.8)	69.8 (65.5, 73.6)
DMFS rate at 18 Months in % (95% CI)†	78.3 (74.4, 81.7)	62.7 (58.3, 66.8)
DMFS rate at 24 Months in % (95% CI)†	73.5 (69.4, 77.2)	56.0 (51.5, 60.3)
DMFS rate at 30 Months in % (95% CI)†	70.3 (66.1, 74.2)	53.5 (48.9, 57.8)
DMFS rate at 36 Months in % (95% CI)†	68.2 (63.9, 72.1)	51.5 (47.0, 55.9)
DMFS rate at 42 Months in % (95% CI)†	65.3 (60.9, 69.5)	49.4 (44.8, 53.8)

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

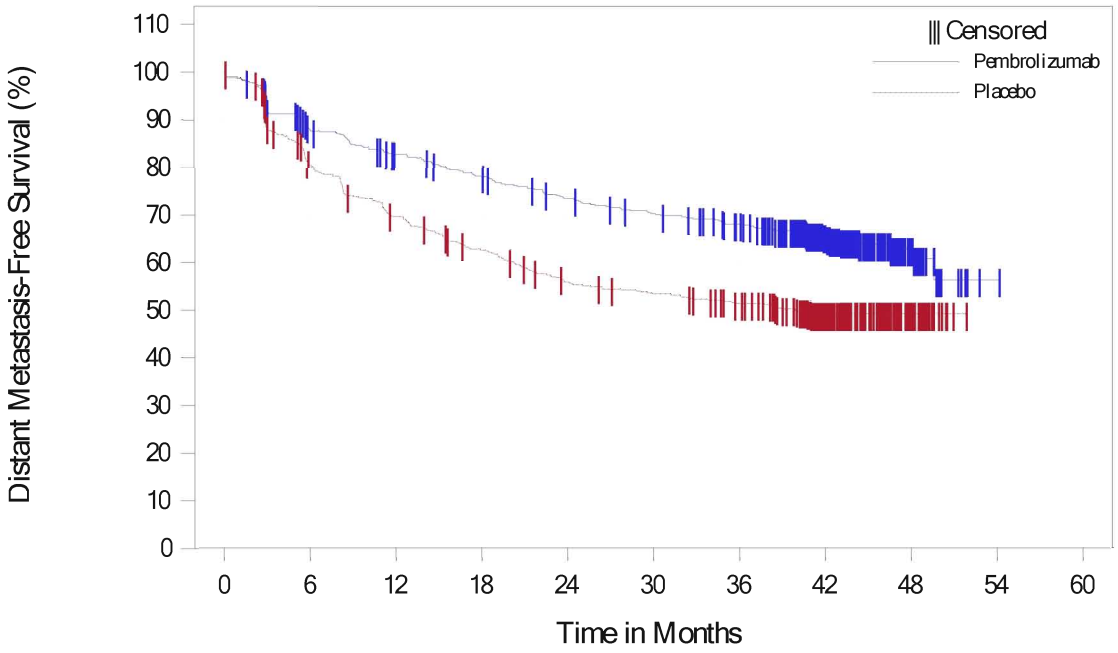
† From the product-limit (Kaplan-Meier) method for censored data.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-2
Kaplan-Meier Estimates of Distant Metastasis-Free Survival

ITT Population – Sensitivity Analysis 1



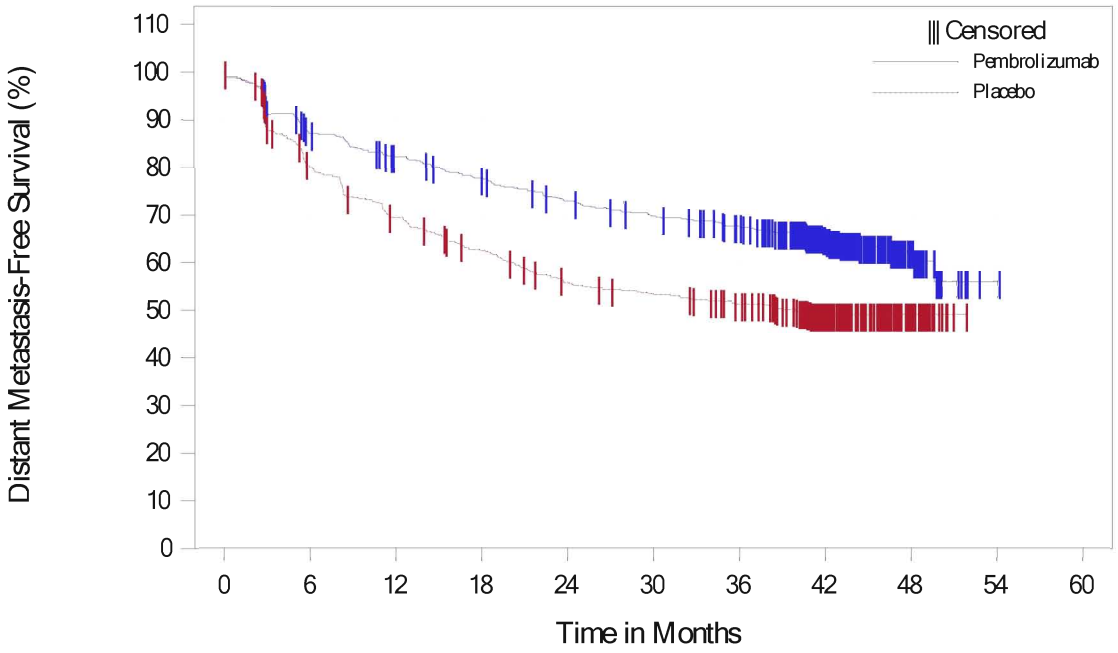
n at risk

Pembrolizumab	514	432	402	376	350	332	312	173	32	1	0
Placebo	505	394	339	301	265	251	235	136	31	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-3
Kaplan-Meier Estimates of Distant Metastasis-Free Survival

ITT Population – Sensitivity Analysis 2



n at risk

Pembrolizumab	514	432	402	376	350	332	312	173	32	1	0
Placebo	505	394	339	301	265	251	235	136	31	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

14.2.2 Efficacy Endpoint: Distant Metastasis-free Survival by PD-L1 Expression

Table 14.2-6
Analysis of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	428	138 (32.2)	13632.1	1.0	Not Reached (49.6, -)	66.7 (61.8, 71.2)	0.61 (0.49, 0.76)	<0.0001
Placebo	425	198 (46.6)	11630.0	1.7	Not Reached (33.8, -)	51.6 (46.6, 56.4)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

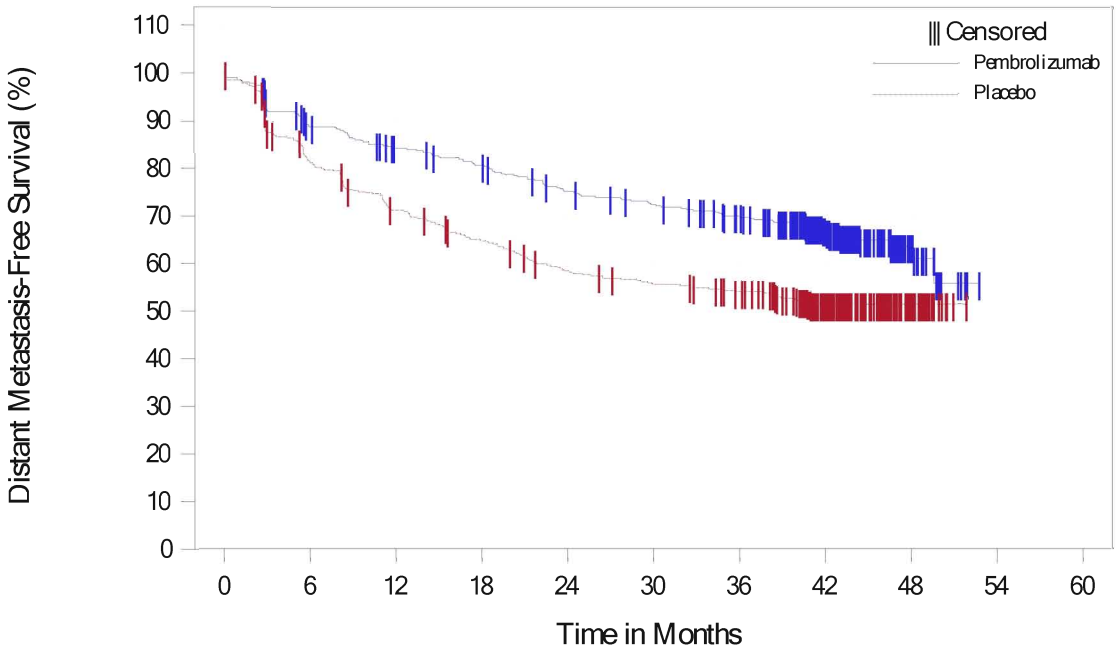
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-4
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population



n at risk

Pembrolizumab	428	365	341	322	297	283	264	144	25	0	0
Placebo	425	339	293	264	235	222	210	123	30	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-7
Analysis of Distant Metastasis-Free Survival
(8th Edition Cancer Stage)
PD-L1 Positive ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	428	138 (32.2)	13632.1	1.0	Not Reached (49.6, -)	66.7 (61.8, 71.2)	0.59 (0.47, 0.73)	<0.0001
Placebo	425	198 (46.6)	11630.0	1.7	Not Reached (33.8, -)	51.6 (46.6, 56.4)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by AJCC 8th Edition cancer stage as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-8
Analysis of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population – Sensitivity Analysis 1

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	428	138 (32.2)	13555.5	1.0	Not Reached (49.6, -)	66.6 (61.6, 71.1)	0.61 (0.49, 0.76)	<0.0001
Placebo	425	198 (46.6)	11626.8	1.7	Not Reached (32.8, -)	51.6 (46.6, 56.4)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-9
Analysis of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population – Sensitivity Analysis 2

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo	
							Hazard Ratio‡ (95% CI)‡	p-Value§
Pembrolizumab	428	141 (32.9)	13555.5	1.0	Not Reached (49.6, -)	66.1 (61.1, 70.6)	0.63 (0.50, 0.78)	0.00001
Placebo	425	199 (46.8)	11626.8	1.7	Not Reached (32.8, -)	51.5 (46.5, 56.2)	---	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

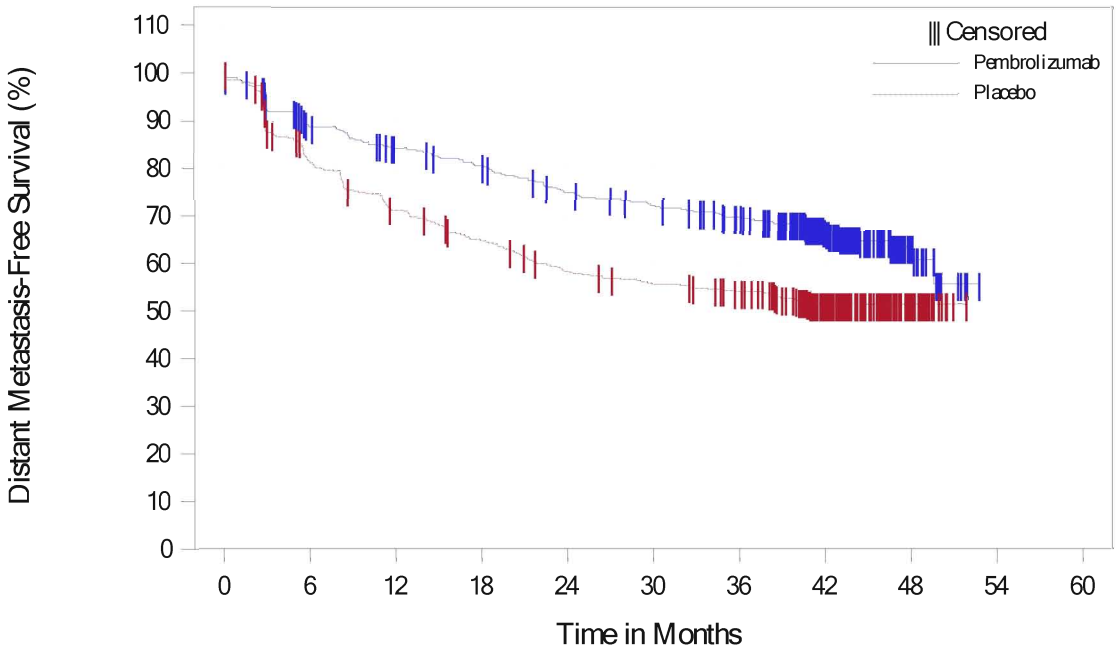
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

§ One-sided p-value based on log-rank test.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-5
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population – Sensitivity Analysis 1

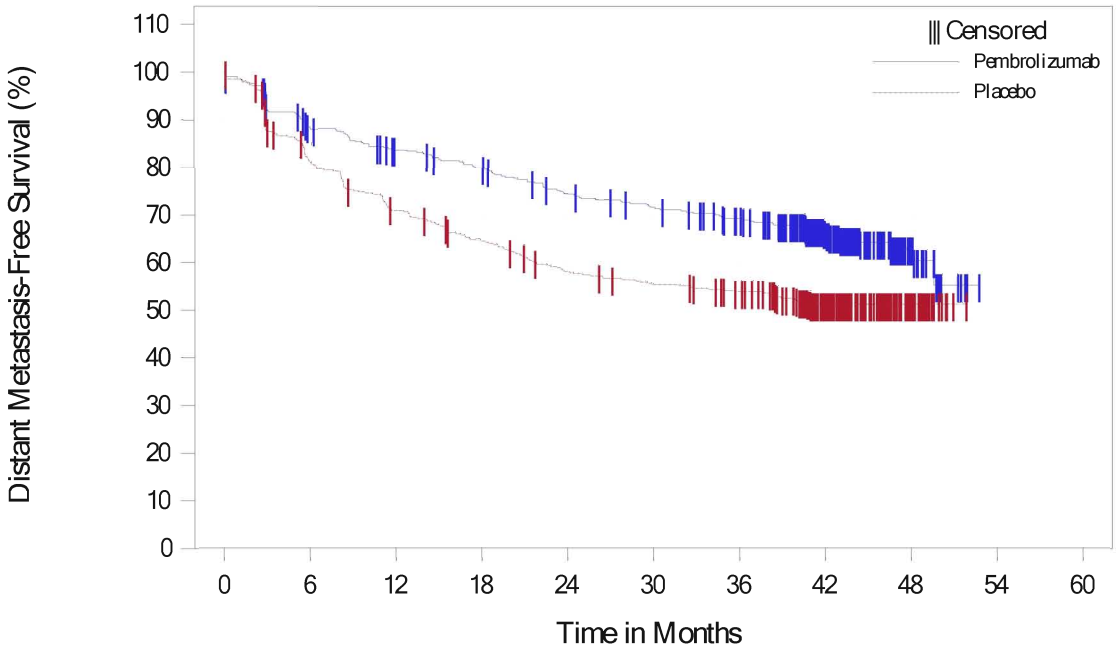


n at risk

Pembrolizumab	428	363	339	320	295	281	262	143	25	0	0
Placebo	425	338	293	264	235	222	210	123	30	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-6
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Positive ITT Population – Sensitivity Analysis 2



n at risk

Pembrolizumab	428	363	339	320	295	281	262	143	25	0	0
Placebo	425	338	293	264	235	222	210	123	30	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-10
Analysis of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	24 (40.7)	1771.2	1.4	Not Reached (25.6, -)	58.0 (44.1, 69.5)	0.49 (0.28, 0.83)
Placebo	57	32 (56.1)	1252.7	2.6	20.3 (10.4, -)	40.2 (27.0, 53.0)	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

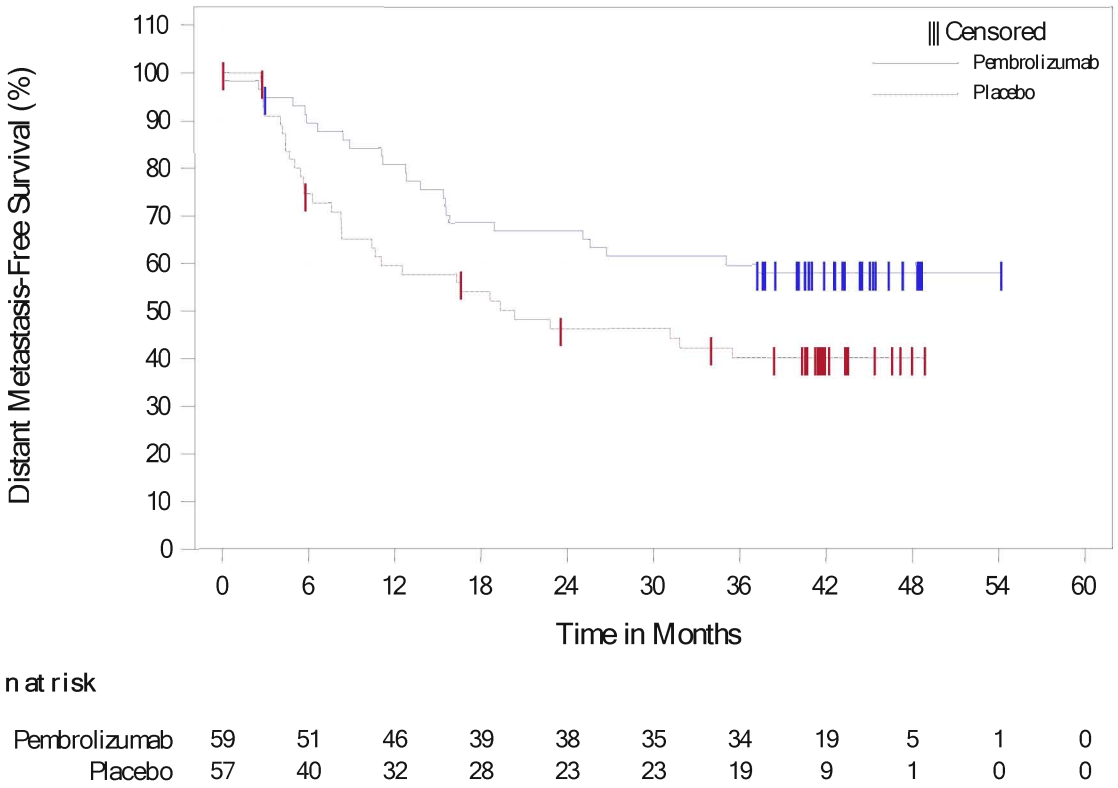
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-7
Kaplan-Meier Estimates of Distant Metastasis-Free Survival

PD-L1 Negative ITT Population



n at risk

Pembrolizumab	59	51	46	39	38	35	34	19	5	1	0
Placebo	57	40	32	28	23	23	19	9	1	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-11
Analysis of Distant Metastasis-Free Survival
(8th Edition Cancer Stage)
PD-L1 Negative ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	24 (40.7)	1771.2	1.4	Not Reached (25.6, -)	58.0 (44.1, 69.5)	0.50 (0.29, 0.88)
Placebo	57	32 (56.1)	1252.7	2.6	20.3 (10.4, -)	40.2 (27.0, 53.0)	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by AJCC 8th Edition cancer stage as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-12
Analysis of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population – Sensitivity Analysis 1

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	24 (40.7)	1771.2	1.4	Not Reached (25.6, -)	58.0 (44.1, 69.5)	0.49 (0.28, 0.83)
Placebo	57	32 (56.1)	1252.7	2.6	20.3 (10.4, -)	40.2 (27.0, 53.0)	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-13
Analysis of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population – Sensitivity Analysis 2

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median DMFS† (Months) (95% CI)	DMFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	24 (40.7)	1771.2	1.4	Not Reached (25.6, -)	58.0 (44.1, 69.5)	0.49 (0.28, 0.83)
Placebo	57	32 (56.1)	1252.7	2.6	20.3 (10.4, -)	40.2 (27.0, 53.0)	---

Distant metastasis-free survival is defined as the time between the date of randomization and the date of first distant metastasis or date of death (whatever the cause), whichever occurs first.

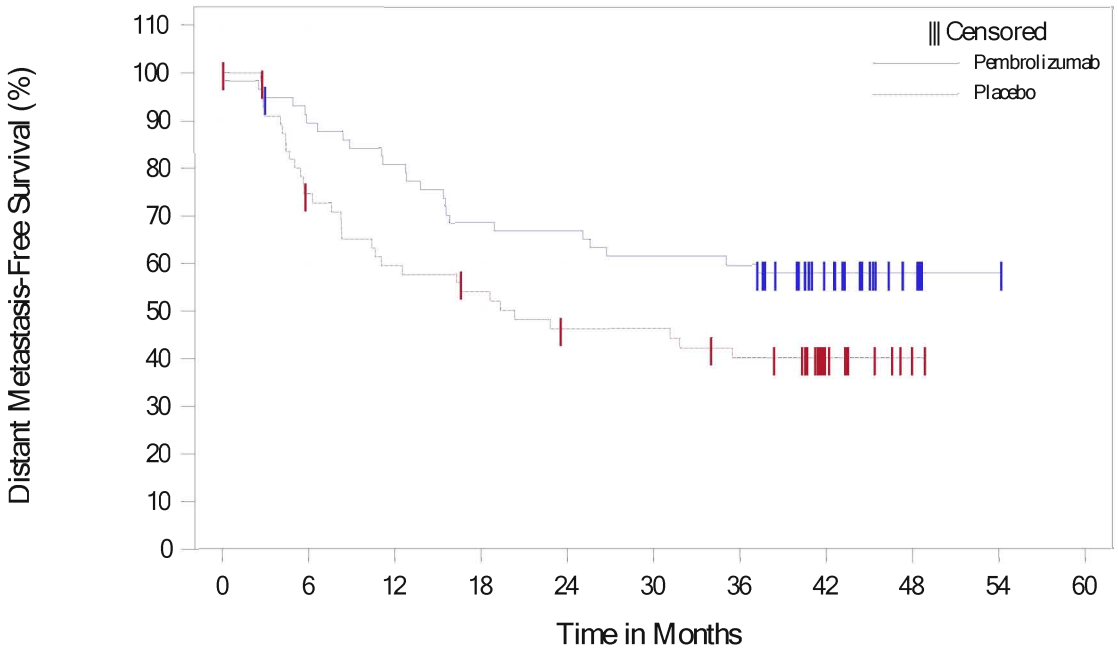
† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-8
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population – Sensitivity Analysis 1

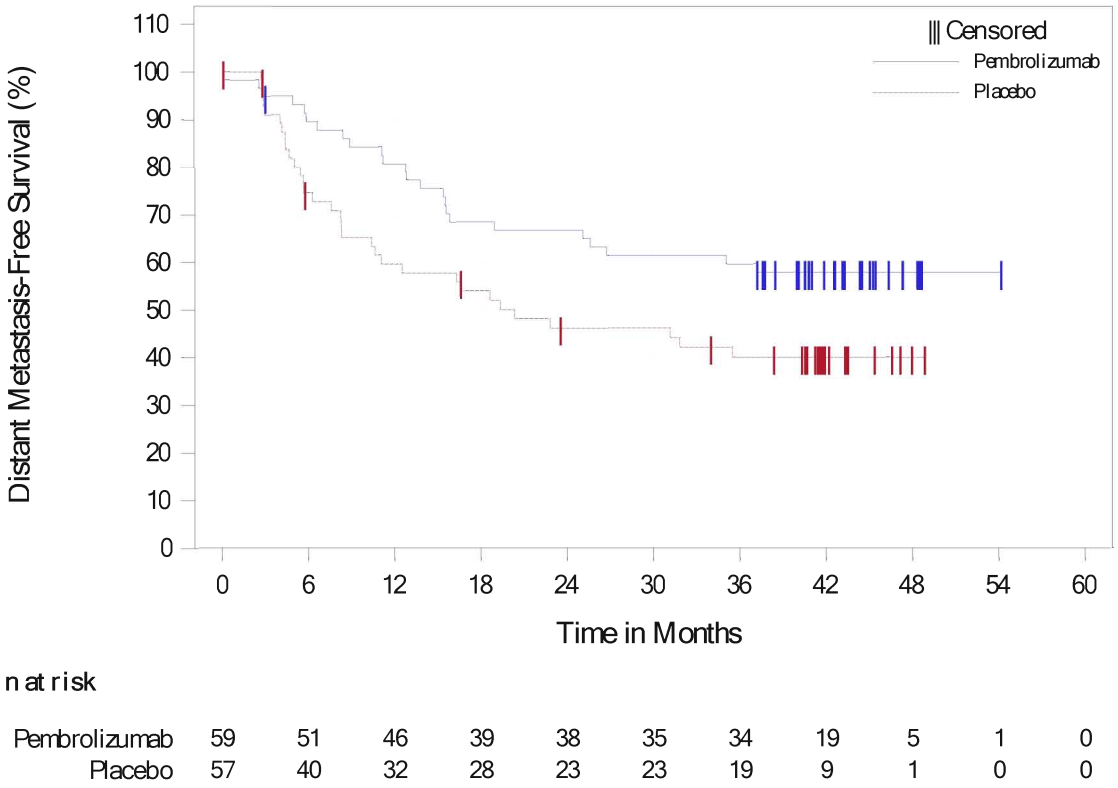


n at risk

Pembrolizumab	59	51	46	39	38	35	34	19	5	1	0
Placebo	57	40	32	28	23	23	19	9	1	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-9
Kaplan-Meier Estimates of Distant Metastasis-Free Survival
PD-L1 Negative ITT Population – Sensitivity Analysis 2



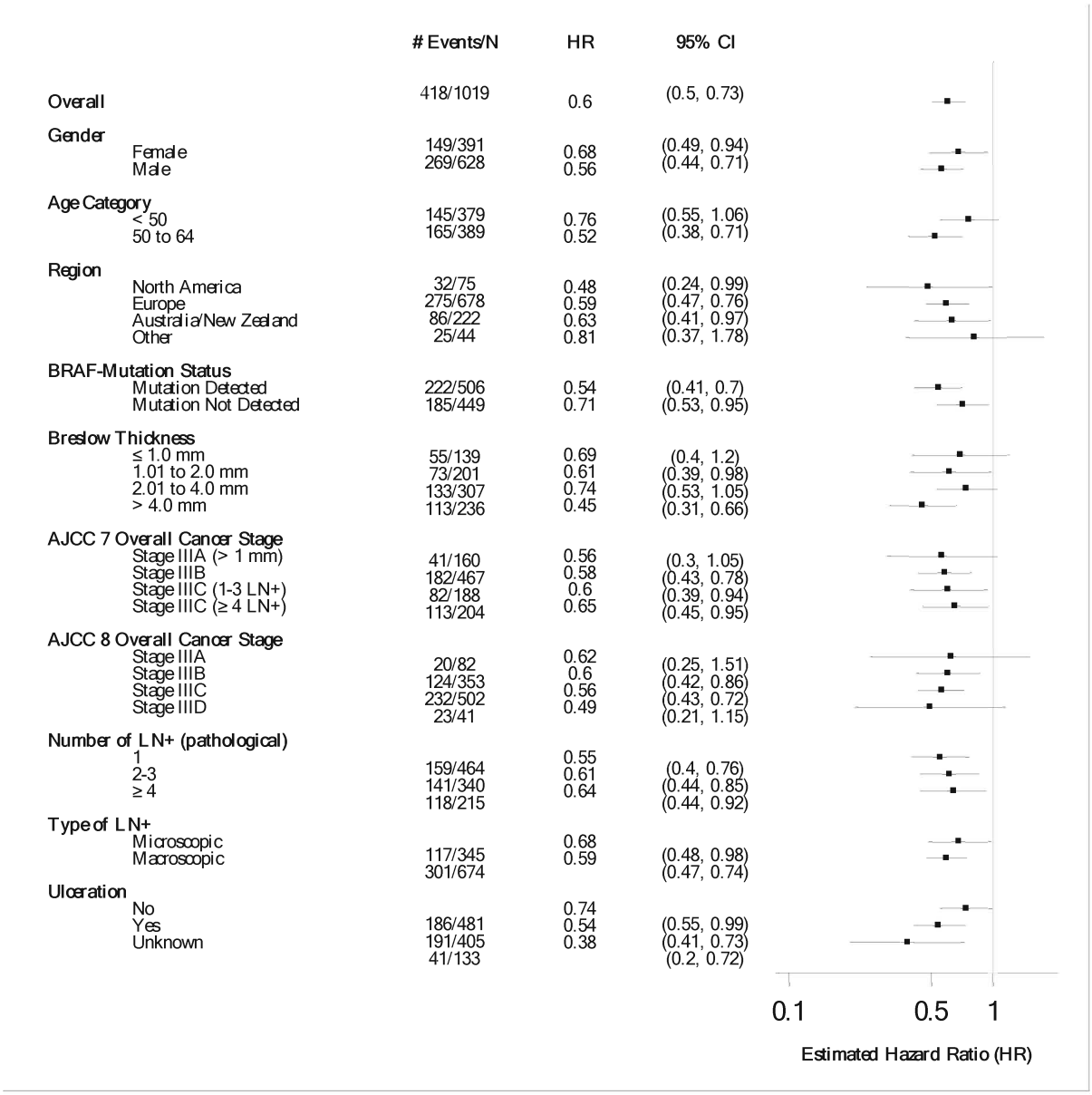
n at risk

Pembrolizumab	59	51	46	39	38	35	34	19	5	1	0
Placebo	57	40	32	28	23	23	19	9	1	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

14.2.3 Distant Metastasis-free Survival by Other Subgroup

Figure 14.2-10
Forest Plot of Distant Metastases-Free Survival Hazard Ratio by Subgroup Factors
ITT Population



(Database Cutoff Date: 03APR2020).
Source: [P054V02MK3475: adam-adsl; adtte]

14.2.4 Efficacy Endpoint: Recurrence-free Survival in All Participants

Table 14.2-14
Analysis of Recurrence-Free Survival
ITT Population

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median RFS† (Months) (95% CI)	RFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	514	203 (39.5)	15278.1	1.3	Not Reached (48.1, -)	59.8 (55.3, 64.1)	0.59 (0.49, 0.70)
Placebo	505	288 (57.0)	11792.0	2.4	21.4 (16.3, 27.0)	41.4 (37.0, 45.8)	---

Recurrence-free survival is defined as time from randomization to the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

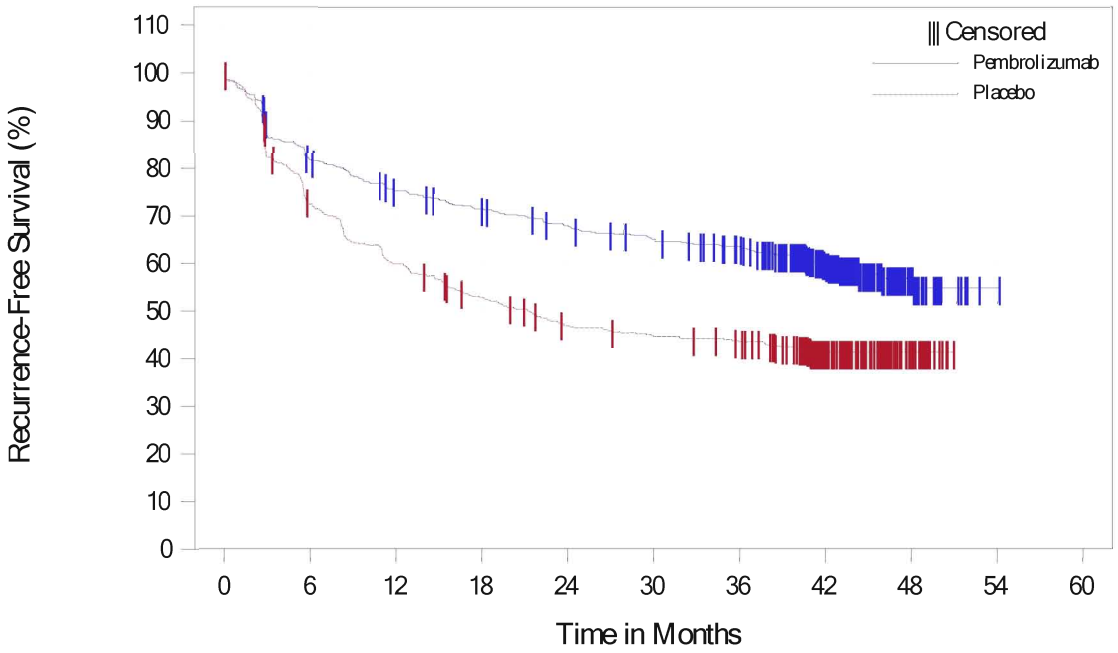
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Figure 14.2-11
Kaplan-Meier Estimates of Recurrence-Free Survival

ITT Population



n at risk

Pembrolizumab	514	412	375	353	333	316	300	163	30	1	0
Placebo	505	359	297	258	225	213	205	115	26	0	0

(Database Cutoff Date: 03APR2020)
Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-15
Recurrence-Free Survival Rate Over Time
(ITT Population)

	Pembrolizumab (N=514)	Placebo (N=505)
RFS rate at 6 Months in % (95% CI)†	81.8 (78.2, 84.9)	72.5 (68.4, 76.2)
RFS rate at 12 Months in % (95% CI)†	75.3 (71.3, 78.8)	60.0 (55.5, 64.1)
RFS rate at 18 Months in % (95% CI)†	71.4 (67.3, 75.2)	52.9 (48.4, 57.2)
RFS rate at 24 Months in % (95% CI)†	68.0 (63.7, 71.9)	46.9 (42.4, 51.2)
RFS rate at 30 Months in % (95% CI)†	65.1 (60.8, 69.1)	44.6 (40.2, 48.9)
RFS rate at 36 Months in % (95% CI)†	63.7 (59.3, 67.7)	43.5 (39.1, 47.9)
RFS rate at 42 Months in % (95% CI)†	59.8 (55.3, 64.1)	41.4 (37.0, 45.8)
RFS rate at 48 Months in % (95% CI)†	57.0 (51.9, 61.7)	41.4 (37.0, 45.8)
RFS rate at 54 Months in % (95% CI)†	55.0 (48.8, 60.8)	Not reached
RFS rate at 60 Months in % (95% CI)†	Not reached	

Recurrence-free survival is defined as time from randomization to the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause), whichever occurs first.

† From the product-limit (Kaplan-Meier) method for censored data.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-16
Disease Status
ITT Population

	Pembrolizumab n (%)	Placebo n (%)
Subjects in population	514	505
Type of First Event in RFS Analysis		
No event	311 (60.5)	217 (43.0)
Event	203 (39.5)	288 (57.0)
Locoregional recurrence	71 (13.8)	93 (18.4)
Distant metastasis	118 (23.0)	165 (32.7)
Both diagnosed within 30 days from each other	8 (1.6)	29 (5.7)
Death	6 (1.2)	1 (0.2)
DMFS Status		
No event	341 (66.3)	260 (51.5)
Event	173 (33.7)	245 (48.5)
(Data Cutoff Date: 03APR2020).		

Source: [P054V02MK3475: adam-adsl; adtte]

14.2.5 Efficacy Endpoint: Recurrence-free Survival by PD-L1 Expression

Table 14.2-17
Analysis of Recurrence-Free Survival
PD-L1 Positive
(ITT Population)

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median RFS† (Months) (95% CI)	RFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	428	163 (38.1)	12982.6	1.3	Not Reached (48.1, -)	60.9 (55.9, 65.6)	0.59 (0.49, 0.73)
Placebo	425	235 (55.3)	10321.8	2.3	22.5 (17.3, 37.8)	43.7 (38.9, 48.4)	---

Recurrence-free survival is defined as time from randomization to the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

Table 14.2-18
Analysis of Recurrence-Free Survival
PD-L1 Negative
(ITT Population)

Treatment	N	Number of Events (%)	Person-Months	Event Rate/ 100 Person-Months	Median RFS† (Months) (95% CI)	RFS Rate at Month 42 in %† (95% CI)	Pembrolizumab vs. Placebo Hazard Ratio‡ (95% CI)‡
Pembrolizumab	59	27 (45.8)	1639.5	1.6	Not Reached (15.5, -)	55.2 (41.6, 66.9)	0.46 (0.27, 0.77)
Placebo	57	37 (64.9)	1112.1	3.3	16.6 (5.7, 31.9)	30.1 (18.2, 43.0)	---

Recurrence-free survival is defined as time from randomization to the date of first recurrence (local, regional, distant metastasis) or death (whatever the cause), whichever occurs first.

† From product-limit (Kaplan-Meier) method for censored data.

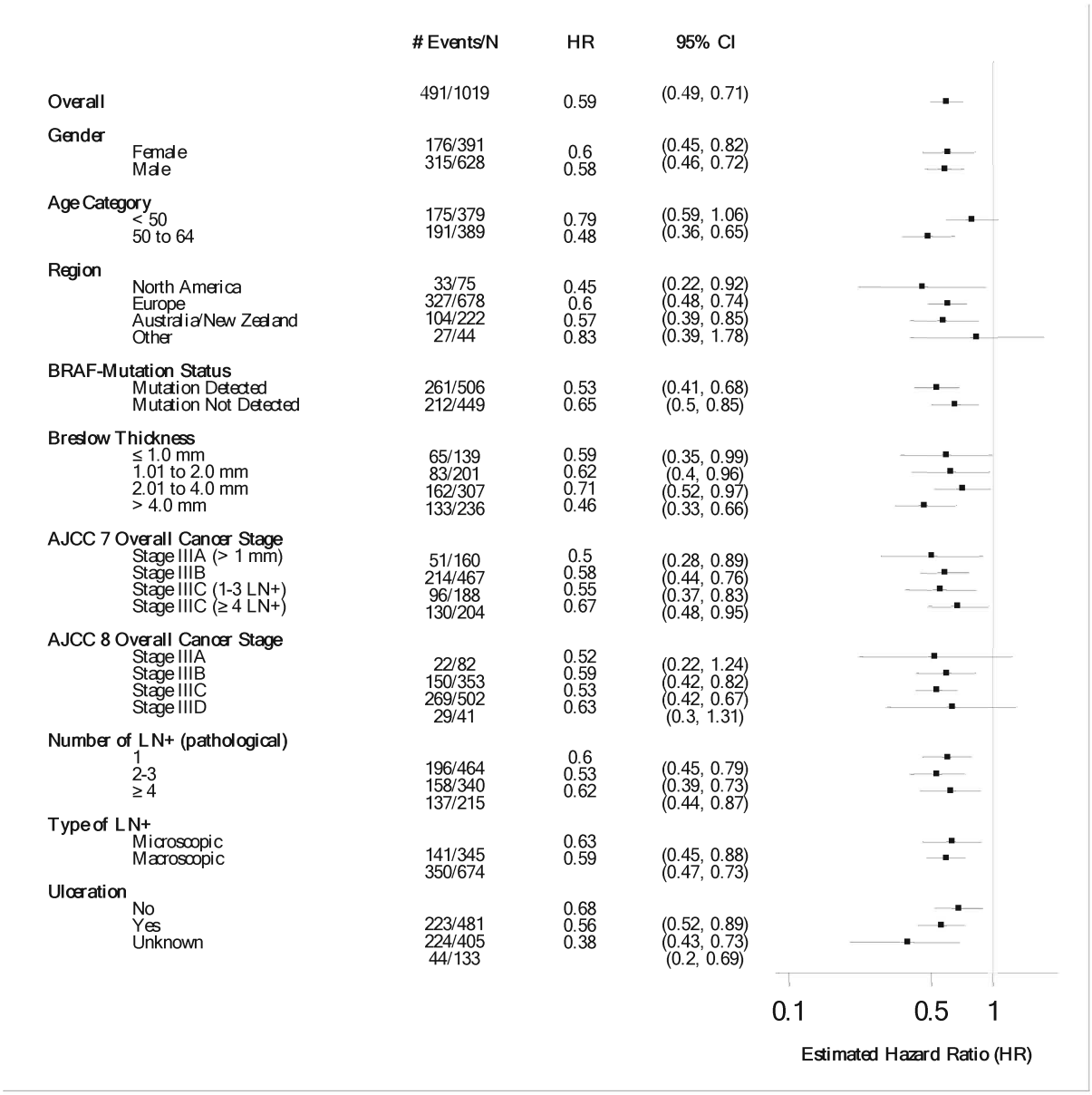
‡ Based on Cox regression model with treatment as a covariate stratified by stage (IIIA [>1 mm metastasis] vs. IIIB vs. IIIC 1-3 nodes vs. IIIC = 4 nodes) as indicated at randomization.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adtte]

14.2.6 Recurrence-free Survival by Other Subgroup

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



(Database Cutoff Date: 03APR2020).
Source: [P054V02MK3475: adam-adsl; adtte]

14.3 Safety Data

14.3.1 Adverse Events

14.3.1.1 All Adverse Events

14.3.1.1.1 Brief Summary of Adverse Events

Table 14.3-1

Adverse Event Summary
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse event	29	(5.7)	48	(9.6)	77	(7.6)
with drug-related† adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with toxicity grade 3-5 adverse events	162	(31.8)	96	(19.1)	258	(25.5)
with toxicity grade 3-5 drug-related adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with serious adverse events	127	(25.0)	83	(16.5)	210	(20.8)
with serious drug-related adverse events	62	(12.2)	6	(1.2)	68	(6.7)
who died	1	(0.2)	0	(0.0)	1	(0.1)
who died due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	71	(13.9)	18	(3.6)	89	(8.8)
discontinued drug due to a drug-related adverse event	62	(12.2)	8	(1.6)	70	(6.9)
discontinued drug due to a serious adverse event	29	(5.7)	11	(2.2)	40	(4.0)
discontinued drug due to a serious drug-related adverse event	22	(4.3)	2	(0.4)	24	(2.4)

† Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-2

Adverse Event Summary
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	149	(87.6)
with no adverse event	21	(12.4)
with drug-related† adverse events	117	(68.8)
with toxicity grade 3-5 adverse events	46	(27.1)
with toxicity grade 3-5 drug-related adverse events	18	(10.6)
with serious adverse events	29	(17.1)
with serious drug-related adverse events	9	(5.3)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued drug due to an adverse event	19	(11.2)
discontinued drug due to a drug-related adverse event	13	(7.6)
discontinued drug due to a serious adverse event	6	(3.5)
discontinued drug due to a serious drug-related adverse event	3	(1.8)

† Determined by the investigator to be related to the drug.

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

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

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-3

Subjects With COVID-19 Related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	0	(0.0)	0	(0.0)	0	(0.0)
with no adverse events	509	(100.0)	502	(100.0)	1,011	(100.0)

Every subject is counted a single time for each applicable row and column.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.1.2 Most Frequently Reported Adverse Events

Table 14.3-4

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)

Every subject 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.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

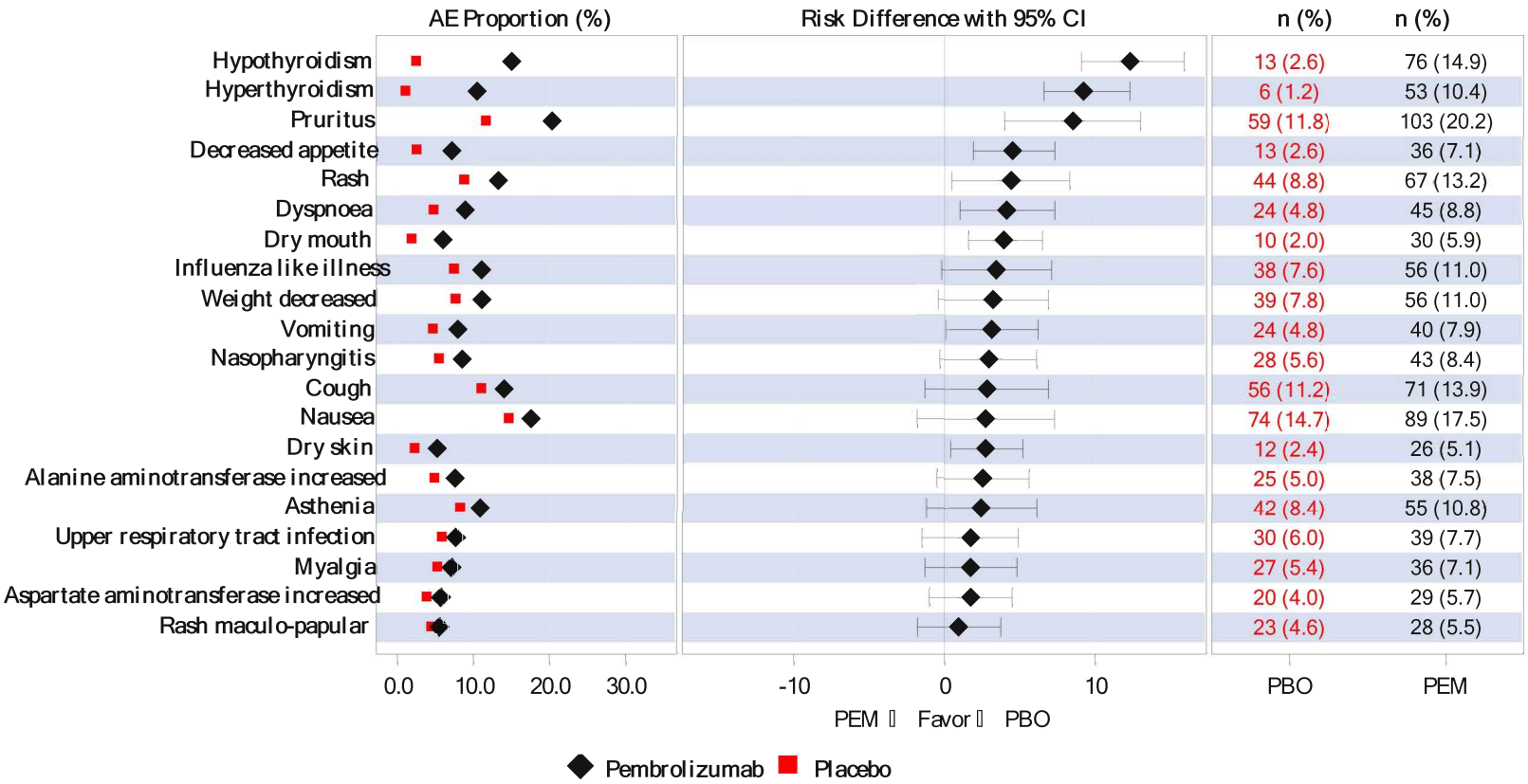
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

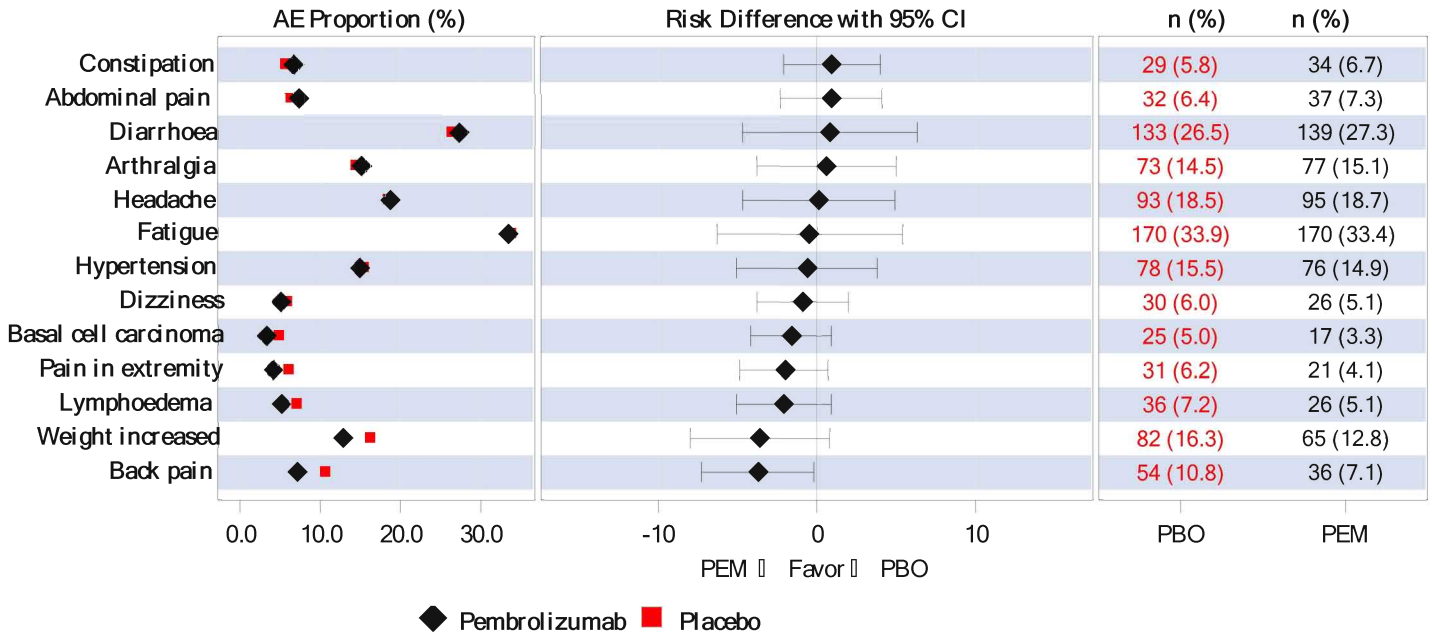
Source: [P054V02MK3475: adam-adsl; adae]

Figure 14.3-1

Between-Treatment Comparisons in Adverse Events
Selected Adverse Events (≥5% Incidence) and Sorted by Risk Difference
(ASaT Population)
Pembrolizumab (N=509) vs. Placebo (N=502)



Between-Treatment Comparisons in Adverse Events
Selected Adverse Events (≥5% Incidence) and Sorted by Risk Difference
(ASaT Population)
Pembrolizumab (N=509) vs. Placebo (N=502) (Continued)



PEM: Pembrolizumab
PBO: Placebo
Database Cutoff Date: 03APR2020
Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-5

Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence ≥ 10% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
Grade 1	69	(13.6)	136	(27.1)	205	(20.3)
Grade 2	249	(48.9)	222	(44.2)	471	(46.6)
Grade 3	147	(28.9)	89	(17.7)	236	(23.3)
Grade 4	14	(2.8)	7	(1.4)	21	(2.1)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Endocrine disorders	**121**	**(23.8)**	**27**	**(5.4)**	**148**	**(14.6)**
Grade 1	38	(7.5)	17	(3.4)	55	(5.4)
Grade 2	80	(15.7)	10	(2.0)	90	(8.9)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Eye disorders	**56**	**(11.0)**	**43**	**(8.6)**	**99**	**(9.8)**
Grade 1	46	(9.0)	35	(7.0)	81	(8.0)
Grade 2	9	(1.8)	7	(1.4)	16	(1.6)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Grade 1	179	(35.2)	175	(34.9)	354	(35.0)
Grade 2	75	(14.7)	46	(9.2)	121	(12.0)
Grade 3	27	(5.3)	10	(2.0)	37	(3.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Grade 1	106	(20.8)	108	(21.5)	214	(21.2)
Grade 2	27	(5.3)	19	(3.8)	46	(4.5)
Grade 3	5	(1.0)	6	(1.2)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence ≥ 10% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Grade 1	76	(14.9)	66	(13.1)	142	(14.0)
Grade 2	12	(2.4)	8	(1.6)	20	(2.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
General disorders and administration site conditions	**280**	**(55.0)**	**260**	**(51.8)**	**540**	**(53.4)**
Grade 1	192	(37.7)	216	(43.0)	408	(40.4)
Grade 2	79	(15.5)	41	(8.2)	120	(11.9)
Grade 3	9	(1.8)	3	(0.6)	12	(1.2)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Grade 1	38	(7.5)	37	(7.4)	75	(7.4)
Grade 2	16	(3.1)	5	(1.0)	21	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Grade 1	122	(24.0)	144	(28.7)	266	(26.3)
Grade 2	44	(8.6)	23	(4.6)	67	(6.6)
Grade 3	4	(0.8)	3	(0.6)	7	(0.7)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Grade 1	46	(9.0)	32	(6.4)	78	(7.7)
Grade 2	10	(2.0)	6	(1.2)	16	(1.6)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Grade 1	72	(14.1)	55	(11.0)	127	(12.6)
Grade 2	134	(26.3)	98	(19.5)	232	(22.9)
Grade 3	18	(3.5)	19	(3.8)	37	(3.7)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Grade 1	22	(4.3)	29	(5.8)	51	(5.0)
Grade 2	14	(2.8)	18	(3.6)	32	(3.2)
Grade 3	3	(0.6)	5	(1.0)	8	(0.8)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence ≥ 10% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Grade 1	130	(25.5)	129	(25.7)	259	(25.6)
Grade 2	57	(11.2)	38	(7.6)	95	(9.4)
Grade 3	13	(2.6)	13	(2.6)	26	(2.6)
Grade 4	5	(1.0)	2	(0.4)	7	(0.7)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Grade 1	48	(9.4)	33	(6.6)	81	(8.0)
Grade 2	8	(1.6)	6	(1.2)	14	(1.4)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Grade 1	49	(9.6)	68	(13.5)	117	(11.6)
Grade 2	16	(3.1)	14	(2.8)	30	(3.0)
Metabolism and nutrition disorders	**90**	**(17.7)**	**52**	**(10.4)**	**142**	**(14.0)**
Grade 1	47	(9.2)	31	(6.2)	78	(7.7)
Grade 2	24	(4.7)	11	(2.2)	35	(3.5)
Grade 3	17	(3.3)	7	(1.4)	24	(2.4)
Grade 4	2	(0.4)	3	(0.6)	5	(0.5)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Grade 1	125	(24.6)	129	(25.7)	254	(25.1)
Grade 2	47	(9.2)	50	(10.0)	97	(9.6)
Grade 3	10	(2.0)	5	(1.0)	15	(1.5)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Grade 1	52	(10.2)	59	(11.8)	111	(11.0)
Grade 2	19	(3.7)	14	(2.8)	33	(3.3)
Grade 3	6	(1.2)	0	(0.0)	6	(0.6)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Grade 1	28	(5.5)	36	(7.2)	64	(6.3)
Grade 2	8	(1.6)	16	(3.2)	24	(2.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence ≥ 10% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Grade 1	27	(5.3)	29	(5.8)	56	(5.5)
Grade 2	31	(6.1)	32	(6.4)	63	(6.2)
Grade 3	14	(2.8)	12	(2.4)	26	(2.6)
Grade 4	1	(0.2)	1	(0.2)	2	(0.2)
Nervous system disorders	**175**	**(34.4)**	**162**	**(32.3)**	**337**	**(33.3)**
Grade 1	132	(25.9)	125	(24.9)	257	(25.4)
Grade 2	37	(7.3)	28	(5.6)	65	(6.4)
Grade 3	6	(1.2)	9	(1.8)	15	(1.5)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Grade 1	75	(14.7)	78	(15.5)	153	(15.1)
Grade 2	20	(3.9)	14	(2.8)	34	(3.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Psychiatric disorders	**43**	**(8.4)**	**61**	**(12.2)**	**104**	**(10.3)**
Grade 1	26	(5.1)	42	(8.4)	68	(6.7)
Grade 2	17	(3.3)	17	(3.4)	34	(3.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**
Grade 1	99	(19.4)	87	(17.3)	186	(18.4)
Grade 2	41	(8.1)	19	(3.8)	60	(5.9)
Grade 3	9	(1.8)	2	(0.4)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Grade 1	63	(12.4)	48	(9.6)	111	(11.0)
Grade 2	8	(1.6)	8	(1.6)	16	(1.6)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Grade 1	190	(37.3)	166	(33.1)	356	(35.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence ≥ 10% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Grade 2	79	(15.5)	31	(6.2)	110	(10.9)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Grade 1	85	(16.7)	56	(11.2)	141	(13.9)
Grade 2	18	(3.5)	3	(0.6)	21	(2.1)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Grade 1	54	(10.6)	40	(8.0)	94	(9.3)
Grade 2	11	(2.2)	4	(0.8)	15	(1.5)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Vascular disorders	**125**	**(24.6)**	**130**	**(25.9)**	**255**	**(25.2)**
Grade 1	47	(9.2)	55	(11.0)	102	(10.1)
Grade 2	47	(9.2)	56	(11.2)	103	(10.2)
Grade 3	31	(6.1)	19	(3.8)	50	(4.9)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Grade 1	9	(1.8)	15	(3.0)	24	(2.4)
Grade 2	39	(7.7)	45	(9.0)	84	(8.3)
Grade 3	28	(5.5)	18	(3.6)	46	(4.5)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-6

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Blood and lymphatic system disorders	**37**	**(7.3)**	**22**	**(4.4)**	**59**	**(5.8)**
Anaemia	7	(1.4)	5	(1.0)	12	(1.2)
Eosinophilia	9	(1.8)	1	(0.2)	10	(1.0)
Leukocytosis	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	2	(0.4)	2	(0.2)
Lymph node pain	2	(0.4)	2	(0.4)	4	(0.4)
Lymphadenopathy	3	(0.6)	4	(0.8)	7	(0.7)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	11	(2.2)	7	(1.4)	18	(1.8)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Cardiac disorders	**24**	**(4.7)**	**20**	**(4.0)**	**44**	**(4.4)**
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)
Angina pectoris	1	(0.2)	1	(0.2)	2	(0.2)
Arrhythmia	1	(0.2)	0	(0.0)	1	(0.1)
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bradycardia	6	(1.2)	8	(1.6)	14	(1.4)
Brugada syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure congestive	1	(0.2)	0	(0.0)	1	(0.1)
Coronary artery disease	0	(0.0)	1	(0.2)	1	(0.1)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Palpitations	6	(1.2)	4	(0.8)	10	(1.0)
Sinus bradycardia	1	(0.2)	3	(0.6)	4	(0.4)
Sinus tachycardia	2	(0.4)	0	(0.0)	2	(0.2)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Tachycardia	2	(0.4)	1	(0.2)	3	(0.3)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**5**	**(1.0)**	7	**(0.7)**

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**5**	**(1.0)**	7	**(0.7)**
Dermoid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Epidermal naevus	0	(0.0)	1	(0.2)	1	(0.1)
Gilbert's syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Hydrocele	0	(0.0)	1	(0.2)	1	(0.1)
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Preauricular cyst	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**21**	**(4.1)**	**21**	**(4.2)**	**42**	**(4.2)**
Deafness	0	(0.0)	1	(0.2)	1	(0.1)
Deafness unilateral	0	(0.0)	1	(0.2)	1	(0.1)
Ear discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Ear pain	5	(1.0)	1	(0.2)	6	(0.6)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
External ear inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Hypoacusis	2	(0.4)	0	(0.0)	2	(0.2)
Middle ear effusion	0	(0.0)	1	(0.2)	1	(0.1)
Middle ear inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Noninfective myringitis	0	(0.0)	1	(0.2)	1	(0.1)
Tinnitus	5	(1.0)	8	(1.6)	13	(1.3)
Vertigo	7	(1.4)	9	(1.8)	16	(1.6)
Vestibular disorder	2	(0.4)	0	(0.0)	2	(0.2)
Endocrine disorders	**121**	**(23.8)**	**27**	**(5.4)**	**148**	**(14.6)**
Adrenal insufficiency	4	(0.8)	3	(0.6)	7	(0.7)
Autoimmune thyroiditis	3	(0.6)	1	(0.2)	4	(0.4)
Cushingoid	2	(0.4)	0	(0.0)	2	(0.2)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhagic thyroid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Hypopituitarism	3	(0.6)	1	(0.2)	4	(0.4)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Endocrine disorders	**121**	**(23.8)**	**27**	**(5.4)**	**148**	**(14.6)**
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**56**	**(11.0)**	**43**	**(8.6)**	**99**	**(9.8)**
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Blepharitis	3	(0.6)	0	(0.0)	3	(0.3)
Blepharospasm	0	(0.0)	1	(0.2)	1	(0.1)
Blindness	1	(0.2)	0	(0.0)	1	(0.1)
Cataract	3	(0.6)	3	(0.6)	6	(0.6)
Chalazion	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Diplopia	1	(0.2)	1	(0.2)	2	(0.2)
Dry eye	14	(2.8)	8	(1.6)	22	(2.2)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Eye haemorrhage	1	(0.2)	1	(0.2)	2	(0.2)
Eye inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Eye irritation	3	(0.6)	0	(0.0)	3	(0.3)
Eye pain	1	(0.2)	3	(0.6)	4	(0.4)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Eyelid disorder	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid oedema	1	(0.2)	1	(0.2)	2	(0.2)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	5	(1.0)	1	(0.2)	6	(0.6)
Lens dislocation	0	(0.0)	1	(0.2)	1	(0.1)
Ocular hyperaemia	2	(0.4)	2	(0.4)	4	(0.4)
Optic ischaemic neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	1	(0.2)	2	(0.2)
Periorbital swelling	2	(0.4)	0	(0.0)	2	(0.2)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	1	(0.2)	3	(0.3)
Presbyopia	0	(0.0)	2	(0.4)	2	(0.2)
Scleral hyperaemia	2	(0.4)	0	(0.0)	2	(0.2)
Swelling of eyelid	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eye disorders	**56**	**(11.0)**	**43**	**(8.6)**	**99**	**(9.8)**
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	8	(1.6)	11	(2.2)	19	(1.9)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)
Visual impairment	3	(0.6)	3	(0.6)	6	(0.6)
Vitreous floaters	2	(0.4)	1	(0.2)	3	(0.3)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal distension	2	(0.4)	2	(0.4)	4	(0.4)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Abdominal pain lower	5	(1.0)	1	(0.2)	6	(0.6)
Abdominal pain upper	23	(4.5)	14	(2.8)	37	(3.7)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Anal haemorrhage	3	(0.6)	0	(0.0)	3	(0.3)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Angular cheilitis	0	(0.0)	2	(0.4)	2	(0.2)
Anorectal varices	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	2	(0.4)	0	(0.0)	2	(0.2)
Colitis	13	(2.6)	2	(0.4)	15	(1.5)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Dental caries	2	(0.4)	1	(0.2)	3	(0.3)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Diverticulum	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulum intestinal	1	(0.2)	0	(0.0)	1	(0.1)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Duodenal polyp	1	(0.2)	0	(0.0)	1	(0.1)
Duodenitis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Dyschezia	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	19	(3.7)	6	(1.2)	25	(2.5)
Dysphagia	1	(0.2)	1	(0.2)	2	(0.2)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Epigastric discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Faeces soft	5	(1.0)	3	(0.6)	8	(0.8)
Flatulence	0	(0.0)	4	(0.8)	4	(0.4)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Gastric ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Gastrointestinal angiectasia	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	7	(1.4)	6	(1.2)	13	(1.3)
Gingival bleeding	2	(0.4)	0	(0.0)	2	(0.2)
Gingival oedema	0	(0.0)	1	(0.2)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Gingival recession	0	(0.0)	1	(0.2)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Haematochezia	4	(0.8)	1	(0.2)	5	(0.5)
Haemorrhoidal haemorrhage	2	(0.4)	0	(0.0)	2	(0.2)
Haemorrhoids	7	(1.4)	1	(0.2)	8	(0.8)
Hyperaesthesia teeth	0	(0.0)	1	(0.2)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Inguinal hernia	2	(0.4)	2	(0.4)	4	(0.4)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine polyp	2	(0.4)	1	(0.2)	3	(0.3)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Lip swelling	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Melaena	1	(0.2)	0	(0.0)	1	(0.1)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	4	(0.8)	7	(1.4)	11	(1.1)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Odynophagia	4	(0.8)	1	(0.2)	5	(0.5)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Oesophageal haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal pain	0	(0.0)	1	(0.2)	1	(0.1)
Oral discomfort	1	(0.2)	1	(0.2)	2	(0.2)
Oral disorder	2	(0.4)	0	(0.0)	2	(0.2)
Oral lichen planus	4	(0.8)	0	(0.0)	4	(0.4)
Oral mucosa erosion	1	(0.2)	0	(0.0)	1	(0.1)
Oral pain	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	1	(0.2)	1	(0.2)	2	(0.2)
Proctalgia	3	(0.6)	1	(0.2)	4	(0.4)
Rectal haemorrhage	4	(0.8)	2	(0.4)	6	(0.6)
Rectal tenesmus	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Stomatitis	7	(1.4)	3	(0.6)	10	(1.0)
Submaxillary gland enlargement	1	(0.2)	1	(0.2)	2	(0.2)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Tongue disorder	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	1	(0.2)	2	(0.2)
Toothache	5	(1.0)	7	(1.4)	12	(1.2)
Umbilical hernia	2	(0.4)	0	(0.0)	2	(0.2)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
General disorders and administration site conditions	**280**	**(55.0)**	**260**	**(51.8)**	**540**	**(53.4)**
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Axillary pain	5	(1.0)	5	(1.0)	10	(1.0)
Catheter site inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Catheter site thrombosis	0	(0.0)	1	(0.2)	1	(0.1)
Chest discomfort	0	(0.0)	2	(0.4)	2	(0.2)
Chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Chills	9	(1.8)	5	(1.0)	14	(1.4)
Cyst	1	(0.2)	0	(0.0)	1	(0.1)
Discomfort	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**280**	**(55.0)**	**260**	**(51.8)**	**540**	**(53.4)**
Face oedema	3	(0.6)	1	(0.2)	4	(0.4)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Feeling cold	2	(0.4)	0	(0.0)	2	(0.2)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Gait disturbance	1	(0.2)	0	(0.0)	1	(0.1)
General physical health deterioration	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Infusion site extravasation	2	(0.4)	0	(0.0)	2	(0.2)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Injection site pain	0	(0.0)	1	(0.2)	1	(0.1)
Injection site rash	1	(0.2)	0	(0.0)	1	(0.1)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.1)
Localised oedema	1	(0.2)	3	(0.6)	4	(0.4)
Malaise	5	(1.0)	4	(0.8)	9	(0.9)
Medical device site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Non-cardiac chest pain	13	(2.6)	7	(1.4)	20	(2.0)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Oedema peripheral	24	(4.7)	18	(3.6)	42	(4.2)
Pain	2	(0.4)	2	(0.4)	4	(0.4)
Peripheral swelling	1	(0.2)	1	(0.2)	2	(0.2)
Pyrexia	24	(4.7)	24	(4.8)	48	(4.7)
Swelling face	0	(0.0)	1	(0.2)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**15**	**(2.9)**	**6**	**(1.2)**	**21**	**(2.1)**
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Cholelithiasis	1	(0.2)	1	(0.2)	2	(0.2)
Cholestasis	1	(0.2)	1	(0.2)	2	(0.2)
Hepatitis	6	(1.2)	1	(0.2)	7	(0.7)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hepatobiliary disorders	**15**	**(2.9)**	**6**	**(1.2)**	**21**	**(2.1)**
Hyperbilirubinaemia	3	(0.6)	0	(0.0)	3	(0.3)
Ocular icterus	0	(0.0)	1	(0.2)	1	(0.1)
Immune system disorders	**21**	**(4.1)**	**6**	**(1.2)**	**27**	**(2.7)**
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to arthropod sting	1	(0.2)	1	(0.2)	2	(0.2)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Contrast media allergy	1	(0.2)	3	(0.6)	4	(0.4)
Drug hypersensitivity	4	(0.8)	0	(0.0)	4	(0.4)
Hypersensitivity	3	(0.6)	0	(0.0)	3	(0.3)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Seasonal allergy	3	(0.6)	0	(0.0)	3	(0.3)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Bacterial disease carrier	0	(0.0)	1	(0.2)	1	(0.1)
Bacterial urethritis	0	(0.0)	1	(0.2)	1	(0.1)
Bacteriuria	0	(0.0)	1	(0.2)	1	(0.1)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Borrelia infection	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	12	(2.4)	15	(3.0)	27	(2.7)
Bronchitis bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Bronchitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	9	(1.8)	12	(2.4)	21	(2.1)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis	7	(1.4)	3	(0.6)	10	(1.0)
Conjunctivitis viral	1	(0.2)	1	(0.2)	2	(0.2)
Cystitis	4	(0.8)	8	(1.6)	12	(1.2)
Dermatophytosis	2	(0.4)	1	(0.2)	3	(0.3)
Device related infection	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	1	(0.2)	1	(0.2)	2	(0.2)
Ear infection	3	(0.6)	4	(0.8)	7	(0.7)
Enterococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Erysipelas	5	(1.0)	5	(1.0)	10	(1.0)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Eye infection	1	(0.2)	1	(0.2)	2	(0.2)
Folliculitis	10	(2.0)	6	(1.2)	16	(1.6)
Fungal pharyngitis	1	(0.2)	0	(0.0)	1	(0.1)
Fungal skin infection	6	(1.2)	4	(0.8)	10	(1.0)
Furuncle	1	(0.2)	2	(0.4)	3	(0.3)
Gastroenteritis	8	(1.6)	10	(2.0)	18	(1.8)
Gastroenteritis viral	5	(1.0)	1	(0.2)	6	(0.6)
Gastrointestinal infection	1	(0.2)	2	(0.4)	3	(0.3)
Genital candidiasis	2	(0.4)	0	(0.0)	2	(0.2)
Gingival abscess	1	(0.2)	0	(0.0)	1	(0.1)
Gingivitis	1	(0.2)	1	(0.2)	2	(0.2)
Groin abscess	0	(0.0)	1	(0.2)	1	(0.1)
Herpes dermatitis	0	(0.0)	1	(0.2)	1	(0.1)
Herpes simplex	1	(0.2)	0	(0.0)	1	(0.1)
Herpes virus infection	1	(0.2)	1	(0.2)	2	(0.2)
Herpes zoster	0	(0.0)	2	(0.4)	2	(0.2)
Hordeolum	1	(0.2)	2	(0.4)	3	(0.3)
Impetigo	1	(0.2)	0	(0.0)	1	(0.1)
Infected bite	1	(0.2)	0	(0.0)	1	(0.1)
Infected dermal cyst	2	(0.4)	1	(0.2)	3	(0.3)
Infected seroma	1	(0.2)	2	(0.4)	3	(0.3)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Influenza	12	(2.4)	4	(0.8)	16	(1.6)
Labyrinthitis	1	(0.2)	0	(0.0)	1	(0.1)
Laryngitis	2	(0.4)	0	(0.0)	2	(0.2)
Lip infection	0	(0.0)	2	(0.4)	2	(0.2)
Lower respiratory tract infection	6	(1.2)	2	(0.4)	8	(0.8)
Lyme disease	0	(0.0)	1	(0.2)	1	(0.1)
Lymph gland infection	0	(0.0)	1	(0.2)	1	(0.1)
Mastitis	2	(0.4)	1	(0.2)	3	(0.3)
Mumps	1	(0.2)	0	(0.0)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Oesophageal infection	1	(0.2)	0	(0.0)	1	(0.1)
Onychomycosis	0	(0.0)	5	(1.0)	5	(0.5)
Oral candidiasis	1	(0.2)	4	(0.8)	5	(0.5)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Oral herpes	7	(1.4)	5	(1.0)	12	(1.2)
Oral infection	0	(0.0)	1	(0.2)	1	(0.1)
Otitis externa	2	(0.4)	4	(0.8)	6	(0.6)
Otitis media	2	(0.4)	1	(0.2)	3	(0.3)
Paronychia	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Pharyngitis	9	(1.8)	11	(2.2)	20	(2.0)
Pharyngitis streptococcal	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	8	(1.6)	6	(1.2)	14	(1.4)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Postoperative wound infection	1	(0.2)	1	(0.2)	2	(0.2)
Pulpitis dental	1	(0.2)	0	(0.0)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Rash pustular	7	(1.4)	2	(0.4)	9	(0.9)
Respiratory tract infection	6	(1.2)	1	(0.2)	7	(0.7)
Respiratory tract infection viral	0	(0.0)	3	(0.6)	3	(0.3)
Rhinitis	20	(3.9)	9	(1.8)	29	(2.9)
Root canal infection	0	(0.0)	1	(0.2)	1	(0.1)
Sinusitis	16	(3.1)	5	(1.0)	21	(2.1)
Skin infection	9	(1.8)	4	(0.8)	13	(1.3)
Soft tissue infection	2	(0.4)	0	(0.0)	2	(0.2)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Tinea pedis	1	(0.2)	4	(0.8)	5	(0.5)
Tinea versicolour	0	(0.0)	3	(0.6)	3	(0.3)
Tonsillitis	2	(0.4)	2	(0.4)	4	(0.4)
Tooth infection	3	(0.6)	2	(0.4)	5	(0.5)
Tracheitis	0	(0.0)	2	(0.4)	2	(0.2)
Upper aerodigestive tract infection	1	(0.2)	0	(0.0)	1	(0.1)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Urinary tract infection	11	(2.2)	10	(2.0)	21	(2.1)
Urinary tract infection viral	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	2	(0.4)	1	(0.2)	3	(0.3)
Viral infection	7	(1.4)	4	(0.8)	11	(1.1)
Viral pharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Viral rhinitis	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Viral upper respiratory tract infection	4	(0.8)	3	(0.6)	7	(0.7)
Vulval abscess	1	(0.2)	0	(0.0)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)	2	(0.2)
Wound infection	2	(0.4)	2	(0.4)	4	(0.4)
Wound infection bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Animal bite	1	(0.2)	1	(0.2)	2	(0.2)
Arthropod bite	2	(0.4)	6	(1.2)	8	(0.8)
Arthropod sting	3	(0.6)	0	(0.0)	3	(0.3)
Chemical burn	0	(0.0)	1	(0.2)	1	(0.1)
Chillblains	0	(0.0)	1	(0.2)	1	(0.1)
Clavicle fracture	2	(0.4)	0	(0.0)	2	(0.2)
Contusion	1	(0.2)	2	(0.4)	3	(0.3)
Eschar	1	(0.2)	0	(0.0)	1	(0.1)
Fall	2	(0.4)	3	(0.6)	5	(0.5)
Foot fracture	0	(0.0)	1	(0.2)	1	(0.1)
Hand fracture	1	(0.2)	1	(0.2)	2	(0.2)
Humerus fracture	0	(0.0)	1	(0.2)	1	(0.1)
Incision site discharge	1	(0.2)	0	(0.0)	1	(0.1)
Incision site pain	0	(0.0)	2	(0.4)	2	(0.2)
Incision site paraesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Joint injury	1	(0.2)	0	(0.0)	1	(0.1)
Ligament injury	1	(0.2)	0	(0.0)	1	(0.1)
Ligament sprain	3	(0.6)	4	(0.8)	7	(0.7)
Limb injury	1	(0.2)	3	(0.6)	4	(0.4)
Meniscus injury	2	(0.4)	1	(0.2)	3	(0.3)
Muscle strain	0	(0.0)	1	(0.2)	1	(0.1)
Nail avulsion	0	(0.0)	2	(0.4)	2	(0.2)
Nail injury	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haematoma	1	(0.2)	1	(0.2)	2	(0.2)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Post-traumatic pain	2	(0.4)	0	(0.0)	2	(0.2)
Procedural pain	2	(0.4)	4	(0.8)	6	(0.6)
Procedural site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Radiation alopecia	1	(0.2)	0	(0.0)	1	(0.1)
Radiation injury	0	(0.0)	1	(0.2)	1	(0.1)
Radiation pneumonitis	0	(0.0)	1	(0.2)	1	(0.1)
Radiation skin injury	2	(0.4)	3	(0.6)	5	(0.5)
Repetitive strain injury	0	(0.0)	1	(0.2)	1	(0.1)
Rib fracture	1	(0.2)	0	(0.0)	1	(0.1)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Seroma	0	(0.0)	2	(0.4)	2	(0.2)
Skin abrasion	0	(0.0)	2	(0.4)	2	(0.2)
Skin graft failure	0	(0.0)	1	(0.2)	1	(0.1)
Skin laceration	1	(0.2)	0	(0.0)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Spinal fracture	1	(0.2)	1	(0.2)	2	(0.2)
Sunburn	2	(0.4)	1	(0.2)	3	(0.3)
Synovial rupture	2	(0.4)	0	(0.0)	2	(0.2)
Thermal burn	0	(0.0)	1	(0.2)	1	(0.1)
Traumatic haematoma	2	(0.4)	0	(0.0)	2	(0.2)
Upper limb fracture	1	(0.2)	0	(0.0)	1	(0.1)
Wound	0	(0.0)	1	(0.2)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Wound secretion	1	(0.2)	0	(0.0)	1	(0.1)
Wrist fracture	1	(0.2)	1	(0.2)	2	(0.2)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Amylase increased	5	(1.0)	1	(0.2)	6	(0.6)
Anti-transglutaminase antibody increased	0	(0.0)	1	(0.2)	1	(0.1)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Bacterial test positive	1	(0.2)	0	(0.0)	1	(0.1)
Blood albumin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	10	(2.0)	4	(0.8)	14	(1.4)
Blood bicarbonate increased	0	(0.0)	4	(0.8)	4	(0.4)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Blood bilirubin increased	14	(2.8)	9	(1.8)	23	(2.3)
Blood calcium decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood cholesterol increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood creatine phosphokinase increased	14	(2.8)	4	(0.8)	18	(1.8)
Blood creatinine increased	15	(2.9)	7	(1.4)	22	(2.2)
Blood glucose increased	2	(0.4)	1	(0.2)	3	(0.3)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood lactate dehydrogenase decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood lactate dehydrogenase increased	3	(0.6)	3	(0.6)	6	(0.6)
Blood potassium increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood testosterone decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood thyroid stimulating hormone decreased	8	(1.6)	2	(0.4)	10	(1.0)
Blood thyroid stimulating hormone increased	5	(1.0)	5	(1.0)	10	(1.0)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea increased	1	(0.2)	3	(0.6)	4	(0.4)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
C-reactive protein increased	16	(3.1)	6	(1.2)	22	(2.2)
Cardiac murmur	1	(0.2)	1	(0.2)	2	(0.2)
Cortisol decreased	1	(0.2)	3	(0.6)	4	(0.4)
Eosinophil count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count increased	7	(1.4)	0	(0.0)	7	(0.7)
Gamma-glutamyltransferase increased	16	(3.1)	7	(1.4)	23	(2.3)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	1	(0.2)	1	(0.2)	2	(0.2)
Haematocrit decreased	1	(0.2)	1	(0.2)	2	(0.2)
Haematocrit increased	1	(0.2)	0	(0.0)	1	(0.1)
Haemoglobin increased	1	(0.2)	3	(0.6)	4	(0.4)
Heart rate decreased	1	(0.2)	0	(0.0)	1	(0.1)
Lipase increased	10	(2.0)	5	(1.0)	15	(1.5)
Lymphocyte count decreased	11	(2.2)	5	(1.0)	16	(1.6)
Monocyte count increased	1	(0.2)	1	(0.2)	2	(0.2)
Neutrophil count decreased	2	(0.4)	10	(2.0)	12	(1.2)
Neutrophil count increased	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Platelet count decreased	4	(0.8)	5	(1.0)	9	(0.9)
Platelet count increased	2	(0.4)	0	(0.0)	2	(0.2)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)	1	(0.1)
Protein total decreased	0	(0.0)	1	(0.2)	1	(0.1)
Protein total increased	1	(0.2)	1	(0.2)	2	(0.2)
Red blood cell count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Urinary sediment present	1	(0.2)	0	(0.0)	1	(0.1)
Urine output decreased	1	(0.2)	0	(0.0)	1	(0.1)
Urobilinogen urine increased	1	(0.2)	0	(0.0)	1	(0.1)
Vitamin D decreased	1	(0.2)	0	(0.0)	1	(0.1)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
White blood cell count decreased	1	(0.2)	7	(1.4)	8	(0.8)
White blood cell count increased	1	(0.2)	1	(0.2)	2	(0.2)
Metabolism and nutrition disorders	**90**	**(17.7)**	**52**	**(10.4)**	**142**	**(14.0)**
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Dehydration	2	(0.4)	0	(0.0)	2	(0.2)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Fluid retention	0	(0.0)	2	(0.4)	2	(0.2)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Gout	3	(0.6)	0	(0.0)	3	(0.3)
Hyperamylasaemia	3	(0.6)	0	(0.0)	3	(0.3)
Hypercalcaemia	2	(0.4)	3	(0.6)	5	(0.5)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	11	(2.2)	15	(3.0)	26	(2.6)
Hyperkalaemia	3	(0.6)	7	(1.4)	10	(1.0)
Hyperlipasaemia	1	(0.2)	1	(0.2)	2	(0.2)
Hyperphosphataemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hyperuricaemia	4	(0.8)	1	(0.2)	5	(0.5)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypocalcaemia	3	(0.6)	2	(0.4)	5	(0.5)
Hypoglycaemia	1	(0.2)	3	(0.6)	4	(0.4)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**90**	**(17.7)**	**52**	**(10.4)**	**142**	**(14.0)**
Hypokalaemia	7	(1.4)	3	(0.6)	10	(1.0)
Hypomagnesaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hyponatraemia	7	(1.4)	5	(1.0)	12	(1.2)
Hypophosphataemia	5	(1.0)	3	(0.6)	8	(0.8)
Hypovitaminosis	0	(0.0)	1	(0.2)	1	(0.1)
Iron deficiency	2	(0.4)	0	(0.0)	2	(0.2)
Polydipsia	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Vitamin B12 deficiency	1	(0.2)	1	(0.2)	2	(0.2)
Vitamin D deficiency	4	(0.8)	4	(0.8)	8	(0.8)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Arthritis	8	(1.6)	1	(0.2)	9	(0.9)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Bone pain	2	(0.4)	1	(0.2)	3	(0.3)
Bursitis	6	(1.2)	5	(1.0)	11	(1.1)
Chondrosis	1	(0.2)	0	(0.0)	1	(0.1)
Clubbing	1	(0.2)	0	(0.0)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Flank pain	2	(0.4)	3	(0.6)	5	(0.5)
Groin pain	3	(0.6)	5	(1.0)	8	(0.8)
Inguinal mass	1	(0.2)	1	(0.2)	2	(0.2)
Intervertebral disc protrusion	2	(0.4)	3	(0.6)	5	(0.5)
Joint effusion	1	(0.2)	1	(0.2)	2	(0.2)
Joint range of motion decreased	2	(0.4)	2	(0.4)	4	(0.4)
Joint swelling	1	(0.2)	0	(0.0)	1	(0.1)
Limb discomfort	2	(0.4)	1	(0.2)	3	(0.3)
Limb mass	0	(0.0)	1	(0.2)	1	(0.1)
Muscle contracture	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Muscle spasms	9	(1.8)	9	(1.8)	18	(1.8)
Muscular weakness	2	(0.4)	7	(1.4)	9	(0.9)
Musculoskeletal chest pain	7	(1.4)	7	(1.4)	14	(1.4)
Musculoskeletal discomfort	2	(0.4)	4	(0.8)	6	(0.6)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Musculoskeletal pain	22	(4.3)	8	(1.6)	30	(3.0)
Musculoskeletal stiffness	3	(0.6)	2	(0.4)	5	(0.5)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Neck mass	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	12	(2.4)	5	(1.0)	17	(1.7)
Osteitis	0	(0.0)	1	(0.2)	1	(0.1)
Osteoarthritis	4	(0.8)	2	(0.4)	6	(0.6)
Osteoporosis	0	(0.0)	2	(0.4)	2	(0.2)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)
Pain in jaw	2	(0.4)	0	(0.0)	2	(0.2)
Plantar fascial fibromatosis	0	(0.0)	1	(0.2)	1	(0.1)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Soft tissue swelling	0	(0.0)	1	(0.2)	1	(0.1)
Spinal pain	2	(0.4)	1	(0.2)	3	(0.3)
Spondylitis	0	(0.0)	1	(0.2)	1	(0.1)
Synovial cyst	2	(0.4)	0	(0.0)	2	(0.2)
Synovitis	2	(0.4)	0	(0.0)	2	(0.2)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Tendon disorder	2	(0.4)	0	(0.0)	2	(0.2)
Tendonitis	5	(1.0)	1	(0.2)	6	(0.6)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.1)
Vertebral osteophyte	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Acanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Adenoma benign	0	(0.0)	1	(0.2)	1	(0.1)
Angiolipoma	0	(0.0)	1	(0.2)	1	(0.1)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Benign breast neoplasm	0	(0.0)	1	(0.2)	1	(0.1)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm	1	(0.2)	1	(0.2)	2	(0.2)
Benign neoplasm of skin	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Bowen's disease	4	(0.8)	1	(0.2)	5	(0.5)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Colon adenoma	2	(0.4)	1	(0.2)	3	(0.3)
Dysplastic naevus	6	(1.2)	5	(1.0)	11	(1.1)
Fibroadenoma of breast	0	(0.0)	1	(0.2)	1	(0.1)
Fibroma	1	(0.2)	1	(0.2)	2	(0.2)
Fibrous histiocytoma	0	(0.0)	2	(0.4)	2	(0.2)
Haemangioma	1	(0.2)	1	(0.2)	2	(0.2)
Haemangioma of liver	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of skin	0	(0.0)	1	(0.2)	1	(0.1)
Hair follicle tumour benign	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Histiocytic necrotising lymphadenitis	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Keratoacanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Lipoma	5	(1.0)	1	(0.2)	6	(0.6)
Malignant melanoma	4	(0.8)	3	(0.6)	7	(0.7)
Malignant melanoma in situ	1	(0.2)	6	(1.2)	7	(0.7)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	16	(3.1)	11	(2.2)	27	(2.7)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	1	(0.2)	1	(0.2)	2	(0.2)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Renal oncocytoma	0	(0.0)	1	(0.2)	1	(0.1)
Seborrhoeic keratosis	9	(1.8)	4	(0.8)	13	(1.3)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Skin papilloma	2	(0.4)	2	(0.4)	4	(0.4)
Squamous cell carcinoma	6	(1.2)	3	(0.6)	9	(0.9)
Squamous cell carcinoma of skin	1	(0.2)	0	(0.0)	1	(0.1)
Superficial spreading melanoma stage unspecified	0	(0.0)	1	(0.2)	1	(0.1)
Sweat gland tumour	0	(0.0)	1	(0.2)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Uterine leiomyoma	0	(0.0)	2	(0.4)	2	(0.2)
Nervous system disorders	**175**	**(34.4)**	**162**	**(32.3)**	**337**	**(33.3)**
Acute motor-sensory axonal neuropathy	0	(0.0)	1	(0.2)	1	(0.1)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Allodynia	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	3	(0.6)	1	(0.2)	4	(0.4)
Anosmia	1	(0.2)	0	(0.0)	1	(0.1)
Aphasia	1	(0.2)	1	(0.2)	2	(0.2)
Ataxia	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	1	(0.2)	2	(0.2)
Carotid arteriosclerosis	1	(0.2)	1	(0.2)	2	(0.2)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Carpal tunnel syndrome	3	(0.6)	0	(0.0)	3	(0.3)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Cervical radiculopathy	1	(0.2)	1	(0.2)	2	(0.2)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	2	(0.4)	2	(0.2)
Complex regional pain syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Disturbance in attention	3	(0.6)	4	(0.8)	7	(0.7)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Dizziness postural	1	(0.2)	1	(0.2)	2	(0.2)
Dysaesthesia	1	(0.2)	2	(0.4)	3	(0.3)
Dysarthria	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	10	(2.0)	10	(2.0)	20	(2.0)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**175**	**(34.4)**	**162**	**(32.3)**	**337**	**(33.3)**
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Hyperaesthesia	2	(0.4)	1	(0.2)	3	(0.3)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	0	(0.0)	3	(0.6)	3	(0.3)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Lethargy	6	(1.2)	8	(1.6)	14	(1.4)
Memory impairment	6	(1.2)	6	(1.2)	12	(1.2)
Migraine	2	(0.4)	4	(0.8)	6	(0.6)
Muscle contractions involuntary	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Nerve compression	0	(0.0)	1	(0.2)	1	(0.1)
Neuralgia	3	(0.6)	4	(0.8)	7	(0.7)
Neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Neuropathy peripheral	0	(0.0)	3	(0.6)	3	(0.3)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	13	(2.6)	13	(2.6)	26	(2.6)
Peripheral sensory neuropathy	6	(1.2)	5	(1.0)	11	(1.1)
Petit mal epilepsy	1	(0.2)	0	(0.0)	1	(0.1)
Presyncope	3	(0.6)	1	(0.2)	4	(0.4)
Radiculopathy	0	(0.0)	1	(0.2)	1	(0.1)
Sciatica	5	(1.0)	6	(1.2)	11	(1.1)
Sensory disturbance	0	(0.0)	1	(0.2)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Taste disorder	4	(0.8)	2	(0.4)	6	(0.6)
Tension headache	0	(0.0)	1	(0.2)	1	(0.1)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Tremor	2	(0.4)	3	(0.6)	5	(0.5)
Trigeminal nerve disorder	1	(0.2)	0	(0.0)	1	(0.1)
Vasogenic cerebral oedema	1	(0.2)	0	(0.0)	1	(0.1)
Vertebrobasilar insufficiency	0	(0.0)	1	(0.2)	1	(0.1)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**43**	**(8.4)**	**61**	**(12.2)**	**104**	**(10.3)**
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**43**	**(8.4)**	**61**	**(12.2)**	**104**	**(10.3)**
Agitation	3	(0.6)	3	(0.6)	6	(0.6)
Anxiety	10	(2.0)	23	(4.6)	33	(3.3)
Confusional state	1	(0.2)	2	(0.4)	3	(0.3)
Depressed mood	0	(0.0)	2	(0.4)	2	(0.2)
Depression	11	(2.2)	10	(2.0)	21	(2.1)
Insomnia	17	(3.3)	19	(3.8)	36	(3.6)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Libido decreased	1	(0.2)	2	(0.4)	3	(0.3)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Mood swings	0	(0.0)	2	(0.4)	2	(0.2)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Nightmare	0	(0.0)	1	(0.2)	1	(0.1)
Sleep disorder	1	(0.2)	3	(0.6)	4	(0.4)
Suicidal ideation	1	(0.2)	1	(0.2)	2	(0.2)
Tension	0	(0.0)	1	(0.2)	1	(0.1)
Thermophobia	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**27**	**(5.3)**	**19**	**(3.8)**	**46**	**(4.5)**
Acute kidney injury	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Bilirubinuria	1	(0.2)	0	(0.0)	1	(0.1)
Bladder cyst	1	(0.2)	0	(0.0)	1	(0.1)
Bladder dysfunction	0	(0.0)	1	(0.2)	1	(0.1)
Cystitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Dysuria	3	(0.6)	1	(0.2)	4	(0.4)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Glycosuria	0	(0.0)	1	(0.2)	1	(0.1)
Haematuria	7	(1.4)	4	(0.8)	11	(1.1)
Hypertonic bladder	0	(0.0)	1	(0.2)	1	(0.1)
Leukocyturia	2	(0.4)	1	(0.2)	3	(0.3)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Nephrolithiasis	2	(0.4)	2	(0.4)	4	(0.4)
Pollakiuria	4	(0.8)	4	(0.8)	8	(0.8)
Polyuria	1	(0.2)	0	(0.0)	1	(0.1)
Proteinuria	2	(0.4)	2	(0.4)	4	(0.4)
Renal colic	2	(0.4)	2	(0.4)	4	(0.4)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**27**	**(5.3)**	**19**	**(3.8)**	**46**	**(4.5)**
Renal failure	3	(0.6)	0	(0.0)	3	(0.3)
Renal pain	0	(0.0)	1	(0.2)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Urinary incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	1	(0.2)	2	(0.2)
Urine abnormality	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**29**	**(5.7)**	**21**	**(4.2)**	**50**	**(4.9)**
Balanoposthitis	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	1	(0.2)	4	(0.8)	5	(0.5)
Breast cyst	0	(0.0)	1	(0.2)	1	(0.1)
Breast disorder	1	(0.2)	0	(0.0)	1	(0.1)
Breast oedema	0	(0.0)	1	(0.2)	1	(0.1)
Breast pain	3	(0.6)	0	(0.0)	3	(0.3)
Breast swelling	1	(0.2)	0	(0.0)	1	(0.1)
Dysmenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Endometrial hypertrophy	1	(0.2)	0	(0.0)	1	(0.1)
Erectile dysfunction	5	(1.0)	2	(0.4)	7	(0.7)
Genital haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Genital rash	1	(0.2)	0	(0.0)	1	(0.1)
Gynaecomastia	1	(0.2)	1	(0.2)	2	(0.2)
Hypomenorrhoea	0	(0.0)	1	(0.2)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	2	(0.4)	2	(0.2)
Nipple pain	1	(0.2)	0	(0.0)	1	(0.1)
Orchitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Ovarian cyst	3	(0.6)	2	(0.4)	5	(0.5)
Pelvic pain	0	(0.0)	2	(0.4)	2	(0.2)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Prostatomegaly	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Scrotal mass	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**29**	**(5.7)**	**21**	**(4.2)**	**50**	**(4.9)**
Testicular swelling	0	(0.0)	1	(0.2)	1	(0.1)
Uterine fibrosis	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	1	(0.2)	1	(0.2)	2	(0.2)
Vaginal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal dryness	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**
Allergic cough	1	(0.2)	0	(0.0)	1	(0.1)
Aphonia	1	(0.2)	0	(0.0)	1	(0.1)
Asthma	3	(0.6)	3	(0.6)	6	(0.6)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	2	(0.4)	1	(0.2)	3	(0.3)
Chronic obstructive pulmonary disease	1	(0.2)	1	(0.2)	2	(0.2)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Dry throat	0	(0.0)	1	(0.2)	1	(0.1)
Dysphonia	5	(1.0)	2	(0.4)	7	(0.7)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Dyspnoea exertional	4	(0.8)	3	(0.6)	7	(0.7)
Epistaxis	6	(1.2)	1	(0.2)	7	(0.7)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal inflammation	3	(0.6)	0	(0.0)	3	(0.3)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal pain	0	(0.0)	1	(0.2)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Nasal congestion	5	(1.0)	5	(1.0)	10	(1.0)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Oropharyngeal discomfort	3	(0.6)	0	(0.0)	3	(0.3)
Oropharyngeal pain	16	(3.1)	16	(3.2)	32	(3.2)
Oropharyngeal plaque	0	(0.0)	1	(0.2)	1	(0.1)
Painful respiration	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**
Paranasal sinus haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngeal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Pharyngeal erythema	1	(0.2)	1	(0.2)	2	(0.2)
Pleural effusion	1	(0.2)	1	(0.2)	2	(0.2)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Pleuritic pain	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonitis	18	(3.5)	3	(0.6)	21	(2.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Productive cough	7	(1.4)	4	(0.8)	11	(1.1)
Pulmonary embolism	5	(1.0)	2	(0.4)	7	(0.7)
Reflux laryngitis	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	11	(2.2)	5	(1.0)	16	(1.6)
Rhinorrhoea	6	(1.2)	2	(0.4)	8	(0.8)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Sinus pain	0	(0.0)	1	(0.2)	1	(0.1)
Sleep apnoea syndrome	1	(0.2)	2	(0.4)	3	(0.3)
Sneezing	1	(0.2)	0	(0.0)	1	(0.1)
Throat tightness	1	(0.2)	0	(0.0)	1	(0.1)
Tonsillolith	0	(0.0)	1	(0.2)	1	(0.1)
Vocal cord inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Wheezing	2	(0.4)	4	(0.8)	6	(0.6)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Acne	2	(0.4)	1	(0.2)	3	(0.3)
Actinic keratosis	9	(1.8)	3	(0.6)	12	(1.2)
Alopecia	12	(2.4)	10	(2.0)	22	(2.2)
Angioedema	1	(0.2)	1	(0.2)	2	(0.2)
Angiokeratoma	0	(0.0)	1	(0.2)	1	(0.1)
Blister	1	(0.2)	0	(0.0)	1	(0.1)
Dermal cyst	5	(1.0)	3	(0.6)	8	(0.8)
Dermatitis	6	(1.2)	5	(1.0)	11	(1.1)
Dermatitis acneiform	11	(2.2)	10	(2.0)	21	(2.1)
Dermatitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	1	(0.2)	2	(0.2)
Dermatitis contact	3	(0.6)	3	(0.6)	6	(0.6)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	3	(0.6)	0	(0.0)	3	(0.3)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Ecchymosis	1	(0.2)	0	(0.0)	1	(0.1)
Eczema	22	(4.3)	10	(2.0)	32	(3.2)
Eczema asteatotic	1	(0.2)	1	(0.2)	2	(0.2)
Erythema	14	(2.8)	6	(1.2)	20	(2.0)
Erythrosis	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma skin	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhage subcutaneous	0	(0.0)	1	(0.2)	1	(0.1)
Hair disorder	2	(0.4)	0	(0.0)	2	(0.2)
Hidradenitis	1	(0.2)	2	(0.4)	3	(0.3)
Hyperhidrosis	0	(0.0)	6	(1.2)	6	(0.6)
Hyperkeratosis	5	(1.0)	3	(0.6)	8	(0.8)
Hypertrophic scar	1	(0.2)	0	(0.0)	1	(0.1)
Ingrowing nail	0	(0.0)	1	(0.2)	1	(0.1)
Intertrigo	5	(1.0)	5	(1.0)	10	(1.0)
Itching scar	1	(0.2)	0	(0.0)	1	(0.1)
Keloid scar	0	(0.0)	1	(0.2)	1	(0.1)
Keratosis pilaris	0	(0.0)	1	(0.2)	1	(0.1)
Lichen planus	2	(0.4)	1	(0.2)	3	(0.3)
Lichen sclerosus	1	(0.2)	1	(0.2)	2	(0.2)
Lichenoid keratosis	5	(1.0)	0	(0.0)	5	(0.5)
Macule	3	(0.6)	0	(0.0)	3	(0.3)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Neurodermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Neutrophilic dermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Night sweats	3	(0.6)	3	(0.6)	6	(0.6)
Onycholysis	2	(0.4)	0	(0.0)	2	(0.2)
Onychomadesis	0	(0.0)	1	(0.2)	1	(0.1)
Pain of skin	3	(0.6)	0	(0.0)	3	(0.3)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Papule	5	(1.0)	2	(0.4)	7	(0.7)
Papulopustular rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Photodermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Photosensitivity reaction	4	(0.8)	3	(0.6)	7	(0.7)
Pigmentation disorder	1	(0.2)	1	(0.2)	2	(0.2)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Pruritus allergic	0	(0.0)	1	(0.2)	1	(0.1)
Psoriasis	4	(0.8)	1	(0.2)	5	(0.5)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Rash erythematous	5	(1.0)	3	(0.6)	8	(0.8)
Rash macular	2	(0.4)	1	(0.2)	3	(0.3)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Rash papular	4	(0.8)	3	(0.6)	7	(0.7)
Rash pruritic	6	(1.2)	1	(0.2)	7	(0.7)
Rash vesicular	2	(0.4)	0	(0.0)	2	(0.2)
Rosacea	4	(0.8)	1	(0.2)	5	(0.5)
Scar pain	5	(1.0)	2	(0.4)	7	(0.7)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic dermatitis	8	(1.6)	3	(0.6)	11	(1.1)
Skin depigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Skin discolouration	0	(0.0)	2	(0.4)	2	(0.2)
Skin erosion	0	(0.0)	1	(0.2)	1	(0.1)
Skin exfoliation	4	(0.8)	0	(0.0)	4	(0.4)
Skin hyperpigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Skin hypertrophy	2	(0.4)	1	(0.2)	3	(0.3)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Skin induration	3	(0.6)	0	(0.0)	3	(0.3)
Skin irritation	1	(0.2)	1	(0.2)	2	(0.2)
Skin lesion	13	(2.6)	8	(1.6)	21	(2.1)
Skin mass	3	(0.6)	2	(0.4)	5	(0.5)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Skin tightness	2	(0.4)	0	(0.0)	2	(0.2)
Skin ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Solar dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Solar lentigo	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	1	(0.2)	2	(0.2)
Transient acantholytic dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	4	(0.8)	2	(0.4)	6	(0.6)
Vitiligo	25	(4.9)	8	(1.6)	33	(3.3)
Vascular disorders	**125**	**(24.6)**	**130**	**(25.9)**	**255**	**(25.2)**
Aortic arteriosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Deep vein thrombosis	3	(0.6)	1	(0.2)	4	(0.4)
Diastolic hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Flushing	4	(0.8)	4	(0.8)	8	(0.8)
Haematoma	4	(0.8)	7	(1.4)	11	(1.1)
Hot flush	6	(1.2)	8	(1.6)	14	(1.4)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Hypotension	5	(1.0)	4	(0.8)	9	(0.9)
Lymphocele	1	(0.2)	1	(0.2)	2	(0.2)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Orthostatic hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Peripheral venous disease	1	(0.2)	1	(0.2)	2	(0.2)
Poor venous access	1	(0.2)	0	(0.0)	1	(0.1)
Prehypertension	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	2	(0.4)	2	(0.4)	4	(0.4)
Thrombophlebitis	2	(0.4)	0	(0.0)	2	(0.2)
Thrombophlebitis superficial	2	(0.4)	3	(0.6)	5	(0.5)
Varicose vein	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Body System or Organ Class and Preferred Term (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**125**	**(24.6)**	**130**	**(25.9)**	**255**	**(25.2)**
Venous thrombosis limb	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-7

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Vitiligo	25	(4.9)	8	(1.6)	33	(3.3)
Oedema peripheral	24	(4.7)	18	(3.6)	42	(4.2)
Pyrexia	24	(4.7)	24	(4.8)	48	(4.7)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Abdominal pain upper	23	(4.5)	14	(2.8)	37	(3.7)
Eczema	22	(4.3)	10	(2.0)	32	(3.2)
Musculoskeletal pain	22	(4.3)	8	(1.6)	30	(3.0)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)
Rhinitis	20	(3.9)	9	(1.8)	29	(2.9)
Dyspepsia	19	(3.7)	6	(1.2)	25	(2.5)
Pneumonitis	18	(3.5)	3	(0.6)	21	(2.1)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)
Insomnia	17	(3.3)	19	(3.8)	36	(3.6)
C-reactive protein increased	16	(3.1)	6	(1.2)	22	(2.2)
Gamma-glutamyltransferase increased	16	(3.1)	7	(1.4)	23	(2.3)
Melanocytic naevus	16	(3.1)	11	(2.2)	27	(2.7)
Oropharyngeal pain	16	(3.1)	16	(3.2)	32	(3.2)
Sinusitis	16	(3.1)	5	(1.0)	21	(2.1)
Blood creatinine increased	15	(2.9)	7	(1.4)	22	(2.2)
Blood bilirubin increased	14	(2.8)	9	(1.8)	23	(2.3)
Blood creatine phosphokinase increased	14	(2.8)	4	(0.8)	18	(1.8)
Dry eye	14	(2.8)	8	(1.6)	22	(2.2)
Erythema	14	(2.8)	6	(1.2)	20	(2.0)
Colitis	13	(2.6)	2	(0.4)	15	(1.5)
Non-cardiac chest pain	13	(2.6)	7	(1.4)	20	(2.0)
Paraesthesia	13	(2.6)	13	(2.6)	26	(2.6)
Skin lesion	13	(2.6)	8	(1.6)	21	(2.1)
Alopecia	12	(2.4)	10	(2.0)	22	(2.2)
Bronchitis	12	(2.4)	15	(3.0)	27	(2.7)
Influenza	12	(2.4)	4	(0.8)	16	(1.6)
Neck pain	12	(2.4)	5	(1.0)	17	(1.7)
Depression	11	(2.2)	10	(2.0)	21	(2.1)
Dermatitis acneiform	11	(2.2)	10	(2.0)	21	(2.1)
Hyperglycaemia	11	(2.2)	15	(3.0)	26	(2.6)
Lymphocyte count decreased	11	(2.2)	5	(1.0)	16	(1.6)
Lymphopenia	11	(2.2)	7	(1.4)	18	(1.8)
Rhinitis allergic	11	(2.2)	5	(1.0)	16	(1.6)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Urinary tract infection	11	(2.2)	10	(2.0)	21	(2.1)
Anxiety	10	(2.0)	23	(4.6)	33	(3.3)
Blood alkaline phosphatase increased	10	(2.0)	4	(0.8)	14	(1.4)
Dysgeusia	10	(2.0)	10	(2.0)	20	(2.0)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Folliculitis	10	(2.0)	6	(1.2)	16	(1.6)
Lipase increased	10	(2.0)	5	(1.0)	15	(1.5)
Actinic keratosis	9	(1.8)	3	(0.6)	12	(1.2)
Cellulitis	9	(1.8)	12	(2.4)	21	(2.1)
Chills	9	(1.8)	5	(1.0)	14	(1.4)
Eosinophilia	9	(1.8)	1	(0.2)	10	(1.0)
Muscle spasms	9	(1.8)	9	(1.8)	18	(1.8)
Pharyngitis	9	(1.8)	11	(2.2)	20	(2.0)
Seborrhoeic keratosis	9	(1.8)	4	(0.8)	13	(1.3)
Skin infection	9	(1.8)	4	(0.8)	13	(1.3)
Arthritis	8	(1.6)	1	(0.2)	9	(0.9)
Blood thyroid stimulating hormone decreased	8	(1.6)	2	(0.4)	10	(1.0)
Gastroenteritis	8	(1.6)	10	(2.0)	18	(1.8)
Pneumonia	8	(1.6)	6	(1.2)	14	(1.4)
Seborrhoeic dermatitis	8	(1.6)	3	(0.6)	11	(1.1)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Vision blurred	8	(1.6)	11	(2.2)	19	(1.9)
Anaemia	7	(1.4)	5	(1.0)	12	(1.2)
Conjunctivitis	7	(1.4)	3	(0.6)	10	(1.0)
Eosinophil count increased	7	(1.4)	0	(0.0)	7	(0.7)
Gastrooesophageal reflux disease	7	(1.4)	6	(1.2)	13	(1.3)
Haematuria	7	(1.4)	4	(0.8)	11	(1.1)
Haemorrhoids	7	(1.4)	1	(0.2)	8	(0.8)
Hypokalaemia	7	(1.4)	3	(0.6)	10	(1.0)
Hyponatraemia	7	(1.4)	5	(1.0)	12	(1.2)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Musculoskeletal chest pain	7	(1.4)	7	(1.4)	14	(1.4)
Oral herpes	7	(1.4)	5	(1.0)	12	(1.2)
Productive cough	7	(1.4)	4	(0.8)	11	(1.1)
Rash pustular	7	(1.4)	2	(0.4)	9	(0.9)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Stomatitis	7	(1.4)	3	(0.6)	10	(1.0)
Vertigo	7	(1.4)	9	(1.8)	16	(1.6)
Viral infection	7	(1.4)	4	(0.8)	11	(1.1)
Bradycardia	6	(1.2)	8	(1.6)	14	(1.4)
Bursitis	6	(1.2)	5	(1.0)	11	(1.1)
Dermatitis	6	(1.2)	5	(1.0)	11	(1.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dysplastic naevus	6	(1.2)	5	(1.0)	11	(1.1)
Epistaxis	6	(1.2)	1	(0.2)	7	(0.7)
Fungal skin infection	6	(1.2)	4	(0.8)	10	(1.0)
Hepatitis	6	(1.2)	1	(0.2)	7	(0.7)
Hot flush	6	(1.2)	8	(1.6)	14	(1.4)
Lethargy	6	(1.2)	8	(1.6)	14	(1.4)
Lower respiratory tract infection	6	(1.2)	2	(0.4)	8	(0.8)
Memory impairment	6	(1.2)	6	(1.2)	12	(1.2)
Palpitations	6	(1.2)	4	(0.8)	10	(1.0)
Peripheral sensory neuropathy	6	(1.2)	5	(1.0)	11	(1.1)
Rash pruritic	6	(1.2)	1	(0.2)	7	(0.7)
Respiratory tract infection	6	(1.2)	1	(0.2)	7	(0.7)
Rhinorrhoea	6	(1.2)	2	(0.4)	8	(0.8)
Squamous cell carcinoma	6	(1.2)	3	(0.6)	9	(0.9)
Abdominal pain lower	5	(1.0)	1	(0.2)	6	(0.6)
Amylase increased	5	(1.0)	1	(0.2)	6	(0.6)
Axillary pain	5	(1.0)	5	(1.0)	10	(1.0)
Blood thyroid stimulating hormone increased	5	(1.0)	5	(1.0)	10	(1.0)
Dermal cyst	5	(1.0)	3	(0.6)	8	(0.8)
Dysphonia	5	(1.0)	2	(0.4)	7	(0.7)
Ear pain	5	(1.0)	1	(0.2)	6	(0.6)
Erectile dysfunction	5	(1.0)	2	(0.4)	7	(0.7)
Erysipelas	5	(1.0)	5	(1.0)	10	(1.0)
Faeces soft	5	(1.0)	3	(0.6)	8	(0.8)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Gastroenteritis viral	5	(1.0)	1	(0.2)	6	(0.6)
Hyperkeratosis	5	(1.0)	3	(0.6)	8	(0.8)
Hypophosphataemia	5	(1.0)	3	(0.6)	8	(0.8)
Hypotension	5	(1.0)	4	(0.8)	9	(0.9)
Intertrigo	5	(1.0)	5	(1.0)	10	(1.0)
Lacrimation increased	5	(1.0)	1	(0.2)	6	(0.6)
Lichenoid keratosis	5	(1.0)	0	(0.0)	5	(0.5)
Lipoma	5	(1.0)	1	(0.2)	6	(0.6)
Malaise	5	(1.0)	4	(0.8)	9	(0.9)
Nasal congestion	5	(1.0)	5	(1.0)	10	(1.0)
Papule	5	(1.0)	2	(0.4)	7	(0.7)
Pulmonary embolism	5	(1.0)	2	(0.4)	7	(0.7)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Rash erythematous	5	(1.0)	3	(0.6)	8	(0.8)
Scar pain	5	(1.0)	2	(0.4)	7	(0.7)
Sciatica	5	(1.0)	6	(1.2)	11	(1.1)
Tendonitis	5	(1.0)	1	(0.2)	6	(0.6)
Tinnitus	5	(1.0)	8	(1.6)	13	(1.3)
Toothache	5	(1.0)	7	(1.4)	12	(1.2)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Adrenal insufficiency	4	(0.8)	3	(0.6)	7	(0.7)
Bowen's disease	4	(0.8)	1	(0.2)	5	(0.5)
Cystitis	4	(0.8)	8	(1.6)	12	(1.2)
Drug hypersensitivity	4	(0.8)	0	(0.0)	4	(0.4)
Dyspnoea exertional	4	(0.8)	3	(0.6)	7	(0.7)
Flushing	4	(0.8)	4	(0.8)	8	(0.8)
Haematochezia	4	(0.8)	1	(0.2)	5	(0.5)
Haematoma	4	(0.8)	7	(1.4)	11	(1.1)
Hyperuricaemia	4	(0.8)	1	(0.2)	5	(0.5)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Malignant melanoma	4	(0.8)	3	(0.6)	7	(0.7)
Mouth ulceration	4	(0.8)	7	(1.4)	11	(1.1)
Odynophagia	4	(0.8)	1	(0.2)	5	(0.5)
Oral lichen planus	4	(0.8)	0	(0.0)	4	(0.4)
Osteoarthritis	4	(0.8)	2	(0.4)	6	(0.6)
Photosensitivity reaction	4	(0.8)	3	(0.6)	7	(0.7)
Platelet count decreased	4	(0.8)	5	(1.0)	9	(0.9)
Pollakiuria	4	(0.8)	4	(0.8)	8	(0.8)
Psoriasis	4	(0.8)	1	(0.2)	5	(0.5)
Rash papular	4	(0.8)	3	(0.6)	7	(0.7)
Rectal haemorrhage	4	(0.8)	2	(0.4)	6	(0.6)
Rosacea	4	(0.8)	1	(0.2)	5	(0.5)
Skin exfoliation	4	(0.8)	0	(0.0)	4	(0.4)
Taste disorder	4	(0.8)	2	(0.4)	6	(0.6)
Urticaria	4	(0.8)	2	(0.4)	6	(0.6)
Viral upper respiratory tract infection	4	(0.8)	3	(0.6)	7	(0.7)
Vitamin D deficiency	4	(0.8)	4	(0.8)	8	(0.8)
Agitation	3	(0.6)	3	(0.6)	6	(0.6)
Amnesia	3	(0.6)	1	(0.2)	4	(0.4)
Anal haemorrhage	3	(0.6)	0	(0.0)	3	(0.3)
Arthropod sting	3	(0.6)	0	(0.0)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Asthma	3	(0.6)	3	(0.6)	6	(0.6)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Autoimmune thyroiditis	3	(0.6)	1	(0.2)	4	(0.4)
Blepharitis	3	(0.6)	0	(0.0)	3	(0.3)
Blood lactate dehydrogenase increased	3	(0.6)	3	(0.6)	6	(0.6)
Breast pain	3	(0.6)	0	(0.0)	3	(0.3)
Carpal tunnel syndrome	3	(0.6)	0	(0.0)	3	(0.3)
Cataract	3	(0.6)	3	(0.6)	6	(0.6)
Chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Deep vein thrombosis	3	(0.6)	1	(0.2)	4	(0.4)
Dermatitis contact	3	(0.6)	3	(0.6)	6	(0.6)
Disturbance in attention	3	(0.6)	4	(0.8)	7	(0.7)
Drug eruption	3	(0.6)	0	(0.0)	3	(0.3)
Dysuria	3	(0.6)	1	(0.2)	4	(0.4)
Ear infection	3	(0.6)	4	(0.8)	7	(0.7)
Eye irritation	3	(0.6)	0	(0.0)	3	(0.3)
Face oedema	3	(0.6)	1	(0.2)	4	(0.4)
Gout	3	(0.6)	0	(0.0)	3	(0.3)
Groin pain	3	(0.6)	5	(1.0)	8	(0.8)
Hyperamylasaemia	3	(0.6)	0	(0.0)	3	(0.3)
Hyperbilirubinaemia	3	(0.6)	0	(0.0)	3	(0.3)
Hyperkalaemia	3	(0.6)	7	(1.4)	10	(1.0)
Hypersensitivity	3	(0.6)	0	(0.0)	3	(0.3)
Hypocalcaemia	3	(0.6)	2	(0.4)	5	(0.5)
Hypopituitarism	3	(0.6)	1	(0.2)	4	(0.4)
Laryngeal inflammation	3	(0.6)	0	(0.0)	3	(0.3)
Ligament sprain	3	(0.6)	4	(0.8)	7	(0.7)
Lymphadenopathy	3	(0.6)	4	(0.8)	7	(0.7)
Macule	3	(0.6)	0	(0.0)	3	(0.3)
Musculoskeletal stiffness	3	(0.6)	2	(0.4)	5	(0.5)
Neuralgia	3	(0.6)	4	(0.8)	7	(0.7)
Night sweats	3	(0.6)	3	(0.6)	6	(0.6)
Oropharyngeal discomfort	3	(0.6)	0	(0.0)	3	(0.3)
Ovarian cyst	3	(0.6)	2	(0.4)	5	(0.5)
Pain of skin	3	(0.6)	0	(0.0)	3	(0.3)
Presyncope	3	(0.6)	1	(0.2)	4	(0.4)
Proctalgia	3	(0.6)	1	(0.2)	4	(0.4)
Renal failure	3	(0.6)	0	(0.0)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Seasonal allergy	3	(0.6)	0	(0.0)	3	(0.3)
Skin induration	3	(0.6)	0	(0.0)	3	(0.3)
Skin mass	3	(0.6)	2	(0.4)	5	(0.5)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Tooth infection	3	(0.6)	2	(0.4)	5	(0.5)
Visual impairment	3	(0.6)	3	(0.6)	6	(0.6)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal distension	2	(0.4)	2	(0.4)	4	(0.4)
Acne	2	(0.4)	1	(0.2)	3	(0.3)
Acute kidney injury	2	(0.4)	0	(0.0)	2	(0.2)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Arthropod bite	2	(0.4)	6	(1.2)	8	(0.8)
Blood glucose increased	2	(0.4)	1	(0.2)	3	(0.3)
Bone pain	2	(0.4)	1	(0.2)	3	(0.3)
Bronchospasm	2	(0.4)	1	(0.2)	3	(0.3)
Chronic gastritis	2	(0.4)	0	(0.0)	2	(0.2)
Clavicle fracture	2	(0.4)	0	(0.0)	2	(0.2)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Colon adenoma	2	(0.4)	1	(0.2)	3	(0.3)
Cushingoid	2	(0.4)	0	(0.0)	2	(0.2)
Dehydration	2	(0.4)	0	(0.0)	2	(0.2)
Dental caries	2	(0.4)	1	(0.2)	3	(0.3)
Dermatophytosis	2	(0.4)	1	(0.2)	3	(0.3)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Fall	2	(0.4)	3	(0.6)	5	(0.5)
Feeling cold	2	(0.4)	0	(0.0)	2	(0.2)
Flank pain	2	(0.4)	3	(0.6)	5	(0.5)
Genital candidiasis	2	(0.4)	0	(0.0)	2	(0.2)
Gingival bleeding	2	(0.4)	0	(0.0)	2	(0.2)
Haemorrhoidal haemorrhage	2	(0.4)	0	(0.0)	2	(0.2)
Hair disorder	2	(0.4)	0	(0.0)	2	(0.2)
Hyperaesthesia	2	(0.4)	1	(0.2)	3	(0.3)
Hypercalcaemia	2	(0.4)	3	(0.6)	5	(0.5)
Hypoacusis	2	(0.4)	0	(0.0)	2	(0.2)
Infected dermal cyst	2	(0.4)	1	(0.2)	3	(0.3)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infusion site extravasation	2	(0.4)	0	(0.0)	2	(0.2)
Inguinal hernia	2	(0.4)	2	(0.4)	4	(0.4)
Intervertebral disc protrusion	2	(0.4)	3	(0.6)	5	(0.5)
Iron deficiency	2	(0.4)	0	(0.0)	2	(0.2)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Joint range of motion decreased	2	(0.4)	2	(0.4)	4	(0.4)
Large intestine polyp	2	(0.4)	1	(0.2)	3	(0.3)
Laryngitis	2	(0.4)	0	(0.0)	2	(0.2)
Leukocyturia	2	(0.4)	1	(0.2)	3	(0.3)
Lichen planus	2	(0.4)	1	(0.2)	3	(0.3)
Limb discomfort	2	(0.4)	1	(0.2)	3	(0.3)
Lymph node pain	2	(0.4)	2	(0.4)	4	(0.4)
Mastitis	2	(0.4)	1	(0.2)	3	(0.3)
Meniscus injury	2	(0.4)	1	(0.2)	3	(0.3)
Migraine	2	(0.4)	4	(0.8)	6	(0.6)
Muscular weakness	2	(0.4)	7	(1.4)	9	(0.9)
Musculoskeletal discomfort	2	(0.4)	4	(0.8)	6	(0.6)
Nephrolithiasis	2	(0.4)	2	(0.4)	4	(0.4)
Neurodermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Neutrophil count decreased	2	(0.4)	10	(2.0)	12	(1.2)
Ocular hyperaemia	2	(0.4)	2	(0.4)	4	(0.4)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Onycholysis	2	(0.4)	0	(0.0)	2	(0.2)
Oral disorder	2	(0.4)	0	(0.0)	2	(0.2)
Oral pain	2	(0.4)	1	(0.2)	3	(0.3)
Otitis externa	2	(0.4)	4	(0.8)	6	(0.6)
Otitis media	2	(0.4)	1	(0.2)	3	(0.3)
Pain	2	(0.4)	2	(0.4)	4	(0.4)
Pain in jaw	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Periorbital swelling	2	(0.4)	0	(0.0)	2	(0.2)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	1	(0.2)	3	(0.3)
Platelet count increased	2	(0.4)	0	(0.0)	2	(0.2)
Post-traumatic pain	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Prehypertension	2	(0.4)	0	(0.0)	2	(0.2)
Procedural pain	2	(0.4)	4	(0.8)	6	(0.6)
Proteinuria	2	(0.4)	2	(0.4)	4	(0.4)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Radiation skin injury	2	(0.4)	3	(0.6)	5	(0.5)
Rash macular	2	(0.4)	1	(0.2)	3	(0.3)
Rash vesicular	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	2	(0.4)	2	(0.4)	4	(0.4)
Renal colic	2	(0.4)	2	(0.4)	4	(0.4)
Scleral hyperaemia	2	(0.4)	0	(0.0)	2	(0.2)
Sinus tachycardia	2	(0.4)	0	(0.0)	2	(0.2)
Skin hypertrophy	2	(0.4)	1	(0.2)	3	(0.3)
Skin papilloma	2	(0.4)	2	(0.4)	4	(0.4)
Skin tightness	2	(0.4)	0	(0.0)	2	(0.2)
Soft tissue infection	2	(0.4)	0	(0.0)	2	(0.2)
Solar dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Spinal pain	2	(0.4)	1	(0.2)	3	(0.3)
Sunburn	2	(0.4)	1	(0.2)	3	(0.3)
Synovial cyst	2	(0.4)	0	(0.0)	2	(0.2)
Synovial rupture	2	(0.4)	0	(0.0)	2	(0.2)
Synovitis	2	(0.4)	0	(0.0)	2	(0.2)
Tachycardia	2	(0.4)	1	(0.2)	3	(0.3)
Tendon disorder	2	(0.4)	0	(0.0)	2	(0.2)
Thrombophlebitis	2	(0.4)	0	(0.0)	2	(0.2)
Thrombophlebitis superficial	2	(0.4)	3	(0.6)	5	(0.5)
Tonsillitis	2	(0.4)	2	(0.4)	4	(0.4)
Traumatic haematoma	2	(0.4)	0	(0.0)	2	(0.2)
Tremor	2	(0.4)	3	(0.6)	5	(0.5)
Umbilical hernia	2	(0.4)	0	(0.0)	2	(0.2)
Vaginal infection	2	(0.4)	1	(0.2)	3	(0.3)
Vestibular disorder	2	(0.4)	0	(0.0)	2	(0.2)
Viral rhinitis	2	(0.4)	1	(0.2)	3	(0.3)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)
Vitreous floaters	2	(0.4)	1	(0.2)	3	(0.3)
Wheezing	2	(0.4)	4	(0.8)	6	(0.6)
Wound infection	2	(0.4)	2	(0.4)	4	(0.4)
Acanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Allergic cough	1	(0.2)	0	(0.0)	1	(0.1)
Allergy to arthropod sting	1	(0.2)	1	(0.2)	2	(0.2)
Allodynia	1	(0.2)	0	(0.0)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Angina pectoris	1	(0.2)	1	(0.2)	2	(0.2)
Angioedema	1	(0.2)	1	(0.2)	2	(0.2)
Animal bite	1	(0.2)	1	(0.2)	2	(0.2)
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Anorectal varices	1	(0.2)	0	(0.0)	1	(0.1)
Anosmia	1	(0.2)	0	(0.0)	1	(0.1)
Aphasia	1	(0.2)	1	(0.2)	2	(0.2)
Aphonia	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Arrhythmia	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Ataxia	1	(0.2)	0	(0.0)	1	(0.1)
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bacterial test positive	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	1	(0.2)	2	(0.2)
Balanoposthitis	1	(0.2)	0	(0.0)	1	(0.1)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm	1	(0.2)	1	(0.2)	2	(0.2)
Benign neoplasm of skin	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	1	(0.2)	4	(0.8)	5	(0.5)
Bilirubinuria	1	(0.2)	0	(0.0)	1	(0.1)
Bladder cyst	1	(0.2)	0	(0.0)	1	(0.1)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Blindness	1	(0.2)	0	(0.0)	1	(0.1)
Blister	1	(0.2)	0	(0.0)	1	(0.1)
Blood albumin decreased	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood urea increased	1	(0.2)	3	(0.6)	4	(0.4)
Borrelia infection	1	(0.2)	0	(0.0)	1	(0.1)
Breast disorder	1	(0.2)	0	(0.0)	1	(0.1)
Breast swelling	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac failure congestive	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac murmur	1	(0.2)	1	(0.2)	2	(0.2)
Carotid arteriosclerosis	1	(0.2)	1	(0.2)	2	(0.2)
Catheter site inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Cervical radiculopathy	1	(0.2)	1	(0.2)	2	(0.2)
Chalazion	1	(0.2)	0	(0.0)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Cholelithiasis	1	(0.2)	1	(0.2)	2	(0.2)
Cholestasis	1	(0.2)	1	(0.2)	2	(0.2)
Chondrosis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	1	(0.2)	2	(0.2)
Clubbing	1	(0.2)	0	(0.0)	1	(0.1)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Confusional state	1	(0.2)	2	(0.4)	3	(0.3)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis viral	1	(0.2)	1	(0.2)	2	(0.2)
Contrast media allergy	1	(0.2)	3	(0.6)	4	(0.4)
Contusion	1	(0.2)	2	(0.4)	3	(0.3)
Cortisol decreased	1	(0.2)	3	(0.6)	4	(0.4)
Cyst	1	(0.2)	0	(0.0)	1	(0.1)
Cystitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	1	(0.2)	2	(0.2)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Device related infection	1	(0.2)	0	(0.0)	1	(0.1)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Diastolic hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Diplopia	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	1	(0.2)	1	(0.2)	2	(0.2)
Diverticulum	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulum intestinal	1	(0.2)	0	(0.0)	1	(0.1)
Dizziness postural	1	(0.2)	1	(0.2)	2	(0.2)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Duodenal polyp	1	(0.2)	0	(0.0)	1	(0.1)
Duodenitis	1	(0.2)	0	(0.0)	1	(0.1)
Dysaesthesia	1	(0.2)	2	(0.4)	3	(0.3)
Dyschezia	1	(0.2)	0	(0.0)	1	(0.1)
Dysmenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Dysphagia	1	(0.2)	1	(0.2)	2	(0.2)
Ear discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Ecchymosis	1	(0.2)	0	(0.0)	1	(0.1)
Eczema asteatotic	1	(0.2)	1	(0.2)	2	(0.2)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Endometrial hypertrophy	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Enterococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Erythrosis	1	(0.2)	0	(0.0)	1	(0.1)
Eschar	1	(0.2)	0	(0.0)	1	(0.1)
External ear inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Eye haemorrhage	1	(0.2)	1	(0.2)	2	(0.2)
Eye infection	1	(0.2)	1	(0.2)	2	(0.2)
Eye pain	1	(0.2)	3	(0.6)	4	(0.4)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid disorder	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid oedema	1	(0.2)	1	(0.2)	2	(0.2)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Fibroma	1	(0.2)	1	(0.2)	2	(0.2)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Fungal pharyngitis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Furuncle	1	(0.2)	2	(0.4)	3	(0.3)
Gait disturbance	1	(0.2)	0	(0.0)	1	(0.1)
Gastric ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal angiectasia	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal infection	1	(0.2)	2	(0.4)	3	(0.3)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal pain	1	(0.2)	0	(0.0)	1	(0.1)
General physical health deterioration	1	(0.2)	0	(0.0)	1	(0.1)
Genital haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Genital rash	1	(0.2)	0	(0.0)	1	(0.1)
Gingival abscess	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Gingivitis	1	(0.2)	1	(0.2)	2	(0.2)
Glomerular filtration rate increased	1	(0.2)	1	(0.2)	2	(0.2)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma skin	1	(0.2)	0	(0.0)	1	(0.1)
Gynaecomastia	1	(0.2)	1	(0.2)	2	(0.2)
Haemangioma	1	(0.2)	1	(0.2)	2	(0.2)
Haematocrit decreased	1	(0.2)	1	(0.2)	2	(0.2)
Haematocrit increased	1	(0.2)	0	(0.0)	1	(0.1)
Haemoglobin increased	1	(0.2)	3	(0.6)	4	(0.4)
Hand fracture	1	(0.2)	1	(0.2)	2	(0.2)
Heart rate decreased	1	(0.2)	0	(0.0)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Herpes simplex	1	(0.2)	0	(0.0)	1	(0.1)
Herpes virus infection	1	(0.2)	1	(0.2)	2	(0.2)
Hidradenitis	1	(0.2)	2	(0.4)	3	(0.3)
Hordeolum	1	(0.2)	2	(0.4)	3	(0.3)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperlipasaemia	1	(0.2)	1	(0.2)	2	(0.2)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Hypertrophic scar	1	(0.2)	0	(0.0)	1	(0.1)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoglycaemia	1	(0.2)	3	(0.6)	4	(0.4)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Impetigo	1	(0.2)	0	(0.0)	1	(0.1)
Incision site discharge	1	(0.2)	0	(0.0)	1	(0.1)
Incision site paraesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Infected bite	1	(0.2)	0	(0.0)	1	(0.1)
Infected seroma	1	(0.2)	2	(0.4)	3	(0.3)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Inguinal mass	1	(0.2)	1	(0.2)	2	(0.2)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Injection site rash	1	(0.2)	0	(0.0)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Itching scar	1	(0.2)	0	(0.0)	1	(0.1)
Joint effusion	1	(0.2)	1	(0.2)	2	(0.2)
Joint injury	1	(0.2)	0	(0.0)	1	(0.1)
Joint swelling	1	(0.2)	0	(0.0)	1	(0.1)
Keratoacanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Labyrinthitis	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Leukocytosis	1	(0.2)	0	(0.0)	1	(0.1)
Libido decreased	1	(0.2)	2	(0.4)	3	(0.3)
Lichen sclerosus	1	(0.2)	1	(0.2)	2	(0.2)
Ligament injury	1	(0.2)	0	(0.0)	1	(0.1)
Limb injury	1	(0.2)	3	(0.6)	4	(0.4)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Lip swelling	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	3	(0.6)	4	(0.4)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocele	1	(0.2)	1	(0.2)	2	(0.2)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Malignant melanoma in situ	1	(0.2)	6	(1.2)	7	(0.7)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Medical device site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Melaena	1	(0.2)	0	(0.0)	1	(0.1)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Monocyte count increased	1	(0.2)	1	(0.2)	2	(0.2)
Mumps	1	(0.2)	0	(0.0)	1	(0.1)
Muscle contractions involuntary	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Neck mass	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Nipple pain	1	(0.2)	0	(0.0)	1	(0.1)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal infection	1	(0.2)	0	(0.0)	1	(0.1)
Optic ischaemic neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral candidiasis	1	(0.2)	4	(0.8)	5	(0.5)
Oral discomfort	1	(0.2)	1	(0.2)	2	(0.2)
Oral mucosa erosion	1	(0.2)	0	(0.0)	1	(0.1)
Orchitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Papulopustular rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Paranasal sinus haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Periodontal disease	1	(0.2)	1	(0.2)	2	(0.2)
Periorbital oedema	1	(0.2)	1	(0.2)	2	(0.2)
Peripheral swelling	1	(0.2)	1	(0.2)	2	(0.2)
Peripheral venous disease	1	(0.2)	1	(0.2)	2	(0.2)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Petit mal epilepsy	1	(0.2)	0	(0.0)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngeal erythema	1	(0.2)	1	(0.2)	2	(0.2)
Pharyngitis streptococcal	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pigmentation disorder	1	(0.2)	1	(0.2)	2	(0.2)
Pleural effusion	1	(0.2)	1	(0.2)	2	(0.2)
Pleuritic pain	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Polydipsia	1	(0.2)	0	(0.0)	1	(0.1)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Polyuria	1	(0.2)	0	(0.0)	1	(0.1)
Poor venous access	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural haematoma	1	(0.2)	1	(0.2)	2	(0.2)
Postoperative wound infection	1	(0.2)	1	(0.2)	2	(0.2)
Preauricular cyst	1	(0.2)	0	(0.0)	1	(0.1)
Procedural site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	1	(0.2)	1	(0.2)	2	(0.2)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)	1	(0.1)
Prostatomegaly	1	(0.2)	0	(0.0)	1	(0.1)
Protein total increased	1	(0.2)	1	(0.2)	2	(0.2)
Pulpitis dental	1	(0.2)	0	(0.0)	1	(0.1)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Radiation alopecia	1	(0.2)	0	(0.0)	1	(0.1)
Red blood cell count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Reflux laryngitis	1	(0.2)	0	(0.0)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Rib fracture	1	(0.2)	0	(0.0)	1	(0.1)
Scrotal mass	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Sinus bradycardia	1	(0.2)	3	(0.6)	4	(0.4)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Skin depigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Skin hyperpigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Skin irritation	1	(0.2)	1	(0.2)	2	(0.2)
Skin laceration	1	(0.2)	0	(0.0)	1	(0.1)
Skin ulcer	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Sleep apnoea syndrome	1	(0.2)	2	(0.4)	3	(0.3)
Sleep disorder	1	(0.2)	3	(0.6)	4	(0.4)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Sneezing	1	(0.2)	0	(0.0)	1	(0.1)
Solar lentigo	1	(0.2)	0	(0.0)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Spinal fracture	1	(0.2)	1	(0.2)	2	(0.2)
Squamous cell carcinoma of skin	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	1	(0.2)	2	(0.2)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Submaxillary gland enlargement	1	(0.2)	1	(0.2)	2	(0.2)
Suicidal ideation	1	(0.2)	1	(0.2)	2	(0.2)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.1)
Thermophobia	1	(0.2)	0	(0.0)	1	(0.1)
Throat tightness	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Tinea pedis	1	(0.2)	4	(0.8)	5	(0.5)
Tongue disorder	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	1	(0.2)	2	(0.2)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Transient acantholytic dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Trigeminal nerve disorder	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Upper aerodigestive tract infection	1	(0.2)	0	(0.0)	1	(0.1)
Upper limb fracture	1	(0.2)	0	(0.0)	1	(0.1)
Urinary incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	1	(0.2)	2	(0.2)
Urinary sediment present	1	(0.2)	0	(0.0)	1	(0.1)
Urinary tract infection viral	1	(0.2)	0	(0.0)	1	(0.1)
Urine abnormality	1	(0.2)	0	(0.0)	1	(0.1)
Urine output decreased	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Urobilinogen urine increased	1	(0.2)	0	(0.0)	1	(0.1)
Uterine fibrosis	1	(0.2)	0	(0.0)	1	(0.1)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	1	(0.2)	1	(0.2)	2	(0.2)
Vaginal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele	1	(0.2)	0	(0.0)	1	(0.1)
Vasogenic cerebral oedema	1	(0.2)	0	(0.0)	1	(0.1)
Venous thrombosis limb	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Vitamin B12 deficiency	1	(0.2)	1	(0.2)	2	(0.2)
Vitamin D decreased	1	(0.2)	0	(0.0)	1	(0.1)
Vulval abscess	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)	2	(0.2)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
White blood cell count decreased	1	(0.2)	7	(1.4)	8	(0.8)
White blood cell count increased	1	(0.2)	1	(0.2)	2	(0.2)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Wound secretion	1	(0.2)	0	(0.0)	1	(0.1)
Wrist fracture	1	(0.2)	1	(0.2)	2	(0.2)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Acute motor-sensory axonal neuropathy	0	(0.0)	1	(0.2)	1	(0.1)
Adenoma benign	0	(0.0)	1	(0.2)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Angiokeratoma	0	(0.0)	1	(0.2)	1	(0.1)
Angiolipoma	0	(0.0)	1	(0.2)	1	(0.1)
Angular cheilitis	0	(0.0)	2	(0.4)	2	(0.2)
Anti-transglutaminase antibody increased	0	(0.0)	1	(0.2)	1	(0.1)
Aortic arteriosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Bacterial disease carrier	0	(0.0)	1	(0.2)	1	(0.1)
Bacterial urethritis	0	(0.0)	1	(0.2)	1	(0.1)
Bacteriuria	0	(0.0)	1	(0.2)	1	(0.1)
Benign breast neoplasm	0	(0.0)	1	(0.2)	1	(0.1)
Bladder dysfunction	0	(0.0)	1	(0.2)	1	(0.1)
Blepharospasm	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood bicarbonate increased	0	(0.0)	4	(0.8)	4	(0.4)
Blood calcium decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood cholesterol increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood lactate dehydrogenase decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood potassium increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood testosterone decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea decreased	0	(0.0)	1	(0.2)	1	(0.1)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Breast cyst	0	(0.0)	1	(0.2)	1	(0.1)
Breast oedema	0	(0.0)	1	(0.2)	1	(0.1)
Bronchitis bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Brugada syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Catheter site thrombosis	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Chemical burn	0	(0.0)	1	(0.2)	1	(0.1)
Chest discomfort	0	(0.0)	2	(0.4)	2	(0.2)
Chillblains	0	(0.0)	1	(0.2)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	2	(0.4)	2	(0.2)
Complex regional pain syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Coronary artery disease	0	(0.0)	1	(0.2)	1	(0.1)
Deafness	0	(0.0)	1	(0.2)	1	(0.1)
Deafness unilateral	0	(0.0)	1	(0.2)	1	(0.1)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Depressed mood	0	(0.0)	2	(0.4)	2	(0.2)
Dermoid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Dry throat	0	(0.0)	1	(0.2)	1	(0.1)
Dysarthria	0	(0.0)	1	(0.2)	1	(0.1)
Epidermal naevus	0	(0.0)	1	(0.2)	1	(0.1)
Epigastric discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Eye inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Fibroadenoma of breast	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Fibrous histiocytoma	0	(0.0)	2	(0.4)	2	(0.2)
Flatulence	0	(0.0)	4	(0.8)	4	(0.4)
Fluid retention	0	(0.0)	2	(0.4)	2	(0.2)
Foot fracture	0	(0.0)	1	(0.2)	1	(0.1)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Gilbert's syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Gingival oedema	0	(0.0)	1	(0.2)	1	(0.1)
Gingival recession	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Glycosuria	0	(0.0)	1	(0.2)	1	(0.1)
Groin abscess	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of liver	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of skin	0	(0.0)	1	(0.2)	1	(0.1)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhage subcutaneous	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhagic thyroid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Hair follicle tumour benign	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Herpes dermatitis	0	(0.0)	1	(0.2)	1	(0.1)
Herpes zoster	0	(0.0)	2	(0.4)	2	(0.2)
Histiocytic necrotising lymphadenitis	0	(0.0)	1	(0.2)	1	(0.1)
Humerus fracture	0	(0.0)	1	(0.2)	1	(0.1)
Hydrocele	0	(0.0)	1	(0.2)	1	(0.1)
Hyperaesthesia teeth	0	(0.0)	1	(0.2)	1	(0.1)
Hyperhidrosis	0	(0.0)	6	(1.2)	6	(0.6)
Hyperphosphataemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertonic bladder	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Hypoaesthesia	0	(0.0)	3	(0.6)	3	(0.3)
Hypomagnesaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypomenorrhoea	0	(0.0)	1	(0.2)	1	(0.1)
Hypovitaminosis	0	(0.0)	1	(0.2)	1	(0.1)
Incision site pain	0	(0.0)	2	(0.4)	2	(0.2)
Inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Ingrowing nail	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injection site pain	0	(0.0)	1	(0.2)	1	(0.1)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Keloid scar	0	(0.0)	1	(0.2)	1	(0.1)
Keratosis pilaris	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal pain	0	(0.0)	1	(0.2)	1	(0.1)
Lens dislocation	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Leukopenia	0	(0.0)	2	(0.4)	2	(0.2)
Limb mass	0	(0.0)	1	(0.2)	1	(0.1)
Lip infection	0	(0.0)	2	(0.4)	2	(0.2)
Lyme disease	0	(0.0)	1	(0.2)	1	(0.1)
Lymph gland infection	0	(0.0)	1	(0.2)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	2	(0.4)	2	(0.2)
Middle ear effusion	0	(0.0)	1	(0.2)	1	(0.1)
Middle ear inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Mood swings	0	(0.0)	2	(0.4)	2	(0.2)
Muscle contracture	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Muscle strain	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Nail avulsion	0	(0.0)	2	(0.4)	2	(0.2)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Nail injury	0	(0.0)	1	(0.2)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Nerve compression	0	(0.0)	1	(0.2)	1	(0.1)
Neuropathy peripheral	0	(0.0)	3	(0.6)	3	(0.3)
Neutrophil count increased	0	(0.0)	1	(0.2)	1	(0.1)
Neutrophilic dermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Nightmare	0	(0.0)	1	(0.2)	1	(0.1)
Noninfective myringitis	0	(0.0)	1	(0.2)	1	(0.1)
Ocular icterus	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oesophageal haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal pain	0	(0.0)	1	(0.2)	1	(0.1)
Onychomadesis	0	(0.0)	1	(0.2)	1	(0.1)
Onychomycosis	0	(0.0)	5	(1.0)	5	(0.5)
Oral infection	0	(0.0)	1	(0.2)	1	(0.1)
Oropharyngeal plaque	0	(0.0)	1	(0.2)	1	(0.1)
Orthostatic hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Osteitis	0	(0.0)	1	(0.2)	1	(0.1)
Osteoporosis	0	(0.0)	2	(0.4)	2	(0.2)
Painful respiration	0	(0.0)	1	(0.2)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Paronychia	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Pelvic pain	0	(0.0)	2	(0.4)	2	(0.2)
Pharyngeal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Photodermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Plantar fascial fibromatosis	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Presbyopia	0	(0.0)	2	(0.4)	2	(0.2)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Protein total decreased	0	(0.0)	1	(0.2)	1	(0.1)
Pruritus allergic	0	(0.0)	1	(0.2)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Radiation injury	0	(0.0)	1	(0.2)	1	(0.1)
Radiation pneumonitis	0	(0.0)	1	(0.2)	1	(0.1)
Radiculopathy	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Rectal tenesmus	0	(0.0)	1	(0.2)	1	(0.1)
Renal oncocytoma	0	(0.0)	1	(0.2)	1	(0.1)
Renal pain	0	(0.0)	1	(0.2)	1	(0.1)
Repetitive strain injury	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	3	(0.6)	3	(0.3)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Root canal infection	0	(0.0)	1	(0.2)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Sensory disturbance	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Seroma	0	(0.0)	2	(0.4)	2	(0.2)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Sinus pain	0	(0.0)	1	(0.2)	1	(0.1)
Skin abrasion	0	(0.0)	2	(0.4)	2	(0.2)
Skin discolouration	0	(0.0)	2	(0.4)	2	(0.2)
Skin erosion	0	(0.0)	1	(0.2)	1	(0.1)
Skin graft failure	0	(0.0)	1	(0.2)	1	(0.1)
Soft tissue swelling	0	(0.0)	1	(0.2)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Spondylitis	0	(0.0)	1	(0.2)	1	(0.1)
Superficial spreading melanoma stage unspecified	0	(0.0)	1	(0.2)	1	(0.1)
Sweat gland tumour	0	(0.0)	1	(0.2)	1	(0.1)
Swelling face	0	(0.0)	1	(0.2)	1	(0.1)
Swelling of eyelid	0	(0.0)	1	(0.2)	1	(0.1)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Tension	0	(0.0)	1	(0.2)	1	(0.1)
Tension headache	0	(0.0)	1	(0.2)	1	(0.1)
Testicular swelling	0	(0.0)	1	(0.2)	1	(0.1)
Thermal burn	0	(0.0)	1	(0.2)	1	(0.1)
Tinea versicolour	0	(0.0)	3	(0.6)	3	(0.3)
Tonsillolith	0	(0.0)	1	(0.2)	1	(0.1)
Tracheitis	0	(0.0)	2	(0.4)	2	(0.2)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Uterine leiomyoma	0	(0.0)	2	(0.4)	2	(0.2)
Varicose vein	0	(0.0)	1	(0.2)	1	(0.1)
Vertebral osteophyte	0	(0.0)	1	(0.2)	1	(0.1)
Vertebrobasilar insufficiency	0	(0.0)	1	(0.2)	1	(0.1)
Viral pharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Vocal cord inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal dryness	0	(0.0)	1	(0.2)	1	(0.1)
Wound	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Wound infection bacterial	0	(0.0)	1	(0.2)	1	(0.1)

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

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-8

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	149	(87.6)
with no adverse events	21	(12.4)
Diarrhoea	35	(20.6)
Fatigue	33	(19.4)
Pruritus	29	(17.1)
Hypothyroidism	24	(14.1)
Arthralgia	19	(11.2)
Hyperthyroidism	17	(10.0)
Nausea	17	(10.0)
Headache	16	(9.4)
Influenza like illness	16	(9.4)
Rash	15	(8.8)
Alanine aminotransferase increased	14	(8.2)
Aspartate aminotransferase increased	12	(7.1)
Back pain	12	(7.1)
Cough	12	(7.1)
Pyrexia	11	(6.5)
Rash maculo-papular	11	(6.5)
Nasopharyngitis	10	(5.9)
Constipation	9	(5.3)
Decreased appetite	8	(4.7)
Hyperglycaemia	8	(4.7)
Oedema peripheral	8	(4.7)
Upper respiratory tract infection	8	(4.7)
Dizziness	7	(4.1)
Dyspnoea	7	(4.1)
Musculoskeletal pain	7	(4.1)
Myalgia	7	(4.1)
Rhinitis	7	(4.1)
Abdominal pain	6	(3.5)
Anaemia	6	(3.5)
Blood creatinine increased	6	(3.5)
Dry mouth	6	(3.5)
Hypertension	6	(3.5)
Pain in extremity	6	(3.5)
Abdominal pain upper	5	(2.9)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Blood alkaline phosphatase increased	5	(2.9)
Bronchitis	5	(2.9)
Dry skin	5	(2.9)
Gamma-glutamyltransferase increased	5	(2.9)
Insomnia	5	(2.9)
Non-cardiac chest pain	5	(2.9)
Peripheral sensory neuropathy	5	(2.9)
Vertigo	5	(2.9)
Vomiting	5	(2.9)
Arthritis	4	(2.4)
Asthenia	4	(2.4)
Blood bilirubin increased	4	(2.4)
Cellulitis	4	(2.4)
Eczema	4	(2.4)
Hot flush	4	(2.4)
Influenza	4	(2.4)
Rash pustular	4	(2.4)
Syncope	4	(2.4)
Vitiligo	4	(2.4)
Weight increased	4	(2.4)
Anxiety	3	(1.8)
Blood lactate dehydrogenase increased	3	(1.8)
Colitis	3	(1.8)
Conjunctivitis	3	(1.8)
Folliculitis	3	(1.8)
Gastritis	3	(1.8)
Hypopituitarism	3	(1.8)
Leukopenia	3	(1.8)
Muscle spasms	3	(1.8)
Musculoskeletal chest pain	3	(1.8)
Neck pain	3	(1.8)
Oropharyngeal pain	3	(1.8)
Paraesthesia	3	(1.8)
Pharyngitis	3	(1.8)
Seborrhoeic keratosis	3	(1.8)
Sinusitis	3	(1.8)
Skin hypopigmentation	3	(1.8)
Stomatitis	3	(1.8)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Toothache	3	(1.8)
Type 1 diabetes mellitus	3	(1.8)
Urinary tract infection	3	(1.8)
Weight decreased	3	(1.8)
Abdominal distension	2	(1.2)
Abdominal pain lower	2	(1.2)
Actinic keratosis	2	(1.2)
Acute kidney injury	2	(1.2)
Alopecia	2	(1.2)
Amylase increased	2	(1.2)
Angina pectoris	2	(1.2)
Arthropod bite	2	(1.2)
Benign prostatic hyperplasia	2	(1.2)
Blood creatine phosphokinase increased	2	(1.2)
Blood thyroid stimulating hormone increased	2	(1.2)
Cataract	2	(1.2)
Confusional state	2	(1.2)
Contusion	2	(1.2)
Depression	2	(1.2)
Dermatitis	2	(1.2)
Dysgeusia	2	(1.2)
Dysphagia	2	(1.2)
Dysuria	2	(1.2)
Eosinophilia	2	(1.2)
Erythema	2	(1.2)
Gastrooesophageal reflux disease	2	(1.2)
Groin pain	2	(1.2)
Hyperkalaemia	2	(1.2)
Hypoalbuminaemia	2	(1.2)
Hyponatraemia	2	(1.2)
Joint swelling	2	(1.2)
Lacrimation increased	2	(1.2)
Lichenoid keratosis	2	(1.2)
Lipoma	2	(1.2)
Lower limb fracture	2	(1.2)
Lymph node pain	2	(1.2)
Lymphadenopathy	2	(1.2)
Lymphopenia	2	(1.2)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Malignant melanoma	2	(1.2)
Night sweats	2	(1.2)
Pain of skin	2	(1.2)
Pancreatitis	2	(1.2)
Peripheral swelling	2	(1.2)
Pneumonia	2	(1.2)
Pneumonitis	2	(1.2)
Presyncope	2	(1.2)
Procedural pain	2	(1.2)
Rash erythematous	2	(1.2)
Rhinitis allergic	2	(1.2)
Sciatica	2	(1.2)
Skin infection	2	(1.2)
Thrombocytopenia	2	(1.2)
Vaginal infection	2	(1.2)
Viral infection	2	(1.2)
Vision blurred	2	(1.2)
White blood cell count decreased	2	(1.2)
Acquired phimosis	1	(0.6)
Adrenal insufficiency	1	(0.6)
Ageusia	1	(0.6)
Amnesia	1	(0.6)
Animal bite	1	(0.6)
Aphthous ulcer	1	(0.6)
Arrhythmia	1	(0.6)
Arteriosclerosis coronary artery	1	(0.6)
Bacterial disease carrier	1	(0.6)
Bilirubin conjugated increased	1	(0.6)
Blood bicarbonate increased	1	(0.6)
Blood thyroid stimulating hormone decreased	1	(0.6)
Blood triglycerides increased	1	(0.6)
Bone pain	1	(0.6)
Bradycardia	1	(0.6)
Bronchopulmonary aspergillosis	1	(0.6)
Bronchospasm	1	(0.6)
C-reactive protein increased	1	(0.6)
Carpal tunnel syndrome	1	(0.6)
Cerebral amyloid angiopathy	1	(0.6)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Chest pain	1	(0.6)
Cholelithiasis	1	(0.6)
Cholestasis	1	(0.6)
Cystitis	1	(0.6)
Cystitis noninfective	1	(0.6)
Defaecation urgency	1	(0.6)
Dehydration	1	(0.6)
Dementia Alzheimer's type	1	(0.6)
Dental caries	1	(0.6)
Depressed mood	1	(0.6)
Dermatitis acneiform	1	(0.6)
Dermatitis allergic	1	(0.6)
Dermatitis contact	1	(0.6)
Device related infection	1	(0.6)
Diverticulitis	1	(0.6)
Dizziness exertional	1	(0.6)
Dizziness postural	1	(0.6)
Dry eye	1	(0.6)
Duodenal ulcer	1	(0.6)
Duodenitis	1	(0.6)
Dyshidrotic eczema	1	(0.6)
Dyspepsia	1	(0.6)
Dysplastic naevus syndrome	1	(0.6)
Ear congestion	1	(0.6)
Ear discomfort	1	(0.6)
Embolism	1	(0.6)
Emotional distress	1	(0.6)
Enanthema	1	(0.6)
Epigastric discomfort	1	(0.6)
Epistaxis	1	(0.6)
Erythema multiforme	1	(0.6)
Erythrasma	1	(0.6)
Eye inflammation	1	(0.6)
Eyelid oedema	1	(0.6)
Eyelid rash	1	(0.6)
Faeces soft	1	(0.6)
Febrile neutropenia	1	(0.6)
Flank pain	1	(0.6)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Flatulence	1	(0.6)
Focal dyscognitive seizures	1	(0.6)
Food poisoning	1	(0.6)
Fungal skin infection	1	(0.6)
Gastrointestinal infection	1	(0.6)
Gastrointestinal motility disorder	1	(0.6)
Gastrointestinal pain	1	(0.6)
Gingivitis	1	(0.6)
Glucocorticoid deficiency	1	(0.6)
Glucose urine present	1	(0.6)
Granuloma annulare	1	(0.6)
Haematoma	1	(0.6)
Haematuria	1	(0.6)
Haemorrhoids	1	(0.6)
Helicobacter infection	1	(0.6)
Hepatic pain	1	(0.6)
Herpes zoster	1	(0.6)
Hordeolum	1	(0.6)
Hypercalcaemia	1	(0.6)
Hypercapnia	1	(0.6)
Hyperkeratosis	1	(0.6)
Hypersensitivity	1	(0.6)
Hypersensitivity vasculitis	1	(0.6)
Hypocalcaemia	1	(0.6)
Hypoglycaemia	1	(0.6)
Hypokalaemia	1	(0.6)
Immune-mediated adverse reaction	1	(0.6)
Immune-mediated arthritis	1	(0.6)
Immune-mediated hepatitis	1	(0.6)
Impaired healing	1	(0.6)
Infection	1	(0.6)
Inflammation	1	(0.6)
Infusion related reaction	1	(0.6)
Ingrowing nail	1	(0.6)
Interstitial lung disease	1	(0.6)
Intertrigo	1	(0.6)
Intervertebral disc protrusion	1	(0.6)
Intussusception	1	(0.6)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Iron deficiency	1	(0.6)
Iron deficiency anaemia	1	(0.6)
Keloid scar	1	(0.6)
Lactic acidosis	1	(0.6)
Large intestine perforation	1	(0.6)
Large intestine polyp	1	(0.6)
Lethargy	1	(0.6)
Leukocytosis	1	(0.6)
Lichen planopilaris	1	(0.6)
Limb injury	1	(0.6)
Lipase increased	1	(0.6)
Liver disorder	1	(0.6)
Lower gastrointestinal haemorrhage	1	(0.6)
Lung opacity	1	(0.6)
Lymphocyte count decreased	1	(0.6)
Lymphoedema	1	(0.6)
Malaise	1	(0.6)
Melanocytic naevus	1	(0.6)
Metastases to central nervous system	1	(0.6)
Middle ear effusion	1	(0.6)
Mouth ulceration	1	(0.6)
Myositis	1	(0.6)
Neutrophil count decreased	1	(0.6)
Neutrophilia	1	(0.6)
Ocular hyperaemia	1	(0.6)
Oral fungal infection	1	(0.6)
Oral herpes	1	(0.6)
Oral pain	1	(0.6)
Osteoporosis	1	(0.6)
Otitis media	1	(0.6)
Pain	1	(0.6)
Palpitations	1	(0.6)
Panniculitis	1	(0.6)
Paranasal sinus mucosal hypertrophy	1	(0.6)
Pericardial effusion	1	(0.6)
Periorbital haematoma	1	(0.6)
Personality change	1	(0.6)
Pharyngeal abscess	1	(0.6)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Photosensitivity reaction	1	(0.6)
Platelet count decreased	1	(0.6)
Pneumothorax	1	(0.6)
Pollakiuria	1	(0.6)
Post procedural inflammation	1	(0.6)
Post procedural oedema	1	(0.6)
Presbyopia	1	(0.6)
Productive cough	1	(0.6)
Prostatomegaly	1	(0.6)
Proteinuria	1	(0.6)
Pulmonary embolism	1	(0.6)
Radiculopathy	1	(0.6)
Rash papular	1	(0.6)
Rash pruritic	1	(0.6)
Rectal abscess	1	(0.6)
Renal cyst	1	(0.6)
Respiratory tract infection viral	1	(0.6)
Restlessness	1	(0.6)
Retinal haemorrhage	1	(0.6)
Retinopathy	1	(0.6)
Rhinorrhoea	1	(0.6)
Road traffic accident	1	(0.6)
Rosacea	1	(0.6)
Sebaceous gland disorder	1	(0.6)
Sepsis	1	(0.6)
Seroma	1	(0.6)
Sjogren's syndrome	1	(0.6)
Skin fibrosis	1	(0.6)
Skin laceration	1	(0.6)
Skin mass	1	(0.6)
Skin papilloma	1	(0.6)
Solar dermatitis	1	(0.6)
Spinal osteoarthritis	1	(0.6)
Spinal pain	1	(0.6)
Spontaneous haematoma	1	(0.6)
Strangury	1	(0.6)
Suprapubic pain	1	(0.6)
Synovial cyst	1	(0.6)

Subjects With Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Tendon rupture	1	(0.6)
Tinea versicolour	1	(0.6)
Tinnitus	1	(0.6)
Tongue ulceration	1	(0.6)
Transaminases increased	1	(0.6)
Transient ischaemic attack	1	(0.6)
Tumour pain	1	(0.6)
Upper-airway cough syndrome	1	(0.6)
Urinary incontinence	1	(0.6)
Urticaria	1	(0.6)
Viral upper respiratory tract infection	1	(0.6)
Wheezing	1	(0.6)
Wound	1	(0.6)
Wrist fracture	1	(0.6)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 2.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 2.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-9

Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
Grade 1	69	(13.6)	136	(27.1)	205	(20.3)
Grade 2	249	(48.9)	222	(44.2)	471	(46.6)
Grade 3	147	(28.9)	89	(17.7)	236	(23.3)
Grade 4	14	(2.8)	7	(1.4)	21	(2.1)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Blood and lymphatic system disorders	**37**	**(7.3)**	**22**	**(4.4)**	**59**	**(5.8)**
Grade 1	22	(4.3)	13	(2.6)	35	(3.5)
Grade 2	13	(2.6)	9	(1.8)	22	(2.2)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Anaemia	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Eosinophilia	9	(1.8)	1	(0.2)	10	(1.0)
Grade 1	8	(1.6)	1	(0.2)	9	(0.9)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Leukocytosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Lymphadenopathy	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	11	(2.2)	7	(1.4)	18	(1.8)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	6	(1.2)	3	(0.6)	9	(0.9)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac disorders	**24**	**(4.7)**	**20**	**(4.0)**	**44**	**(4.4)**
Grade 1	17	(3.3)	17	(3.4)	34	(3.4)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	4	(0.8)	1	(0.2)	5	(0.5)
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Angina pectoris	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Arrhythmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bradycardia	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Brugada syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure congestive	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Coronary artery disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Palpitations	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Sinus bradycardia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Sinus tachycardia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tachycardia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**5**	**(1.0)**	**7**	**(0.7)**
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Dermoid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Epidermal naevus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Gilbert's syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hydrocele	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Preauricular cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**21**	**(4.1)**	**21**	**(4.2)**	**42**	**(4.2)**
Grade 1	13	(2.6)	19	(3.8)	32	(3.2)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Deafness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Deafness unilateral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Ear discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ear pain	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
External ear inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hypoacusis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Middle ear effusion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Middle ear inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Noninfective myringitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tinnitus	5	(1.0)	8	(1.6)	13	(1.3)
Grade 1	4	(0.8)	7	(1.4)	11	(1.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Vertigo	7	(1.4)	9	(1.8)	16	(1.6)
Grade 1	5	(1.0)	9	(1.8)	14	(1.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Vestibular disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Endocrine disorders	**121**	**(23.8)**	**27**	**(5.4)**	**148**	**(14.6)**
Grade 1	38	(7.5)	17	(3.4)	55	(5.4)
Grade 2	80	(15.7)	10	(2.0)	90	(8.9)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Adrenal insufficiency	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Autoimmune thyroiditis	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cushingoid	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhagic thyroid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	8	(1.6)	1	(0.2)	9	(0.9)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**56**	**(11.0)**	**43**	**(8.6)**	**99**	**(9.8)**
Grade 1	46	(9.0)	35	(7.0)	81	(8.0)
Grade 2	9	(1.8)	7	(1.4)	16	(1.6)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blepharitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Blepharospasm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blindness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Cataract	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Chalazion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diplopia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Dry eye	14	(2.8)	8	(1.6)	22	(2.2)
Grade 1	13	(2.6)	8	(1.6)	21	(2.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye haemorrhage	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Eye inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye irritation	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eye pain	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eyelid disorder	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eyelid disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Lens dislocation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Ocular hyperaemia	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Optic ischaemic neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Periorbital swelling	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Presbyopia	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Scleral hyperaemia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Swelling of eyelid	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	8	(1.6)	11	(2.2)	19	(1.9)
Grade 1	8	(1.6)	8	(1.6)	16	(1.6)
Grade 2	0	(0.0)	3	(0.6)	3	(0.3)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Visual impairment	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Vitreous floaters	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Grade 1	179	(35.2)	175	(34.9)	354	(35.0)
Grade 2	75	(14.7)	46	(9.2)	121	(12.0)
Grade 3	27	(5.3)	10	(2.0)	37	(3.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal distension	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Grade 1	32	(6.3)	27	(5.4)	59	(5.8)
Grade 2	5	(1.0)	4	(0.8)	9	(0.9)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Abdominal pain lower	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Abdominal pain upper	23	(4.5)	14	(2.8)	37	(3.7)
Grade 1	19	(3.7)	13	(2.6)	32	(3.2)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Anal haemorrhage	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Angular cheilitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Anorectal varices	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	13	(2.6)	2	(0.4)	15	(1.5)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Grade 3	7	(1.4)	0	(0.0)	7	(0.7)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Grade 1	27	(5.3)	24	(4.8)	51	(5.0)
Grade 2	6	(1.2)	5	(1.0)	11	(1.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dental caries	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Grade 1	106	(20.8)	108	(21.5)	214	(21.2)
Grade 2	27	(5.3)	19	(3.8)	46	(4.5)
Grade 3	5	(1.0)	6	(1.2)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulum	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulum intestinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Grade 1	29	(5.7)	10	(2.0)	39	(3.9)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Duodenal polyp	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Duodenitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dyschezia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	19	(3.7)	6	(1.2)	25	(2.5)
Grade 1	12	(2.4)	3	(0.6)	15	(1.5)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Dysphagia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Epigastric discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Faeces soft	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Flatulence	0	(0.0)	4	(0.8)	4	(0.4)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Gastric ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal angiectasia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	7	(1.4)	6	(1.2)	13	(1.3)
Grade 1	4	(0.8)	5	(1.0)	9	(0.9)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Gingival bleeding	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Gingival oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gingival recession	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haematochezia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Haemorrhoidal haemorrhage	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Haemorrhoids	7	(1.4)	1	(0.2)	8	(0.8)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hyperaesthesia teeth	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Inguinal hernia	2	(0.4)	2	(0.4)	4	(0.4)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Inguinal hernia	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine polyp	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Melaena	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	4	(0.8)	7	(1.4)	11	(1.1)
Grade 1	4	(0.8)	7	(1.4)	11	(1.1)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Grade 1	76	(14.9)	66	(13.1)	142	(14.0)
Grade 2	12	(2.4)	8	(1.6)	20	(2.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Odynophagia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Oesophageal haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Oral discomfort	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Oral disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Oral lichen planus	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Oral mucosa erosion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Oral pain	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oral pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Proctalgia	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Rectal haemorrhage	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Rectal tenesmus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Stomatitis	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Submaxillary gland enlargement	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tongue disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Toothache	5	(1.0)	7	(1.4)	12	(1.2)
Grade 1	4	(0.8)	5	(1.0)	9	(0.9)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Umbilical hernia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
Grade 1	31	(6.1)	18	(3.6)	49	(4.8)
Grade 2	9	(1.8)	5	(1.0)	14	(1.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
General disorders and administration site conditions	**280**	**(55.0)**	**260**	**(51.8)**	**540**	**(53.4)**
Grade 1	192	(37.7)	216	(43.0)	408	(40.4)
Grade 2	79	(15.5)	41	(8.2)	120	(11.9)
Grade 3	9	(1.8)	3	(0.6)	12	(1.2)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Grade 1	38	(7.5)	37	(7.4)	75	(7.4)
Grade 2	16	(3.1)	5	(1.0)	21	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Axillary pain	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Catheter site inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Catheter site thrombosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chest discomfort	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Chills	9	(1.8)	5	(1.0)	14	(1.4)
Grade 1	9	(1.8)	5	(1.0)	14	(1.4)
Cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Face oedema	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Grade 1	122	(24.0)	144	(28.7)	266	(26.3)
Grade 2	44	(8.6)	23	(4.6)	67	(6.6)
Grade 3	4	(0.8)	3	(0.6)	7	(0.7)
Feeling cold	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gait disturbance	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
General physical health deterioration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Grade 1	46	(9.0)	32	(6.4)	78	(7.7)
Grade 2	10	(2.0)	6	(1.2)	16	(1.6)
Infusion site extravasation	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Injection site rash	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Localised oedema	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Malaise	5	(1.0)	4	(0.8)	9	(0.9)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Medical device site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Non-cardiac chest pain	13	(2.6)	7	(1.4)	20	(2.0)
Grade 1	10	(2.0)	6	(1.2)	16	(1.6)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Oedema peripheral	24	(4.7)	18	(3.6)	42	(4.2)
Grade 1	20	(3.9)	15	(3.0)	35	(3.5)
Grade 2	4	(0.8)	3	(0.6)	7	(0.7)
Pain	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral swelling	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Pyrexia	24	(4.7)	24	(4.8)	48	(4.7)
Grade 1	17	(3.3)	19	(3.8)	36	(3.6)
Grade 2	5	(1.0)	5	(1.0)	10	(1.0)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Swelling face	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**15**	**(2.9)**	**6**	**(1.2)**	**21**	**(2.1)**
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	7	(1.4)	2	(0.4)	9	(0.9)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Cholelithiasis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cholestasis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hepatitis	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Hyperbilirubinaemia	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ocular icterus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Immune system disorders	**21**	**(4.1)**	**6**	**(1.2)**	**27**	**(2.7)**
Grade 1	15	(2.9)	5	(1.0)	20	(2.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to arthropod sting	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Contrast media allergy	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Drug hypersensitivity	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypersensitivity	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Seasonal allergy	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Grade 1	72	(14.1)	55	(11.0)	127	(12.6)
Grade 2	134	(26.3)	98	(19.5)	232	(22.9)
Grade 3	18	(3.5)	19	(3.8)	37	(3.7)
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bacterial disease carrier	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bacterial urethritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bacteriuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Borrelia infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	12	(2.4)	15	(3.0)	27	(2.7)
Grade 1	1	(0.2)	4	(0.8)	5	(0.5)
Grade 2	10	(2.0)	11	(2.2)	21	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bronchitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	9	(1.8)	12	(2.4)	21	(2.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	6	(1.2)	11	(1.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cellulitis	9	(1.8)	12	(2.4)	21	(2.1)
Grade 3	3	(0.6)	6	(1.2)	9	(0.9)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Conjunctivitis viral	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Cystitis	4	(0.8)	8	(1.6)	12	(1.2)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	3	(0.6)	6	(1.2)	9	(0.9)
Dermatophytosis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Device related infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Ear infection	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)
Enterococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erysipelas	5	(1.0)	5	(1.0)	10	(1.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	2	(0.4)	4	(0.8)	6	(0.6)
Eye infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Folliculitis	10	(2.0)	6	(1.2)	16	(1.6)
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Fungal pharyngitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Fungal skin infection	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Furuncle	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Furuncle	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Gastroenteritis	8	(1.6)	10	(2.0)	18	(1.8)
Grade 1	5	(1.0)	8	(1.6)	13	(1.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Gastroenteritis viral	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal infection	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Genital candidiasis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Gingival abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gingivitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Groin abscess	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Herpes dermatitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Herpes simplex	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Herpes virus infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Herpes zoster	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Hordeolum	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Impetigo	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Infected bite	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Infected dermal cyst	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infected seroma	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Influenza	12	(2.4)	4	(0.8)	16	(1.6)
Grade 1	10	(2.0)	3	(0.6)	13	(1.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Labyrinthitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Laryngitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Lip infection	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Lower respiratory tract infection	6	(1.2)	2	(0.4)	8	(0.8)
Grade 2	6	(1.2)	2	(0.4)	8	(0.8)
Lyme disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymph gland infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Mastitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Mumps	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Grade 1	32	(6.3)	23	(4.6)	55	(5.4)
Grade 2	11	(2.2)	5	(1.0)	16	(1.6)
Oesophageal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Onychomycosis	0	(0.0)	5	(1.0)	5	(0.5)
Grade 1	0	(0.0)	5	(1.0)	5	(0.5)
Oral candidiasis	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Oral herpes	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oral herpes	7	(1.4)	5	(1.0)	12	(1.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Oral infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Otitis externa	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Otitis media	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Paronychia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pharyngitis	9	(1.8)	11	(2.2)	20	(2.0)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	9	(1.8)	10	(2.0)	19	(1.9)
Pharyngitis streptococcal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	8	(1.6)	6	(1.2)	14	(1.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	6	(1.2)	4	(0.8)	10	(1.0)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Postoperative wound infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Pulpitis dental	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Rash pustular	7	(1.4)	2	(0.4)	9	(0.9)
Grade 1	7	(1.4)	1	(0.2)	8	(0.8)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Respiratory tract infection viral	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Rhinitis	20	(3.9)	9	(1.8)	29	(2.9)
Grade 1	14	(2.8)	6	(1.2)	20	(2.0)
Grade 2	6	(1.2)	3	(0.6)	9	(0.9)
Root canal infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sinusitis	16	(3.1)	5	(1.0)	21	(2.1)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	14	(2.8)	5	(1.0)	19	(1.9)
Skin infection	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	7	(1.4)	1	(0.2)	8	(0.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Soft tissue infection	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tinea pedis	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Tinea versicolour	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Tonsillitis	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tooth infection	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Tracheitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Upper aerodigestive tract infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Grade 1	11	(2.2)	8	(1.6)	19	(1.9)
Grade 2	28	(5.5)	21	(4.2)	49	(4.8)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Urinary tract infection	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	11	(2.2)	9	(1.8)	20	(2.0)
Urinary tract infection viral	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Viral infection	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Viral pharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Viral rhinitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Viral upper respiratory tract infection	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Vulval abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Wound infection	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Wound infection bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Grade 1	22	(4.3)	29	(5.8)	51	(5.0)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Grade 2	14	(2.8)	18	(3.6)	32	(3.2)
Grade 3	3	(0.6)	5	(1.0)	8	(0.8)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Animal bite	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Arthropod bite	2	(0.4)	6	(1.2)	8	(0.8)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	3	(0.6)	3	(0.3)
Arthropod sting	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chemical burn	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Chillblains	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Clavicle fracture	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Contusion	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Eschar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Fall	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Foot fracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hand fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Humerus fracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Incision site discharge	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Incision site pain	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Incision site paraesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Joint injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ligament injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ligament sprain	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Limb injury	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Meniscus injury	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Muscle strain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nail avulsion	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Nail injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haematoma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Post-traumatic pain	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Procedural pain	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Procedural site reaction	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Procedural site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Radiation alopecia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Radiation injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Radiation pneumonitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Radiation skin injury	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Repetitive strain injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Rib fracture	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Seroma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Skin abrasion	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Skin graft failure	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Skin laceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Spinal fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sunburn	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Synovial rupture	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Thermal burn	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Traumatic haematoma	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Upper limb fracture	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Wound	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Wound secretion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Wrist fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Grade 1	130	(25.5)	129	(25.7)	259	(25.6)
Grade 2	57	(11.2)	38	(7.6)	95	(9.4)
Grade 3	13	(2.6)	13	(2.6)	26	(2.6)
Grade 4	5	(1.0)	2	(0.4)	7	(0.7)
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Grade 1	30	(5.9)	21	(4.2)	51	(5.0)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Amylase increased	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Anti-transglutaminase antibody increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Grade 1	19	(3.7)	15	(3.0)	34	(3.4)
Grade 2	9	(1.8)	4	(0.8)	13	(1.3)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Bacterial test positive	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Blood albumin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	10	(2.0)	4	(0.8)	14	(1.4)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood alkaline phosphatase increased	10	(2.0)	4	(0.8)	14	(1.4)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Blood bicarbonate increased	0	(0.0)	4	(0.8)	4	(0.4)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Blood bilirubin increased	14	(2.8)	9	(1.8)	23	(2.3)
Grade 1	6	(1.2)	5	(1.0)	11	(1.1)
Grade 2	8	(1.6)	3	(0.6)	11	(1.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Blood calcium decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood cholesterol increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood creatine phosphokinase increased	14	(2.8)	4	(0.8)	18	(1.8)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Grade 4	3	(0.6)	1	(0.2)	4	(0.4)
Blood creatinine increased	15	(2.9)	7	(1.4)	22	(2.2)
Grade 1	12	(2.4)	6	(1.2)	18	(1.8)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Blood glucose increased	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood lactate dehydrogenase decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood lactate dehydrogenase increased	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Blood potassium increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood testosterone decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood thyroid stimulating hormone decreased	8	(1.6)	2	(0.4)	10	(1.0)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood thyroid stimulating hormone decreased	8	(1.6)	2	(0.4)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone increased	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea increased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
C-reactive protein increased	16	(3.1)	6	(1.2)	22	(2.2)
Grade 1	14	(2.8)	6	(1.2)	20	(2.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Cardiac murmur	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Cortisol decreased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Eosinophil count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count increased	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Gamma-glutamyltransferase increased	16	(3.1)	7	(1.4)	23	(2.3)
Grade 1	11	(2.2)	3	(0.6)	14	(1.4)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Grade 3	3	(0.6)	2	(0.4)	5	(0.5)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haematocrit decreased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Haematocrit increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Haemoglobin increased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Heart rate decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lipase increased	10	(2.0)	5	(1.0)	15	(1.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	4	(0.8)	4	(0.8)	8	(0.8)
Grade 4	2	(0.4)	1	(0.2)	3	(0.3)
Lymphocyte count decreased	11	(2.2)	5	(1.0)	16	(1.6)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	6	(1.2)	1	(0.2)	7	(0.7)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Monocyte count increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Neutrophil count decreased	2	(0.4)	10	(2.0)	12	(1.2)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Neutrophil count increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Platelet count decreased	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Platelet count increased	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Protein total decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Protein total increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Red blood cell count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urinary sediment present	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urine output decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urobilinogen urine increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vitamin D decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Grade 1	48	(9.4)	33	(6.6)	81	(8.0)
Grade 2	8	(1.6)	6	(1.2)	14	(1.4)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Grade 1	49	(9.6)	68	(13.5)	117	(11.6)
Grade 2	16	(3.1)	14	(2.8)	30	(3.0)
White blood cell count decreased	1	(0.2)	7	(1.4)	8	(0.8)
Grade 1	0	(0.0)	5	(1.0)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
White blood cell count increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Metabolism and nutrition disorders	**90**	**(17.7)**	**52**	**(10.4)**	**142**	**(14.0)**
Grade 1	47	(9.2)	31	(6.2)	78	(7.7)
Grade 2	24	(4.7)	11	(2.2)	35	(3.5)
Grade 3	17	(3.3)	7	(1.4)	24	(2.4)
Grade 4	2	(0.4)	3	(0.6)	5	(0.5)
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Grade 1	27	(5.3)	12	(2.4)	39	(3.9)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Dehydration	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Fluid retention	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gout	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Hyperamylasaemia	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypercalcaemia	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	11	(2.2)	15	(3.0)	26	(2.6)
Grade 1	6	(1.2)	12	(2.4)	18	(1.8)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hyperkalaemia	3	(0.6)	7	(1.4)	10	(1.0)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	1	(0.2)	4	(0.8)	5	(0.5)
Hyperlipasaemia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Hyperphosphataemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hyperuricaemia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypocalcaemia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypoglycaemia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hypokalaemia	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Hypomagnesaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hyponatraemia	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3	5	(1.0)	1	(0.2)	6	(0.6)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Hypophosphataemia	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Hypovitaminosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Iron deficiency	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Polydipsia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Vitamin B12 deficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Vitamin D deficiency	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Grade 1	125	(24.6)	129	(25.7)	254	(25.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Grade 2	47	(9.2)	50	(10.0)	97	(9.6)
Grade 3	10	(2.0)	5	(1.0)	15	(1.5)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Grade 1	52	(10.2)	59	(11.8)	111	(11.0)
Grade 2	19	(3.7)	14	(2.8)	33	(3.3)
Grade 3	6	(1.2)	0	(0.0)	6	(0.6)
Arthritis	8	(1.6)	1	(0.2)	9	(0.9)
Grade 1	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Grade 1	28	(5.5)	36	(7.2)	64	(6.3)
Grade 2	8	(1.6)	16	(3.2)	24	(2.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Bone pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Bursitis	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	2	(0.4)	5	(1.0)	7	(0.7)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Chondrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Clubbing	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Flank pain	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Groin pain	3	(0.6)	5	(1.0)	8	(0.8)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Inguinal mass	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Intervertebral disc protrusion	2	(0.4)	3	(0.6)	5	(0.5)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Intervertebral disc protrusion	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Joint effusion	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Joint range of motion decreased	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Joint swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Limb discomfort	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Limb mass	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Muscle contracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Muscle spasms	9	(1.8)	9	(1.8)	18	(1.8)
Grade 1	8	(1.6)	7	(1.4)	15	(1.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Muscular weakness	2	(0.4)	7	(1.4)	9	(0.9)
Grade 1	2	(0.4)	6	(1.2)	8	(0.8)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal chest pain	7	(1.4)	7	(1.4)	14	(1.4)
Grade 1	6	(1.2)	6	(1.2)	12	(1.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal discomfort	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Musculoskeletal pain	22	(4.3)	8	(1.6)	30	(3.0)
Grade 1	18	(3.5)	5	(1.0)	23	(2.3)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal stiffness	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Grade 1	33	(6.5)	24	(4.8)	57	(5.6)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Neck mass	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	12	(2.4)	5	(1.0)	17	(1.7)
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Osteitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Osteoarthritis	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Osteoporosis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)
Grade 1	17	(3.3)	24	(4.8)	41	(4.1)
Grade 2	3	(0.6)	7	(1.4)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pain in jaw	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Plantar fascial fibromatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Soft tissue swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Spinal pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Spondylitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Synovial cyst	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Synovitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tendon disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Tendonitis	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vertebral osteophyte	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Grade 1	27	(5.3)	29	(5.8)	56	(5.5)
Grade 2	31	(6.1)	32	(6.4)	63	(6.2)
Grade 3	14	(2.8)	12	(2.4)	26	(2.6)
Grade 4	1	(0.2)	1	(0.2)	2	(0.2)
Acanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Adenoma benign	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Angiolipoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	10	(2.0)	18	(3.6)	28	(2.8)
Grade 3	5	(1.0)	3	(0.6)	8	(0.8)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Benign breast neoplasm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Benign neoplasm of skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bowen's disease	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Colon adenoma	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Dysplastic naevus	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Fibroadenoma of breast	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Fibroma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Fibrous histiocytoma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Haemangioma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of liver	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of skin	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hair follicle tumour benign	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Histiocytic necrotising lymphadenitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Keratoacanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Lipoma	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Malignant melanoma	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Malignant melanoma in situ	1	(0.2)	6	(1.2)	7	(0.7)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	16	(3.1)	11	(2.2)	27	(2.7)
Grade 1	11	(2.2)	8	(1.6)	19	(1.9)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Grade 4	1	(0.2)	1	(0.2)	2	(0.2)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Renal oncocytoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Seborrhoeic keratosis	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Skin papilloma	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Squamous cell carcinoma	6	(1.2)	3	(0.6)	9	(0.9)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Squamous cell carcinoma of skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Superficial spreading melanoma stage unspecified	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sweat gland tumour	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Uterine leiomyoma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Nervous system disorders	**175**	**(34.4)**	**162**	**(32.3)**	**337**	**(33.3)**
Grade 1	132	(25.9)	125	(24.9)	257	(25.4)
Grade 2	37	(7.3)	28	(5.6)	65	(6.4)
Grade 3	6	(1.2)	9	(1.8)	15	(1.5)
Acute motor-sensory axonal neuropathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Allodynia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Amnesia	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Anosmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphasia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Ataxia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Carotid arteriosclerosis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Carpal tunnel syndrome	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cervical radiculopathy	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Complex regional pain syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Disturbance in attention	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Grade 1	25	(4.9)	26	(5.2)	51	(5.0)
Grade 2	1	(0.2)	4	(0.8)	5	(0.5)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dizziness postural	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Dysaesthesia	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Dysarthria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	10	(2.0)	10	(2.0)	20	(2.0)
Grade 1	8	(1.6)	10	(2.0)	18	(1.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Grade 1	75	(14.7)	78	(15.5)	153	(15.1)
Grade 2	20	(3.9)	14	(2.8)	34	(3.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hyperaesthesia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lethargy	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	5	(1.0)	6	(1.2)	11	(1.1)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Memory impairment	6	(1.2)	6	(1.2)	12	(1.2)
Grade 1	5	(1.0)	6	(1.2)	11	(1.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Migraine	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Muscle contractions involuntary	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nerve compression	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neuralgia	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Neuropathy peripheral	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	13	(2.6)	13	(2.6)	26	(2.6)
Grade 1	13	(2.6)	13	(2.6)	26	(2.6)
Peripheral sensory neuropathy	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Petit mal epilepsy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Presyncope	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Radiculopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sciatica	5	(1.0)	6	(1.2)	11	(1.1)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Sensory disturbance	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Grade 3	1	(0.2)	4	(0.8)	5	(0.5)
Taste disorder	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Tension headache	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Tremor	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Trigeminal nerve disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vasogenic cerebral oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vertebrobasilar insufficiency	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**43**	**(8.4)**	**61**	**(12.2)**	**104**	**(10.3)**
Grade 1	26	(5.1)	42	(8.4)	68	(6.7)
Grade 2	17	(3.3)	17	(3.4)	34	(3.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Agitation	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	10	(2.0)	23	(4.6)	33	(3.3)
Grade 1	7	(1.4)	13	(2.6)	20	(2.0)
Grade 2	3	(0.6)	9	(1.8)	12	(1.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Confusional state	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Depressed mood	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Depression	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Insomnia	17	(3.3)	19	(3.8)	36	(3.6)
Grade 1	10	(2.0)	12	(2.4)	22	(2.2)
Grade 2	7	(1.4)	7	(1.4)	14	(1.4)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Libido decreased	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Mood swings	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nightmare	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sleep disorder	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Suicidal ideation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Tension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Thermophobia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**27**	**(5.3)**	**19**	**(3.8)**	**46**	**(4.5)**
Grade 1	17	(3.3)	12	(2.4)	29	(2.9)
Grade 2	6	(1.2)	5	(1.0)	11	(1.1)
Grade 3	4	(0.8)	2	(0.4)	6	(0.6)
Acute kidney injury	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bilirubinuria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bladder cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Bladder dysfunction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cystitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dysuria	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Glycosuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Haematuria	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	7	(1.4)	4	(0.8)	11	(1.1)
Hypertonic bladder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Leukocyturia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nephrolithiasis	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pollakiuria	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Polyuria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Proteinuria	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Renal colic	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Renal failure	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Urinary incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Urine abnormality	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**29**	**(5.7)**	**21**	**(4.2)**	**50**	**(4.9)**
Grade 1	22	(4.3)	15	(3.0)	37	(3.7)
Grade 2	7	(1.4)	4	(0.8)	11	(1.1)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Balanoposthitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Breast cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Breast disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Breast oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Breast pain	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Breast swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dysmenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Endometrial hypertrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erectile dysfunction	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Genital haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Genital rash	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gynaecomastia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Hypomenorrhoea	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Nipple pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Orchitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ovarian cyst	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Pelvic pain	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Prostatomegaly	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Scrotal mass	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Testicular swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Uterine fibrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Vaginal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal dryness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**
Grade 1	99	(19.4)	87	(17.3)	186	(18.4)
Grade 2	41	(8.1)	19	(3.8)	60	(5.9)
Grade 3	9	(1.8)	2	(0.4)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Allergic cough	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphonia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Asthma	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Chronic obstructive pulmonary disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Grade 1	63	(12.4)	48	(9.6)	111	(11.0)
Grade 2	8	(1.6)	8	(1.6)	16	(1.6)
Dry throat	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysphonia	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Grade 1	36	(7.1)	24	(4.8)	60	(5.9)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea exertional	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Epistaxis	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal inflammation	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nasal congestion	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	5	(1.0)	4	(0.8)	9	(0.9)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oropharyngeal discomfort	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Oropharyngeal pain	16	(3.1)	16	(3.2)	32	(3.2)
Grade 1	14	(2.8)	15	(3.0)	29	(2.9)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Oropharyngeal plaque	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Painful respiration	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Paranasal sinus haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngeal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Pharyngeal erythema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Pleural effusion	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pleuritic pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonitis	18	(3.5)	3	(0.6)	21	(2.1)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	14	(2.8)	2	(0.4)	16	(1.6)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Productive cough	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary embolism	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	4	(0.8)	1	(0.2)	5	(0.5)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Reflux laryngitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	11	(2.2)	5	(1.0)	16	(1.6)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Rhinitis allergic	11	(2.2)	5	(1.0)	16	(1.6)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	6	(1.2)	2	(0.4)	8	(0.8)
Rhinorrhoea	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sinus pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Sleep apnoea syndrome	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sneezing	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Throat tightness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tonsillolith	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vocal cord inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Wheezing	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	1	(0.2)	4	(0.8)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Grade 1	190	(37.3)	166	(33.1)	356	(35.2)
Grade 2	79	(15.5)	31	(6.2)	110	(10.9)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
Acne	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Actinic keratosis	9	(1.8)	3	(0.6)	12	(1.2)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Alopecia	12	(2.4)	10	(2.0)	22	(2.2)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Angioedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Angiokeratoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Blister	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dermal cyst	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Dermatitis	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis acneiform	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	10	(2.0)	10	(2.0)	20	(2.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Dermatitis contact	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Grade 1	23	(4.5)	10	(2.0)	33	(3.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ecchymosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eczema	22	(4.3)	10	(2.0)	32	(3.2)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	10	(2.0)	1	(0.2)	11	(1.1)
Eczema asteatotic	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erythema	14	(2.8)	6	(1.2)	20	(2.0)
Grade 1	11	(2.2)	5	(1.0)	16	(1.6)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Erythrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhage subcutaneous	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hair disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Hidradenitis	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hyperhidrosis	0	(0.0)	6	(1.2)	6	(0.6)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hyperkeratosis	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Hypertrophic scar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ingrowing nail	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Intertrigo	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Itching scar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Keloid scar	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Keratosis pilaris	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Keratosis pilaris	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lichen planus	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lichen sclerosus	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lichenoid keratosis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Macule	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neurodermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Neutrophilic dermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Night sweats	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Onycholysis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Onychomadesis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pain of skin	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Papule	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Papulopustular rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Photodermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Photosensitivity reaction	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pigmentation disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Grade 1	85	(16.7)	56	(11.2)	141	(13.9)
Grade 2	18	(3.5)	3	(0.6)	21	(2.1)
Pruritus allergic	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Psoriasis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Grade 1	54	(10.6)	40	(8.0)	94	(9.3)
Grade 2	11	(2.2)	4	(0.8)	15	(1.5)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Rash erythematous	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash macular	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Grade 1	20	(3.9)	21	(4.2)	41	(4.1)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Rash papular	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash pruritic	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Rash vesicular	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Scar pain	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic dermatitis	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Skin depigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin discolouration	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Skin erosion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Skin exfoliation	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin hyperpigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin hypertrophy	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin induration	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin irritation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin lesion	13	(2.6)	8	(1.6)	21	(2.1)
Grade 1	9	(1.8)	6	(1.2)	15	(1.5)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Skin mass	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Skin tightness	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Skin ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Solar dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Solar lentigo	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Transient acantholytic dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vitiligo	25	(4.9)	8	(1.6)	33	(3.3)
Grade 1	24	(4.7)	7	(1.4)	31	(3.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Vascular disorders	**125**	**(24.6)**	**130**	**(25.9)**	**255**	**(25.2)**
Grade 1	47	(9.2)	55	(11.0)	102	(10.1)
Grade 2	47	(9.2)	56	(11.2)	103	(10.2)
Grade 3	31	(6.1)	19	(3.8)	50	(4.9)
Aortic arteriosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Deep vein thrombosis	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Diastolic hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Flushing	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Haematoma	4	(0.8)	7	(1.4)	11	(1.1)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hot flush	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Grade 1	9	(1.8)	15	(3.0)	24	(2.4)
Grade 2	39	(7.7)	45	(9.0)	84	(8.3)
Grade 3	28	(5.5)	18	(3.6)	46	(4.5)
Hypotension	5	(1.0)	4	(0.8)	9	(0.9)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocele	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Grade 1	21	(4.1)	29	(5.8)	50	(4.9)
Grade 2	4	(0.8)	7	(1.4)	11	(1.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Orthostatic hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Peripheral venous disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Poor venous access	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Prehypertension	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Thrombophlebitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Thrombophlebitis superficial	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)

Subjects With Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Varicose vein	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Venous thrombosis limb	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-10

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	480	(94.3)	454	(90.4)	934	(92.4)
Grade 1	69	(13.6)	136	(27.1)	205	(20.3)
Grade 2	249	(48.9)	222	(44.2)	471	(46.6)
Grade 3	147	(28.9)	89	(17.7)	236	(23.3)
Grade 4	14	(2.8)	7	(1.4)	21	(2.1)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
with no adverse events	29	(5.7)	48	(9.6)	77	(7.6)
Blood and lymphatic system disorders	**37**	**(7.3)**	**22**	**(4.4)**	**59**	**(5.8)**
Grade 1	22	(4.3)	13	(2.6)	35	(3.5)
Grade 2	13	(2.6)	9	(1.8)	22	(2.2)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Lymphopenia	11	(2.2)	7	(1.4)	18	(1.8)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	6	(1.2)	3	(0.6)	9	(0.9)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Eosinophilia	9	(1.8)	1	(0.2)	10	(1.0)
Grade 1	8	(1.6)	1	(0.2)	9	(0.9)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anaemia	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Lymphadenopathy	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Leukocytosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac disorders	**24**	**(4.7)**	**20**	**(4.0)**	**44**	**(4.4)**
Grade 1	17	(3.3)	17	(3.4)	34	(3.4)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	4	(0.8)	1	(0.2)	5	(0.5)
Bradycardia	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Palpitations	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Sinus tachycardia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Tachycardia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Angina pectoris	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Arrhythmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac failure congestive	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Sinus bradycardia	1	(0.2)	3	(0.6)	4	(0.4)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Sinus bradycardia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Brugada syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Coronary artery disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**5**	**(1.0)**	**7**	**(0.7)**
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Preauricular cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dermoid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Epidermal naevus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Gilbert's syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hydrocele	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Ear and labyrinth disorders	**21**	**(4.1)**	**21**	**(4.2)**	**42**	**(4.2)**
Grade 1	13	(2.6)	19	(3.8)	32	(3.2)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vertigo	7	(1.4)	9	(1.8)	16	(1.6)
Grade 1	5	(1.0)	9	(1.8)	14	(1.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Ear pain	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tinnitus	5	(1.0)	8	(1.6)	13	(1.3)
Grade 1	4	(0.8)	7	(1.4)	11	(1.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hypoacusis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Vestibular disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Ear discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
External ear inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Deafness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Deafness unilateral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Middle ear effusion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Middle ear inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Noninfective myringitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Endocrine disorders	**121**	**(23.8)**	**27**	**(5.4)**	**148**	**(14.6)**
Grade 1	38	(7.5)	17	(3.4)	55	(5.4)
Grade 2	80	(15.7)	10	(2.0)	90	(8.9)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	8	(1.6)	1	(0.2)	9	(0.9)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal insufficiency	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Autoimmune thyroiditis	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hypopituitarism	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cushingoid	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhagic thyroid cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eye disorders	**56**	**(11.0)**	**43**	**(8.6)**	**99**	**(9.8)**
Grade 1	46	(9.0)	35	(7.0)	81	(8.0)
Grade 2	9	(1.8)	7	(1.4)	16	(1.6)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Dry eye	14	(2.8)	8	(1.6)	22	(2.2)
Grade 1	13	(2.6)	8	(1.6)	21	(2.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	8	(1.6)	11	(2.2)	19	(1.9)
Grade 1	8	(1.6)	8	(1.6)	16	(1.6)
Grade 2	0	(0.0)	3	(0.6)	3	(0.3)
Lacrimation increased	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Blepharitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Cataract	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Eye irritation	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Visual impairment	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Ocular hyperaemia	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Periorbital swelling	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Scleral hyperaemia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Visual acuity reduced	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vitreous floaters	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Blindness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Chalazion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctival hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diplopia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye haemorrhage	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Eye pain	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eyelid oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Optic ischaemic neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blepharospasm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lens dislocation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Presbyopia	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Swelling of eyelid	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal disorders	**282**	**(55.4)**	**231**	**(46.0)**	**513**	**(50.7)**
Grade 1	179	(35.2)	175	(34.9)	354	(35.0)
Grade 2	75	(14.7)	46	(9.2)	121	(12.0)
Grade 3	27	(5.3)	10	(2.0)	37	(3.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	139	(27.3)	133	(26.5)	272	(26.9)
Grade 1	106	(20.8)	108	(21.5)	214	(21.2)
Grade 2	27	(5.3)	19	(3.8)	46	(4.5)
Grade 3	5	(1.0)	6	(1.2)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	89	(17.5)	74	(14.7)	163	(16.1)
Grade 1	76	(14.9)	66	(13.1)	142	(14.0)
Grade 2	12	(2.4)	8	(1.6)	20	(2.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	40	(7.9)	24	(4.8)	64	(6.3)
Grade 1	31	(6.1)	18	(3.6)	49	(4.8)
Grade 2	9	(1.8)	5	(1.0)	14	(1.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Grade 1	32	(6.3)	27	(5.4)	59	(5.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Abdominal pain	37	(7.3)	32	(6.4)	69	(6.8)
Grade 2	5	(1.0)	4	(0.8)	9	(0.9)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Constipation	34	(6.7)	29	(5.8)	63	(6.2)
Grade 1	27	(5.3)	24	(4.8)	51	(5.0)
Grade 2	6	(1.2)	5	(1.0)	11	(1.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dry mouth	30	(5.9)	10	(2.0)	40	(4.0)
Grade 1	29	(5.7)	10	(2.0)	39	(3.9)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	23	(4.5)	14	(2.8)	37	(3.7)
Grade 1	19	(3.7)	13	(2.6)	32	(3.2)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	19	(3.7)	6	(1.2)	25	(2.5)
Grade 1	12	(2.4)	3	(0.6)	15	(1.5)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Colitis	13	(2.6)	2	(0.4)	15	(1.5)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Grade 3	7	(1.4)	0	(0.0)	7	(0.7)
Gastrooesophageal reflux disease	7	(1.4)	6	(1.2)	13	(1.3)
Grade 1	4	(0.8)	5	(1.0)	9	(0.9)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Haemorrhoids	7	(1.4)	1	(0.2)	8	(0.8)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Stomatitis	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Abdominal pain lower	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Faeces soft	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastritis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Toothache	5	(1.0)	7	(1.4)	12	(1.2)
Grade 1	4	(0.8)	5	(1.0)	9	(0.9)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Haematochezia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Mouth ulceration	4	(0.8)	7	(1.4)	11	(1.1)
Grade 1	4	(0.8)	7	(1.4)	11	(1.1)
Odynophagia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Oral lichen planus	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rectal haemorrhage	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Anal haemorrhage	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Proctalgia	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal distension	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dental caries	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Gingival bleeding	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Haemorrhoidal haemorrhage	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Inguinal hernia	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Large intestine polyp	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Oral disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Oral pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Umbilical hernia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anorectal varices	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Diverticulum	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulum intestinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Duodenal polyp	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Duodenitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dyschezia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dysphagia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Gastric ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal angiectasia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Melaena	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Melaena	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Oral discomfort	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Oral mucosa erosion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Periodontal disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Submaxillary gland enlargement	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tongue disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Angular cheilitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Epigastric discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Flatulence	0	(0.0)	4	(0.8)	4	(0.4)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Flatulence	0	(0.0)	4	(0.8)	4	(0.4)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Gingival oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Gingival recession	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hyperaesthesia teeth	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Rectal tenesmus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
General disorders and administration site conditions	**280**	**(55.0)**	**260**	**(51.8)**	**540**	**(53.4)**
Grade 1	192	(37.7)	216	(43.0)	408	(40.4)
Grade 2	79	(15.5)	41	(8.2)	120	(11.9)
Grade 3	9	(1.8)	3	(0.6)	12	(1.2)
Fatigue	170	(33.4)	170	(33.9)	340	(33.6)
Grade 1	122	(24.0)	144	(28.7)	266	(26.3)
Grade 2	44	(8.6)	23	(4.6)	67	(6.6)
Grade 3	4	(0.8)	3	(0.6)	7	(0.7)
Influenza like illness	56	(11.0)	38	(7.6)	94	(9.3)
Grade 1	46	(9.0)	32	(6.4)	78	(7.7)
Grade 2	10	(2.0)	6	(1.2)	16	(1.6)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Grade 1	38	(7.5)	37	(7.4)	75	(7.4)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Asthenia	55	(10.8)	42	(8.4)	97	(9.6)
Grade 2	16	(3.1)	5	(1.0)	21	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Oedema peripheral	24	(4.7)	18	(3.6)	42	(4.2)
Grade 1	20	(3.9)	15	(3.0)	35	(3.5)
Grade 2	4	(0.8)	3	(0.6)	7	(0.7)
Pyrexia	24	(4.7)	24	(4.8)	48	(4.7)
Grade 1	17	(3.3)	19	(3.8)	36	(3.6)
Grade 2	5	(1.0)	5	(1.0)	10	(1.0)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Non-cardiac chest pain	13	(2.6)	7	(1.4)	20	(2.0)
Grade 1	10	(2.0)	6	(1.2)	16	(1.6)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Chills	9	(1.8)	5	(1.0)	14	(1.4)
Grade 1	9	(1.8)	5	(1.0)	14	(1.4)
Axillary pain	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Malaise	5	(1.0)	4	(0.8)	9	(0.9)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Face oedema	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Feeling cold	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Infusion site extravasation	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Pain	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Catheter site inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gait disturbance	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
General physical health deterioration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site rash	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Medical device site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral swelling	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Catheter site thrombosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chest discomfort	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Injection site pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Swelling face	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hepatobiliary disorders	**15**	**(2.9)**	**6**	**(1.2)**	**21**	**(2.1)**
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	7	(1.4)	2	(0.4)	9	(0.9)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hyperbilirubinaemia	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Cholelithiasis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cholestasis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Ocular icterus	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Immune system disorders	**21**	**(4.1)**	**6**	**(1.2)**	**27**	**(2.7)**
Grade 1	15	(2.9)	5	(1.0)	20	(2.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Immune system disorders	**21**	**(4.1)**	**6**	**(1.2)**	**27**	**(2.7)**
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Drug hypersensitivity	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Seasonal allergy	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Allergy to arthropod sting	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Contrast media allergy	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Infections and infestations	**224**	**(44.0)**	**172**	**(34.3)**	**396**	**(39.2)**
Grade 1	72	(14.1)	55	(11.0)	127	(12.6)
Grade 2	134	(26.3)	98	(19.5)	232	(22.9)
Grade 3	18	(3.5)	19	(3.8)	37	(3.7)
Nasopharyngitis	43	(8.4)	28	(5.6)	71	(7.0)
Grade 1	32	(6.3)	23	(4.6)	55	(5.4)
Grade 2	11	(2.2)	5	(1.0)	16	(1.6)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Upper respiratory tract infection	39	(7.7)	30	(6.0)	69	(6.8)
Grade 1	11	(2.2)	8	(1.6)	19	(1.9)
Grade 2	28	(5.5)	21	(4.2)	49	(4.8)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Rhinitis	20	(3.9)	9	(1.8)	29	(2.9)
Grade 1	14	(2.8)	6	(1.2)	20	(2.0)
Grade 2	6	(1.2)	3	(0.6)	9	(0.9)
Sinusitis	16	(3.1)	5	(1.0)	21	(2.1)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	14	(2.8)	5	(1.0)	19	(1.9)
Bronchitis	12	(2.4)	15	(3.0)	27	(2.7)
Grade 1	1	(0.2)	4	(0.8)	5	(0.5)
Grade 2	10	(2.0)	11	(2.2)	21	(2.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Influenza	12	(2.4)	4	(0.8)	16	(1.6)
Grade 1	10	(2.0)	3	(0.6)	13	(1.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Urinary tract infection	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	11	(2.2)	9	(1.8)	20	(2.0)
Folliculitis	10	(2.0)	6	(1.2)	16	(1.6)
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cellulitis	9	(1.8)	12	(2.4)	21	(2.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	6	(1.2)	11	(1.1)
Grade 3	3	(0.6)	6	(1.2)	9	(0.9)
Pharyngitis	9	(1.8)	11	(2.2)	20	(2.0)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	9	(1.8)	10	(2.0)	19	(1.9)
Skin infection	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	7	(1.4)	1	(0.2)	8	(0.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Gastroenteritis	8	(1.6)	10	(2.0)	18	(1.8)
Grade 1	5	(1.0)	8	(1.6)	13	(1.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pneumonia	8	(1.6)	6	(1.2)	14	(1.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	6	(1.2)	4	(0.8)	10	(1.0)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Conjunctivitis	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Oral herpes	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Rash pustular	7	(1.4)	2	(0.4)	9	(0.9)
Grade 1	7	(1.4)	1	(0.2)	8	(0.8)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Viral infection	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Fungal skin infection	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Lower respiratory tract infection	6	(1.2)	2	(0.4)	8	(0.8)
Grade 2	6	(1.2)	2	(0.4)	8	(0.8)
Respiratory tract infection	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Erysipelas	5	(1.0)	5	(1.0)	10	(1.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	2	(0.4)	4	(0.8)	6	(0.6)
Gastroenteritis viral	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cystitis	4	(0.8)	8	(1.6)	12	(1.2)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	3	(0.6)	6	(1.2)	9	(0.9)
Viral upper respiratory tract infection	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Viral upper respiratory tract infection	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Ear infection	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)
Tooth infection	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Dermatophytosis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Genital candidiasis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Infected dermal cyst	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Laryngitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Mastitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Otitis externa	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Otitis media	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Soft tissue infection	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Tonsillitis	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Viral rhinitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Wound infection	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Borrelia infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis viral	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Device related infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Enterococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eye infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Fungal pharyngitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Furuncle	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Gastrointestinal infection	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Gingival abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gingivitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Herpes simplex	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Herpes virus infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hordeolum	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Impetigo	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Infected bite	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Infected seroma	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Labyrinthitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Mumps	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Oral candidiasis	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Pharyngitis streptococcal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Postoperative wound infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Pulpitis dental	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tinea pedis	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Upper aerodigestive tract infection	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Upper aerodigestive tract infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urinary tract infection viral	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vulval abscess	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal mycotic infection	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Bacterial disease carrier	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bacterial urethritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bacteriuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Bronchitis bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Groin abscess	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Herpes dermatitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Herpes zoster	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Lip infection	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Lyme disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymph gland infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Onychomycosis	0	(0.0)	5	(1.0)	5	(0.5)
Grade 1	0	(0.0)	5	(1.0)	5	(0.5)
Oral infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Paronychia	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Paronychia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Root canal infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Tinea versicolour	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Tracheitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Viral pharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Wound infection bacterial	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**39**	**(7.7)**	**53**	**(10.6)**	**92**	**(9.1)**
Grade 1	22	(4.3)	29	(5.8)	51	(5.0)
Grade 2	14	(2.8)	18	(3.6)	32	(3.2)
Grade 3	3	(0.6)	5	(1.0)	8	(0.8)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Arthropod sting	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ligament sprain	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Arthropod bite	2	(0.4)	6	(1.2)	8	(0.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Arthropod bite	2	(0.4)	6	(1.2)	8	(0.8)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	3	(0.6)	3	(0.3)
Clavicle fracture	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Fall	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Meniscus injury	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Post-traumatic pain	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Procedural pain	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Radiation skin injury	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Sunburn	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Synovial rupture	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Traumatic haematoma	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Animal bite	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Contusion	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Eschar	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eschar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hand fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Incision site discharge	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Incision site paraesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Joint injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ligament injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Limb injury	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Post procedural haematoma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Procedural site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Radiation alopecia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rib fracture	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin laceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Spinal fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Upper limb fracture	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Wound secretion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Wrist fracture	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Wrist fracture	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Chemical burn	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Chillblains	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Foot fracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Humerus fracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Incision site pain	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Muscle strain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nail avulsion	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Nail injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Radiation injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Radiation pneumonitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Repetitive strain injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Seroma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Skin abrasion	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Skin graft failure	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Thermal burn	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Wound	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Investigations	**205**	**(40.3)**	**182**	**(36.3)**	**387**	**(38.3)**
Grade 1	130	(25.5)	129	(25.7)	259	(25.6)
Grade 2	57	(11.2)	38	(7.6)	95	(9.4)
Grade 3	13	(2.6)	13	(2.6)	26	(2.6)
Grade 4	5	(1.0)	2	(0.4)	7	(0.7)
Weight increased	65	(12.8)	82	(16.3)	147	(14.5)
Grade 1	49	(9.6)	68	(13.5)	117	(11.6)
Grade 2	16	(3.1)	14	(2.8)	30	(3.0)
Weight decreased	56	(11.0)	39	(7.8)	95	(9.4)
Grade 1	48	(9.4)	33	(6.6)	81	(8.0)
Grade 2	8	(1.6)	6	(1.2)	14	(1.4)
Alanine aminotransferase increased	38	(7.5)	25	(5.0)	63	(6.2)
Grade 1	30	(5.9)	21	(4.2)	51	(5.0)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Aspartate aminotransferase increased	29	(5.7)	20	(4.0)	49	(4.8)
Grade 1	19	(3.7)	15	(3.0)	34	(3.4)
Grade 2	9	(1.8)	4	(0.8)	13	(1.3)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
C-reactive protein increased	16	(3.1)	6	(1.2)	22	(2.2)
Grade 1	14	(2.8)	6	(1.2)	20	(2.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	16	(3.1)	7	(1.4)	23	(2.3)
Grade 1	11	(2.2)	3	(0.6)	14	(1.4)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Grade 3	3	(0.6)	2	(0.4)	5	(0.5)
Blood creatinine increased	15	(2.9)	7	(1.4)	22	(2.2)
Grade 1	12	(2.4)	6	(1.2)	18	(1.8)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Blood bilirubin increased	14	(2.8)	9	(1.8)	23	(2.3)
Grade 1	6	(1.2)	5	(1.0)	11	(1.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood bilirubin increased	14	(2.8)	9	(1.8)	23	(2.3)
Grade 2	8	(1.6)	3	(0.6)	11	(1.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Blood creatine phosphokinase increased	14	(2.8)	4	(0.8)	18	(1.8)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Grade 4	3	(0.6)	1	(0.2)	4	(0.4)
Lymphocyte count decreased	11	(2.2)	5	(1.0)	16	(1.6)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	6	(1.2)	1	(0.2)	7	(0.7)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Blood alkaline phosphatase increased	10	(2.0)	4	(0.8)	14	(1.4)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Lipase increased	10	(2.0)	5	(1.0)	15	(1.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	4	(0.8)	4	(0.8)	8	(0.8)
Grade 4	2	(0.4)	1	(0.2)	3	(0.3)
Blood thyroid stimulating hormone decreased	8	(1.6)	2	(0.4)	10	(1.0)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count increased	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Amylase increased	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone increased	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Platelet count decreased	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Platelet count decreased	4	(0.8)	5	(1.0)	9	(0.9)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Blood lactate dehydrogenase increased	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Blood glucose increased	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Neutrophil count decreased	2	(0.4)	10	(2.0)	12	(1.2)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Platelet count increased	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Bacterial test positive	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Blood albumin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood urea increased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Cardiac murmur	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Cortisol decreased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Eosinophil count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Glomerular filtration rate increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haematocrit decreased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Haematocrit increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Haemoglobin increased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Haemoglobin increased	1	(0.2)	3	(0.6)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Heart rate decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Monocyte count increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Prostatic specific antigen increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Protein total increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Red blood cell count decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urinary sediment present	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urine output decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urobilinogen urine increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vitamin D decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
White blood cell count decreased	1	(0.2)	7	(1.4)	8	(0.8)
Grade 1	0	(0.0)	5	(1.0)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
White blood cell count increased	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Anti-transglutaminase antibody increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood bicarbonate increased	0	(0.0)	4	(0.8)	4	(0.4)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Blood calcium decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood cholesterol increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood lactate dehydrogenase decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood potassium increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood testosterone decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Neutrophil count increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Protein total decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Metabolism and nutrition disorders	**90**	**(17.7)**	**52**	**(10.4)**	**142**	**(14.0)**
Grade 1	47	(9.2)	31	(6.2)	78	(7.7)
Grade 2	24	(4.7)	11	(2.2)	35	(3.5)
Grade 3	17	(3.3)	7	(1.4)	24	(2.4)
Grade 4	2	(0.4)	3	(0.6)	5	(0.5)
Decreased appetite	36	(7.1)	13	(2.6)	49	(4.8)
Grade 1	27	(5.3)	12	(2.4)	39	(3.9)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Hyperglycaemia	11	(2.2)	15	(3.0)	26	(2.6)
Grade 1	6	(1.2)	12	(2.4)	18	(1.8)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hypokalaemia	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Hyponatraemia	7	(1.4)	5	(1.0)	12	(1.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hyponatraemia	7	(1.4)	5	(1.0)	12	(1.2)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 3	5	(1.0)	1	(0.2)	6	(0.6)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Hypophosphataemia	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Hyperuricaemia	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Vitamin D deficiency	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)
Gout	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Hyperamylasaemia	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hyperkalaemia	3	(0.6)	7	(1.4)	10	(1.0)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	1	(0.2)	4	(0.8)	5	(0.5)
Hypocalcaemia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dehydration	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hypercalcaemia	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Iron deficiency	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperlipasaemia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypoglycaemia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Polydipsia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vitamin B12 deficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Fluid retention	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Hyperphosphataemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hypomagnesaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypovitaminosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Grade 1	125	(24.6)	129	(25.7)	254	(25.1)
Grade 2	47	(9.2)	50	(10.0)	97	(9.6)
Grade 3	10	(2.0)	5	(1.0)	15	(1.5)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**183**	**(36.0)**	**184**	**(36.7)**	**367**	**(36.3)**
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	77	(15.1)	73	(14.5)	150	(14.8)
Grade 1	52	(10.2)	59	(11.8)	111	(11.0)
Grade 2	19	(3.7)	14	(2.8)	33	(3.3)
Grade 3	6	(1.2)	0	(0.0)	6	(0.6)
Back pain	36	(7.1)	54	(10.8)	90	(8.9)
Grade 1	28	(5.5)	36	(7.2)	64	(6.3)
Grade 2	8	(1.6)	16	(3.2)	24	(2.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Myalgia	36	(7.1)	27	(5.4)	63	(6.2)
Grade 1	33	(6.5)	24	(4.8)	57	(5.6)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Musculoskeletal pain	22	(4.3)	8	(1.6)	30	(3.0)
Grade 1	18	(3.5)	5	(1.0)	23	(2.3)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pain in extremity	21	(4.1)	31	(6.2)	52	(5.1)
Grade 1	17	(3.3)	24	(4.8)	41	(4.1)
Grade 2	3	(0.6)	7	(1.4)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	12	(2.4)	5	(1.0)	17	(1.7)
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Muscle spasms	9	(1.8)	9	(1.8)	18	(1.8)
Grade 1	8	(1.6)	7	(1.4)	15	(1.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Arthritis	8	(1.6)	1	(0.2)	9	(0.9)
Grade 1	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Musculoskeletal chest pain	7	(1.4)	7	(1.4)	14	(1.4)
Grade 1	6	(1.2)	6	(1.2)	12	(1.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Bursitis	6	(1.2)	5	(1.0)	11	(1.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Bursitis	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	2	(0.4)	5	(1.0)	7	(0.7)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Tendonitis	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Osteoarthritis	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Groin pain	3	(0.6)	5	(1.0)	8	(0.8)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal stiffness	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Bone pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Flank pain	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Intervertebral disc protrusion	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Joint range of motion decreased	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Limb discomfort	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Muscular weakness	2	(0.4)	7	(1.4)	9	(0.9)
Grade 1	2	(0.4)	6	(1.2)	8	(0.8)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal discomfort	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Pain in jaw	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Spinal pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Synovial cyst	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Synovitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tendon disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Chondrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Clubbing	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Inguinal mass	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Joint effusion	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Joint swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Neck mass	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Limb mass	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Muscle contracture	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Muscle contracture	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Osteitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Osteoporosis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Plantar fascial fibromatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Soft tissue swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Spondylitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Temporomandibular joint syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vertebral osteophyte	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**73**	**(14.3)**	**74**	**(14.7)**	**147**	**(14.5)**
Grade 1	27	(5.3)	29	(5.8)	56	(5.5)
Grade 2	31	(6.1)	32	(6.4)	63	(6.2)
Grade 3	14	(2.8)	12	(2.4)	26	(2.6)
Grade 4	1	(0.2)	1	(0.2)	2	(0.2)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	10	(2.0)	18	(3.6)	28	(2.8)
Grade 3	5	(1.0)	3	(0.6)	8	(0.8)
Melanocytic naevus	16	(3.1)	11	(2.2)	27	(2.7)
Grade 1	11	(2.2)	8	(1.6)	19	(1.9)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Seborrhoeic keratosis	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	7	(1.4)	2	(0.4)	9	(0.9)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Dysplastic naevus	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Squamous cell carcinoma	6	(1.2)	3	(0.6)	9	(0.9)
Grade 2	5	(1.0)	3	(0.6)	8	(0.8)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lipoma	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Bowen's disease	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Malignant melanoma	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Colon adenoma	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Skin papilloma	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Acanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Benign neoplasm of skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Fibroma	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Fibroma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Haemangioma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Keratoacanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Malignant melanoma in situ	1	(0.2)	6	(1.2)	7	(0.7)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Grade 4	1	(0.2)	1	(0.2)	2	(0.2)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Squamous cell carcinoma of skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Adenoma benign	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Angiolipoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Benign breast neoplasm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Fibroadenoma of breast	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Fibrous histiocytoma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Haemangioma of liver	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Haemangioma of skin	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hair follicle tumour benign	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Histiocytic necrotising lymphadenitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Renal oncocytoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Superficial spreading melanoma stage unspecified	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sweat gland tumour	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Uterine leiomyoma	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Nervous system disorders	**175**	**(34.4)**	**162**	**(32.3)**	**337**	**(33.3)**
Grade 1	132	(25.9)	125	(24.9)	257	(25.4)
Grade 2	37	(7.3)	28	(5.6)	65	(6.4)
Grade 3	6	(1.2)	9	(1.8)	15	(1.5)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Headache	95	(18.7)	93	(18.5)	188	(18.6)
Grade 1	75	(14.7)	78	(15.5)	153	(15.1)
Grade 2	20	(3.9)	14	(2.8)	34	(3.4)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness	26	(5.1)	30	(6.0)	56	(5.5)
Grade 1	25	(4.9)	26	(5.2)	51	(5.0)
Grade 2	1	(0.2)	4	(0.8)	5	(0.5)
Paraesthesia	13	(2.6)	13	(2.6)	26	(2.6)
Grade 1	13	(2.6)	13	(2.6)	26	(2.6)
Dysgeusia	10	(2.0)	10	(2.0)	20	(2.0)
Grade 1	8	(1.6)	10	(2.0)	18	(1.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Lethargy	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	5	(1.0)	6	(1.2)	11	(1.1)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Memory impairment	6	(1.2)	6	(1.2)	12	(1.2)
Grade 1	5	(1.0)	6	(1.2)	11	(1.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Sciatica	5	(1.0)	6	(1.2)	11	(1.1)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Taste disorder	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Amnesia	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Carpal tunnel syndrome	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Disturbance in attention	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Neuralgia	3	(0.6)	4	(0.8)	7	(0.7)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Presyncope	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hyperaesthesia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Migraine	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Tremor	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Allodynia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Anosmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphasia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Ataxia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Carotid arteriosclerosis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cervical radiculopathy	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dizziness postural	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Dysaesthesia	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Muscle contractions involuntary	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Petit mal epilepsy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Grade 3	1	(0.2)	4	(0.8)	5	(0.5)
Trigeminal nerve disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vasogenic cerebral oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Acute motor-sensory axonal neuropathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cognitive disorder	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Complex regional pain syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Dysarthria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypoaesthesia	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Nerve compression	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neuropathy peripheral	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Radiculopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sensory disturbance	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tension headache	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Vertebrobasilar insufficiency	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Psychiatric disorders	**43**	**(8.4)**	**61**	**(12.2)**	**104**	**(10.3)**
Grade 1	26	(5.1)	42	(8.4)	68	(6.7)
Grade 2	17	(3.3)	17	(3.4)	34	(3.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Insomnia	17	(3.3)	19	(3.8)	36	(3.6)
Grade 1	10	(2.0)	12	(2.4)	22	(2.2)
Grade 2	7	(1.4)	7	(1.4)	14	(1.4)
Depression	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Anxiety	10	(2.0)	23	(4.6)	33	(3.3)
Grade 1	7	(1.4)	13	(2.6)	20	(2.0)
Grade 2	3	(0.6)	9	(1.8)	12	(1.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Anxiety	10	(2.0)	23	(4.6)	33	(3.3)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Agitation	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Confusional state	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Libido decreased	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	1	(0.2)	3	(0.6)	4	(0.4)
Suicidal ideation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Thermophobia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Depressed mood	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Mood swings	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nightmare	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Tension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**27**	**(5.3)**	**19**	**(3.8)**	**46**	**(4.5)**

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**27**	**(5.3)**	**19**	**(3.8)**	**46**	**(4.5)**
Grade 1	17	(3.3)	12	(2.4)	29	(2.9)
Grade 2	6	(1.2)	5	(1.0)	11	(1.1)
Grade 3	4	(0.8)	2	(0.4)	6	(0.6)
Haematuria	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	7	(1.4)	4	(0.8)	11	(1.1)
Pollakiuria	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dysuria	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Renal failure	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Acute kidney injury	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Leukocyturia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Nephrolithiasis	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Proteinuria	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Renal colic	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Bilirubinuria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bladder cyst	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Bladder cyst	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Cystitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polyuria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Urinary incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Urine abnormality	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bladder dysfunction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Glycosuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypertonic bladder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Renal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Reproductive system and breast disorders	**29**	**(5.7)**	**21**	**(4.2)**	**50**	**(4.9)**
Grade 1	22	(4.3)	15	(3.0)	37	(3.7)
Grade 2	7	(1.4)	4	(0.8)	11	(1.1)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Erectile dysfunction	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Breast pain	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ovarian cyst	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Balanoposthitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	1	(0.2)	4	(0.8)	5	(0.5)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Breast disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Breast swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dysmenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Endometrial hypertrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Genital haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Genital rash	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gynaecomastia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Nipple pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Orchitis noninfective	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Prostatomegaly	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Scrotal mass	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Uterine fibrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Vaginal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Breast cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Breast oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hypomenorrhoea	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Pelvic pain	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Testicular swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Vulvovaginal dryness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**150**	**(29.5)**	**108**	**(21.5)**	**258**	**(25.5)**
Grade 1	99	(19.4)	87	(17.3)	186	(18.4)
Grade 2	41	(8.1)	19	(3.8)	60	(5.9)
Grade 3	9	(1.8)	2	(0.4)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Cough	71	(13.9)	56	(11.2)	127	(12.6)
Grade 1	63	(12.4)	48	(9.6)	111	(11.0)
Grade 2	8	(1.6)	8	(1.6)	16	(1.6)
Dyspnoea	45	(8.8)	24	(4.8)	69	(6.8)
Grade 1	36	(7.1)	24	(4.8)	60	(5.9)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonitis	18	(3.5)	3	(0.6)	21	(2.1)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	14	(2.8)	2	(0.4)	16	(1.6)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Oropharyngeal pain	16	(3.1)	16	(3.2)	32	(3.2)
Grade 1	14	(2.8)	15	(3.0)	29	(2.9)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Rhinitis allergic	11	(2.2)	5	(1.0)	16	(1.6)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	6	(1.2)	2	(0.4)	8	(0.8)
Productive cough	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Epistaxis	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Rhinorrhoea	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)
Dysphonia	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nasal congestion	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	5	(1.0)	4	(0.8)	9	(0.9)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nasal congestion	5	(1.0)	5	(1.0)	10	(1.0)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Pulmonary embolism	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	4	(0.8)	1	(0.2)	5	(0.5)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea exertional	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Asthma	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Laryngeal inflammation	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Oropharyngeal discomfort	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Bronchospasm	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Wheezing	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	1	(0.2)	4	(0.8)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Allergic cough	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aphonia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Paranasal sinus haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngeal erythema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Pleural effusion	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pleuritic pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Reflux laryngitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sleep apnoea syndrome	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Sneezing	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Throat tightness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dry throat	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Oropharyngeal plaque	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Painful respiration	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pharyngeal cyst	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pharyngeal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Sinus pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tonsillolith	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vocal cord inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Skin and subcutaneous tissue disorders	**276**	**(54.2)**	**198**	**(39.4)**	**474**	**(46.9)**
Grade 1	190	(37.3)	166	(33.1)	356	(35.2)
Grade 2	79	(15.5)	31	(6.2)	110	(10.9)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	103	(20.2)	59	(11.8)	162	(16.0)
Grade 1	85	(16.7)	56	(11.2)	141	(13.9)
Grade 2	18	(3.5)	3	(0.6)	21	(2.1)
Rash	67	(13.2)	44	(8.8)	111	(11.0)
Grade 1	54	(10.6)	40	(8.0)	94	(9.3)
Grade 2	11	(2.2)	4	(0.8)	15	(1.5)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Rash maculo-papular	28	(5.5)	23	(4.6)	51	(5.0)
Grade 1	20	(3.9)	21	(4.2)	41	(4.1)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dry skin	26	(5.1)	12	(2.4)	38	(3.8)
Grade 1	23	(4.5)	10	(2.0)	33	(3.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Vitiligo	25	(4.9)	8	(1.6)	33	(3.3)
Grade 1	24	(4.7)	7	(1.4)	31	(3.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Eczema	22	(4.3)	10	(2.0)	32	(3.2)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	10	(2.0)	1	(0.2)	11	(1.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Erythema	14	(2.8)	6	(1.2)	20	(2.0)
Grade 1	11	(2.2)	5	(1.0)	16	(1.6)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Skin lesion	13	(2.6)	8	(1.6)	21	(2.1)
Grade 1	9	(1.8)	6	(1.2)	15	(1.5)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Alopecia	12	(2.4)	10	(2.0)	22	(2.2)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Dermatitis acneiform	11	(2.2)	10	(2.0)	21	(2.1)
Grade 1	10	(2.0)	10	(2.0)	20	(2.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Actinic keratosis	9	(1.8)	3	(0.6)	12	(1.2)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Seborrhoeic dermatitis	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis	6	(1.2)	5	(1.0)	11	(1.1)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash pruritic	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Dermal cyst	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Hyperkeratosis	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Intertrigo	5	(1.0)	5	(1.0)	10	(1.0)
Grade 1	5	(1.0)	5	(1.0)	10	(1.0)
Lichenoid keratosis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lichenoid keratosis	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Papule	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Rash erythematous	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Scar pain	5	(1.0)	2	(0.4)	7	(0.7)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Photosensitivity reaction	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Psoriasis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Rash papular	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Skin exfoliation	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis contact	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Drug eruption	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Macule	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Night sweats	3	(0.6)	3	(0.6)	6	(0.6)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Night sweats	3	(0.6)	3	(0.6)	6	(0.6)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Pain of skin	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Skin induration	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Skin mass	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Acne	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hair disorder	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Lichen planus	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Onycholysis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Rash macular	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Rash vesicular	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin hypertrophy	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Skin tightness	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Solar dermatitis	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Solar dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Angioedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Blister	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Grade 5	1	(0.2)	0	(0.0)	1	(0.1)
Ecchymosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eczema asteatotic	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erythrosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma skin	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hypertrophic scar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Itching scar	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lichen sclerosus	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Papulopustular rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pigmentation disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin depigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin hyperpigmentation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin irritation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin ulcer	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Solar lentigo	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Transient acantholytic dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Angiokeratoma	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhage subcutaneous	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hyperhidrosis	0	(0.0)	6	(1.2)	6	(0.6)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hyperhidrosis	0	(0.0)	6	(1.2)	6	(0.6)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Ingrowing nail	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Keloid scar	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Keratosis pilaris	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neutrophilic dermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Onychomadesis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Photodermatosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pruritus allergic	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Skin discolouration	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Skin erosion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vascular disorders	**125**	**(24.6)**	**130**	**(25.9)**	**255**	**(25.2)**
Grade 1	47	(9.2)	55	(11.0)	102	(10.1)
Grade 2	47	(9.2)	56	(11.2)	103	(10.2)
Grade 3	31	(6.1)	19	(3.8)	50	(4.9)
Hypertension	76	(14.9)	78	(15.5)	154	(15.2)
Grade 1	9	(1.8)	15	(3.0)	24	(2.4)
Grade 2	39	(7.7)	45	(9.0)	84	(8.3)
Grade 3	28	(5.5)	18	(3.6)	46	(4.5)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Grade 1	21	(4.1)	29	(5.8)	50	(4.9)
Grade 2	4	(0.8)	7	(1.4)	11	(1.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lymphoedema	26	(5.1)	36	(7.2)	62	(6.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hot flush	6	(1.2)	8	(1.6)	14	(1.4)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Hypotension	5	(1.0)	4	(0.8)	9	(0.9)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Flushing	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Haematoma	4	(0.8)	7	(1.4)	11	(1.1)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Deep vein thrombosis	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Prehypertension	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Thrombophlebitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Thrombophlebitis superficial	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	2	(0.4)	3	(0.6)	5	(0.5)
Diastolic hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocele	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Peripheral venous disease	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Poor venous access	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Venous thrombosis limb	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aortic arteriosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Orthostatic hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Varicose vein	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.1.3 Related to Study Intervention

Table 14.3-11

Subjects With Drug-related Adverse Events by Decreasing Incidence
(Incidence ≥ 5% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)

Every subject 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.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-12

Subjects With Drug-related Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)
Decreased appetite	25	(4.9)	8	(1.6)	33	(3.3)
Rash maculo-papular	24	(4.7)	20	(4.0)	44	(4.4)
Vitiligo	24	(4.7)	7	(1.4)	31	(3.1)
Dry mouth	23	(4.5)	10	(2.0)	33	(3.3)
Abdominal pain	20	(3.9)	14	(2.8)	34	(3.4)
Aspartate aminotransferase increased	20	(3.9)	14	(2.8)	34	(3.4)
Dry skin	20	(3.9)	8	(1.6)	28	(2.8)
Cough	18	(3.5)	16	(3.2)	34	(3.4)
Pneumonitis	17	(3.3)	3	(0.6)	20	(2.0)
Vomiting	16	(3.1)	9	(1.8)	25	(2.5)
Weight increased	16	(3.1)	4	(0.8)	20	(2.0)
Influenza like illness	15	(2.9)	9	(1.8)	24	(2.4)
Colitis	13	(2.6)	1	(0.2)	14	(1.4)
Eczema	13	(2.6)	3	(0.6)	16	(1.6)
Weight decreased	13	(2.6)	11	(2.2)	24	(2.4)
Constipation	12	(2.4)	8	(1.6)	20	(2.0)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Dizziness	10	(2.0)	13	(2.6)	23	(2.3)
Abdominal pain upper	9	(1.8)	10	(2.0)	19	(1.9)
Alopecia	9	(1.8)	8	(1.6)	17	(1.7)
Gamma-glutamyltransferase increased	9	(1.8)	4	(0.8)	13	(1.3)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood bilirubin increased	8	(1.6)	3	(0.6)	11	(1.1)
Dyspepsia	8	(1.6)	2	(0.4)	10	(1.0)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Blood creatine phosphokinase increased	7	(1.4)	2	(0.4)	9	(0.9)
Blood thyroid stimulating hormone decreased	7	(1.4)	1	(0.2)	8	(0.8)
Dermatitis acneiform	7	(1.4)	6	(1.2)	13	(1.3)
Dry eye	7	(1.4)	4	(0.8)	11	(1.1)
Dysgeusia	7	(1.4)	8	(1.6)	15	(1.5)
Erythema	7	(1.4)	3	(0.6)	10	(1.0)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Lipase increased	7	(1.4)	3	(0.6)	10	(1.0)
Pain in extremity	7	(1.4)	3	(0.6)	10	(1.0)
Arthritis	6	(1.2)	0	(0.0)	6	(0.6)
Blood alkaline phosphatase increased	6	(1.2)	2	(0.4)	8	(0.8)
Blood creatinine increased	6	(1.2)	2	(0.4)	8	(0.8)
Chills	6	(1.2)	4	(0.8)	10	(1.0)
Eosinophil count increased	6	(1.2)	0	(0.0)	6	(0.6)
Lymphocyte count decreased	6	(1.2)	2	(0.4)	8	(0.8)
Lymphopenia	6	(1.2)	1	(0.2)	7	(0.7)
Sarcoidosis	6	(1.2)	0	(0.0)	6	(0.6)
Eosinophilia	5	(1.0)	1	(0.2)	6	(0.6)
Hyperglycaemia	5	(1.0)	3	(0.6)	8	(0.8)
Hypophosphataemia	5	(1.0)	1	(0.2)	6	(0.6)
Muscle spasms	5	(1.0)	1	(0.2)	6	(0.6)
Musculoskeletal pain	5	(1.0)	3	(0.6)	8	(0.8)
Oedema peripheral	5	(1.0)	3	(0.6)	8	(0.8)
Pyrexia	5	(1.0)	6	(1.2)	11	(1.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Adrenal insufficiency	4	(0.8)	1	(0.2)	5	(0.5)
Amylase increased	4	(0.8)	0	(0.0)	4	(0.4)
Back pain	4	(0.8)	6	(1.2)	10	(1.0)
Blood thyroid stimulating hormone increased	4	(0.8)	5	(1.0)	9	(0.9)
Conjunctivitis	4	(0.8)	1	(0.2)	5	(0.5)
Faeces soft	4	(0.8)	3	(0.6)	7	(0.7)
Gastritis	4	(0.8)	0	(0.0)	4	(0.4)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypertension	4	(0.8)	5	(1.0)	9	(0.9)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Lethargy	4	(0.8)	6	(1.2)	10	(1.0)
Lichenoid keratosis	4	(0.8)	0	(0.0)	4	(0.4)
Memory impairment	4	(0.8)	3	(0.6)	7	(0.7)
Palpitations	4	(0.8)	1	(0.2)	5	(0.5)
Paraesthesia	4	(0.8)	4	(0.8)	8	(0.8)
Peripheral sensory neuropathy	4	(0.8)	1	(0.2)	5	(0.5)
Psoriasis	4	(0.8)	0	(0.0)	4	(0.4)
Rash erythematous	4	(0.8)	2	(0.4)	6	(0.6)
Rash pruritic	4	(0.8)	1	(0.2)	5	(0.5)
Rash pustular	4	(0.8)	1	(0.2)	5	(0.5)
Sinusitis	4	(0.8)	0	(0.0)	4	(0.4)
Stomatitis	4	(0.8)	1	(0.2)	5	(0.5)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Autoimmune thyroiditis	3	(0.6)	0	(0.0)	3	(0.3)
C-reactive protein increased	3	(0.6)	0	(0.0)	3	(0.3)
Dyspnoea exertional	3	(0.6)	1	(0.2)	4	(0.4)
Ear pain	3	(0.6)	0	(0.0)	3	(0.3)
Erectile dysfunction	3	(0.6)	0	(0.0)	3	(0.3)
Hypopituitarism	3	(0.6)	0	(0.0)	3	(0.3)
Insomnia	3	(0.6)	7	(1.4)	10	(1.0)
Non-cardiac chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Oral lichen planus	3	(0.6)	0	(0.0)	3	(0.3)
Photosensitivity reaction	3	(0.6)	2	(0.4)	5	(0.5)
Productive cough	3	(0.6)	0	(0.0)	3	(0.3)
Rash papular	3	(0.6)	1	(0.2)	4	(0.4)
Rhinitis	3	(0.6)	0	(0.0)	3	(0.3)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Amnesia	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Bronchitis	2	(0.4)	1	(0.2)	3	(0.3)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Dermatitis	2	(0.4)	4	(0.8)	6	(0.6)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Dysphonia	2	(0.4)	1	(0.2)	3	(0.3)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Flushing	2	(0.4)	1	(0.2)	3	(0.3)
Folliculitis	2	(0.4)	1	(0.2)	3	(0.3)
Hot flush	2	(0.4)	4	(0.8)	6	(0.6)
Hyperbilirubinaemia	2	(0.4)	0	(0.0)	2	(0.2)
Hyponatraemia	2	(0.4)	3	(0.6)	5	(0.5)
Influenza	2	(0.4)	0	(0.0)	2	(0.2)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Lymphoedema	2	(0.4)	0	(0.0)	2	(0.2)
Melanocytic naevus	2	(0.4)	0	(0.0)	2	(0.2)
Mouth ulceration	2	(0.4)	4	(0.8)	6	(0.6)
Muscular weakness	2	(0.4)	2	(0.4)	4	(0.4)
Neck pain	2	(0.4)	0	(0.0)	2	(0.2)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Neutrophil count decreased	2	(0.4)	7	(1.4)	9	(0.9)
Odynophagia	2	(0.4)	0	(0.0)	2	(0.2)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Pain	2	(0.4)	1	(0.2)	3	(0.3)
Pain of skin	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Papule	2	(0.4)	0	(0.0)	2	(0.2)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	0	(0.0)	2	(0.2)
Platelet count decreased	2	(0.4)	3	(0.6)	5	(0.5)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	1	(0.2)	3	(0.3)
Rhinorrhoea	2	(0.4)	0	(0.0)	2	(0.2)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Skin lesion	2	(0.4)	2	(0.4)	4	(0.4)
Taste disorder	2	(0.4)	2	(0.4)	4	(0.4)
Tinnitus	2	(0.4)	2	(0.4)	4	(0.4)
Vision blurred	2	(0.4)	4	(0.8)	6	(0.6)
Visual impairment	2	(0.4)	1	(0.2)	3	(0.3)
Abdominal distension	1	(0.2)	2	(0.4)	3	(0.3)
Acne	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Actinic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Agitation	1	(0.2)	1	(0.2)	2	(0.2)
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Angina pectoris	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	0	(0.0)	1	(0.1)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	1	(0.2)	0	(0.0)	1	(0.1)
Bursitis	1	(0.2)	1	(0.2)	2	(0.2)
Cataract	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	1	(0.2)	1	(0.2)	2	(0.2)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chest pain	1	(0.2)	0	(0.0)	1	(0.1)
Cholestasis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Dehydration	1	(0.2)	0	(0.0)	1	(0.1)
Depression	1	(0.2)	2	(0.4)	3	(0.3)
Dermatitis atopic	1	(0.2)	0	(0.0)	1	(0.1)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Dysplastic naevus	1	(0.2)	0	(0.0)	1	(0.1)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Erysipelas	1	(0.2)	0	(0.0)	1	(0.1)
Eye irritation	1	(0.2)	0	(0.0)	1	(0.1)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Face oedema	1	(0.2)	1	(0.2)	2	(0.2)
Feeling cold	1	(0.2)	0	(0.0)	1	(0.1)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Gout	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	1	(0.2)	0	(0.0)	1	(0.1)
Hair disorder	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperkalaemia	1	(0.2)	3	(0.6)	4	(0.4)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	1	(0.2)	0	(0.0)	1	(0.1)
Libido decreased	1	(0.2)	0	(0.0)	1	(0.1)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	0	(0.0)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Macule	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	1	(0.2)	2	(0.4)	3	(0.3)
Mastitis	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal chest pain	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal stiffness	1	(0.2)	1	(0.2)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Night sweats	1	(0.2)	0	(0.0)	1	(0.1)
Ocular hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Onycholysis	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Oral disorder	1	(0.2)	0	(0.0)	1	(0.1)
Oral herpes	1	(0.2)	0	(0.0)	1	(0.1)
Oral pain	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital swelling	1	(0.2)	0	(0.0)	1	(0.1)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	1	(0.2)	1	(0.2)	2	(0.2)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Protein total increased	1	(0.2)	0	(0.0)	1	(0.1)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Rash macular	1	(0.2)	1	(0.2)	2	(0.2)
Rash vesicular	1	(0.2)	0	(0.0)	1	(0.1)
Raynaud's phenomenon	1	(0.2)	1	(0.2)	2	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Skin exfoliation	1	(0.2)	0	(0.0)	1	(0.1)
Skin induration	1	(0.2)	0	(0.0)	1	(0.1)
Skin ulcer	1	(0.2)	1	(0.2)	2	(0.2)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Synovitis	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thrombophlebitis superficial	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Tremor	1	(0.2)	2	(0.4)	3	(0.3)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	0	(0.0)	1	(0.1)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	1	(0.2)	0	(0.0)	1	(0.1)
Vertigo	1	(0.2)	1	(0.2)	2	(0.2)
Vestibular disorder	1	(0.2)	0	(0.0)	1	(0.1)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Vitreous floaters	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
White blood cell count increased	1	(0.2)	0	(0.0)	1	(0.1)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Blood bicarbonate increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood glucose increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea increased	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)
Confusional state	0	(0.0)	1	(0.2)	1	(0.1)
Cortisol decreased	0	(0.0)	2	(0.4)	2	(0.2)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Depressed mood	0	(0.0)	1	(0.2)	1	(0.1)
Dermatitis contact	0	(0.0)	1	(0.2)	1	(0.1)
Disturbance in attention	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness postural	0	(0.0)	1	(0.2)	1	(0.1)
Dysaesthesia	0	(0.0)	1	(0.2)	1	(0.1)
Dysphagia	0	(0.0)	1	(0.2)	1	(0.1)
Eye pain	0	(0.0)	1	(0.2)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Flatulence	0	(0.0)	3	(0.6)	3	(0.3)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Gastroenteritis	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	0	(0.0)	1	(0.2)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Haemoglobin increased	0	(0.0)	1	(0.2)	1	(0.1)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Hyperhidrosis	0	(0.0)	2	(0.4)	2	(0.2)
Hypocalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypoglycaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Joint effusion	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	2	(0.4)	2	(0.2)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Leukopenia	0	(0.0)	1	(0.2)	1	(0.1)
Lip infection	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy	0	(0.0)	1	(0.2)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Menstruation irregular	0	(0.0)	1	(0.2)	1	(0.1)
Migraine	0	(0.0)	2	(0.4)	2	(0.2)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Neuropathy peripheral	0	(0.0)	2	(0.4)	2	(0.2)
Osteoarthritis	0	(0.0)	1	(0.2)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Pelvic pain	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	0	(0.0)	1	(0.2)	1	(0.1)
Peripheral swelling	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Pollakiuria	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	2	(0.4)	2	(0.2)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Skin abrasion	0	(0.0)	1	(0.2)	1	(0.1)
Sleep disorder	0	(0.0)	1	(0.2)	1	(0.1)
Visual acuity reduced	0	(0.0)	1	(0.2)	1	(0.1)
Wheezing	0	(0.0)	1	(0.2)	1	(0.1)
White blood cell count decreased	0	(0.0)	5	(1.0)	5	(0.5)

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

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-13

Subjects With Drug-Related Adverse Events by Decreasing Incidence
(Incidence > 0%)
(ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	117	(68.8)
with no adverse events	53	(31.2)
Fatigue	31	(18.2)
Diarrhoea	25	(14.7)
Pruritus	25	(14.7)
Hypothyroidism	23	(13.5)
Hyperthyroidism	17	(10.0)
Arthralgia	14	(8.2)
Rash	11	(6.5)
Nausea	10	(5.9)
Rash maculo-papular	9	(5.3)
Alanine aminotransferase increased	8	(4.7)
Aspartate aminotransferase increased	8	(4.7)
Headache	6	(3.5)
Myalgia	6	(3.5)
Decreased appetite	5	(2.9)
Dry mouth	5	(2.9)
Eczema	4	(2.4)
Vitiligo	4	(2.4)
Arthritis	3	(1.8)
Asthenia	3	(1.8)
Blood alkaline phosphatase increased	3	(1.8)
Blood creatinine increased	3	(1.8)
Colitis	3	(1.8)
Cough	3	(1.8)
Dry skin	3	(1.8)
Gamma-glutamyltransferase increased	3	(1.8)
Hot flush	3	(1.8)
Influenza like illness	3	(1.8)
Leukopenia	3	(1.8)
Rash pustular	3	(1.8)
Skin hypopigmentation	3	(1.8)
Type 1 diabetes mellitus	3	(1.8)
Abdominal pain upper	2	(1.2)
Blood thyroid stimulating hormone increased	2	(1.2)
Bronchitis	2	(1.2)

Subjects With Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0%) (ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Dizziness	2	(1.2)
Dysgeusia	2	(1.2)
Dyspnoea	2	(1.2)
Eosinophilia	2	(1.2)
Folliculitis	2	(1.2)
Gastritis	2	(1.2)
Hyperglycaemia	2	(1.2)
Hypopituitarism	2	(1.2)
Oedema peripheral	2	(1.2)
Pancreatitis	2	(1.2)
Peripheral sensory neuropathy	2	(1.2)
Pneumonitis	2	(1.2)
Rhinitis	2	(1.2)
Weight increased	2	(1.2)
White blood cell count decreased	2	(1.2)
Abdominal distension	1	(0.6)
Abdominal pain	1	(0.6)
Actinic keratosis	1	(0.6)
Adrenal insufficiency	1	(0.6)
Amylase increased	1	(0.6)
Anaemia	1	(0.6)
Angina pectoris	1	(0.6)
Aphthous ulcer	1	(0.6)
Arrhythmia	1	(0.6)
Blood bicarbonate increased	1	(0.6)
Blood bilirubin increased	1	(0.6)
Blood creatine phosphokinase increased	1	(0.6)
Blood lactate dehydrogenase increased	1	(0.6)
Blood thyroid stimulating hormone decreased	1	(0.6)
Bone pain	1	(0.6)
Constipation	1	(0.6)
Depressed mood	1	(0.6)
Dermatitis	1	(0.6)
Dermatitis acneiform	1	(0.6)
Dry eye	1	(0.6)
Duodenitis	1	(0.6)
Dysphagia	1	(0.6)
Dysuria	1	(0.6)

Subjects With Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0%) (ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Enanthema	1	(0.6)
Epistaxis	1	(0.6)
Erythema	1	(0.6)
Erythema multiforme	1	(0.6)
Eye inflammation	1	(0.6)
Eyelid oedema	1	(0.6)
Eyelid rash	1	(0.6)
Flatulence	1	(0.6)
Glucocorticoid deficiency	1	(0.6)
Granuloma annulare	1	(0.6)
Helicobacter infection	1	(0.6)
Hepatic pain	1	(0.6)
Herpes zoster	1	(0.6)
Hyperkeratosis	1	(0.6)
Hypersensitivity	1	(0.6)
Hypertension	1	(0.6)
Hypoalbuminaemia	1	(0.6)
Hyponatraemia	1	(0.6)
Immune-mediated adverse reaction	1	(0.6)
Immune-mediated arthritis	1	(0.6)
Immune-mediated hepatitis	1	(0.6)
Influenza	1	(0.6)
Infusion related reaction	1	(0.6)
Interstitial lung disease	1	(0.6)
Joint swelling	1	(0.6)
Lacrimation increased	1	(0.6)
Lichen planopilaris	1	(0.6)
Lichenoid keratosis	1	(0.6)
Lipase increased	1	(0.6)
Liver disorder	1	(0.6)
Lung opacity	1	(0.6)
Lymphocyte count decreased	1	(0.6)
Lymphopenia	1	(0.6)
Mouth ulceration	1	(0.6)
Muscle spasms	1	(0.6)
Musculoskeletal chest pain	1	(0.6)
Musculoskeletal pain	1	(0.6)
Myositis	1	(0.6)

Subjects With Drug-Related Adverse Events by Decreasing Incidence (Incidence > 0%) (ASaT Population-Part 2)

	Pembrolizumab	
	n	(%)
Nasopharyngitis	1	(0.6)
Neutrophil count decreased	1	(0.6)
Pain of skin	1	(0.6)
Pericardial effusion	1	(0.6)
Peripheral swelling	1	(0.6)
Personality change	1	(0.6)
Photosensitivity reaction	1	(0.6)
Platelet count decreased	1	(0.6)
Pyrexia	1	(0.6)
Rash erythematous	1	(0.6)
Rash pruritic	1	(0.6)
Restlessness	1	(0.6)
Rhinitis allergic	1	(0.6)
Rhinorrhoea	1	(0.6)
Sinusitis	1	(0.6)
Sjogren's syndrome	1	(0.6)
Stomatitis	1	(0.6)
Strangury	1	(0.6)
Thrombocytopenia	1	(0.6)
Transaminases increased	1	(0.6)
Urticaria	1	(0.6)
Vaginal infection	1	(0.6)
Vertigo	1	(0.6)
Vomiting	1	(0.6)
Weight decreased	1	(0.6)

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

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

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

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 2.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-14

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Blood and lymphatic system disorders	**18**	**(3.5)**	**8**	**(1.6)**	**26**	**(2.6)**
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophilia	5	(1.0)	1	(0.2)	6	(0.6)
Leukopenia	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	6	(1.2)	1	(0.2)	7	(0.7)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Cardiac disorders	**6**	**(1.2)**	**1**	**(0.2)**	7	**(0.7)**
Angina pectoris	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Palpitations	4	(0.8)	1	(0.2)	5	(0.5)
Congenital, familial and genetic disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**6**	**(1.2)**	**3**	**(0.6)**	**9**	**(0.9)**
Ear pain	3	(0.6)	0	(0.0)	3	(0.3)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Tinnitus	2	(0.4)	2	(0.4)	4	(0.4)
Vertigo	1	(0.2)	1	(0.2)	2	(0.2)
Vestibular disorder	1	(0.2)	0	(0.0)	1	(0.1)
Endocrine disorders	**116**	**(22.8)**	**19**	**(3.8)**	**135**	**(13.4)**
Adrenal insufficiency	4	(0.8)	1	(0.2)	5	(0.5)
Autoimmune thyroiditis	3	(0.6)	0	(0.0)	3	(0.3)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Endocrine disorders	**116**	**(22.8)**	**19**	**(3.8)**	**135**	**(13.4)**
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Hypopituitarism	3	(0.6)	0	(0.0)	3	(0.3)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**26**	**(5.1)**	**13**	**(2.6)**	**39**	**(3.9)**
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Cataract	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Dry eye	7	(1.4)	4	(0.8)	11	(1.1)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Eye irritation	1	(0.2)	0	(0.0)	1	(0.1)
Eye pain	0	(0.0)	1	(0.2)	1	(0.1)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	1	(0.2)	0	(0.0)	1	(0.1)
Ocular hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital swelling	1	(0.2)	0	(0.0)	1	(0.1)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	0	(0.0)	2	(0.2)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	2	(0.4)	4	(0.8)	6	(0.6)
Visual acuity reduced	0	(0.0)	1	(0.2)	1	(0.1)
Visual impairment	2	(0.4)	1	(0.2)	3	(0.3)
Vitreous floaters	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Abdominal distension	1	(0.2)	2	(0.4)	3	(0.3)
Abdominal pain	20	(3.9)	14	(2.8)	34	(3.4)
Abdominal pain upper	9	(1.8)	10	(2.0)	19	(1.9)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	13	(2.6)	1	(0.2)	14	(1.4)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Constipation	12	(2.4)	8	(1.6)	20	(2.0)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Dry mouth	23	(4.5)	10	(2.0)	33	(3.3)
Dyspepsia	8	(1.6)	2	(0.4)	10	(1.0)
Dysphagia	0	(0.0)	1	(0.2)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Faeces soft	4	(0.8)	3	(0.6)	7	(0.7)
Flatulence	0	(0.0)	3	(0.6)	3	(0.3)
Gastritis	4	(0.8)	0	(0.0)	4	(0.4)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Haemorrhoids	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	2	(0.4)	4	(0.8)	6	(0.6)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Odynophagia	2	(0.4)	0	(0.0)	2	(0.2)
Oral discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Oral disorder	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	3	(0.6)	0	(0.0)	3	(0.3)
Oral pain	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Stomatitis	4	(0.8)	1	(0.2)	5	(0.5)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	16	(3.1)	9	(1.8)	25	(2.5)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Chest pain	1	(0.2)	0	(0.0)	1	(0.1)
Chills	6	(1.2)	4	(0.8)	10	(1.0)
Face oedema	1	(0.2)	1	(0.2)	2	(0.2)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Feeling cold	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Influenza like illness	15	(2.9)	9	(1.8)	24	(2.4)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	1	(0.2)	2	(0.4)	3	(0.3)
Non-cardiac chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Oedema peripheral	5	(1.0)	3	(0.6)	8	(0.8)
Pain	2	(0.4)	1	(0.2)	3	(0.3)
Peripheral swelling	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
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	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**
Pyrexia	5	(1.0)	6	(1.2)	11	(1.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**10**	**(2.0)**	**3**	**(0.6)**	**13**	**(1.3)**
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Cholestasis	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Hyperbilirubinaemia	2	(0.4)	0	(0.0)	2	(0.2)
Immune system disorders	**6**	**(1.2)**	**2**	**(0.4)**	**8**	**(0.8)**
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Sarcoidosis	6	(1.2)	0	(0.0)	6	(0.6)
Infections and infestations	**28**	**(5.5)**	**13**	**(2.6)**	**41**	**(4.1)**
Bronchitis	2	(0.4)	1	(0.2)	3	(0.3)
Cellulitis	1	(0.2)	1	(0.2)	2	(0.2)
Conjunctivitis	4	(0.8)	1	(0.2)	5	(0.5)
Diverticulitis	1	(0.2)	0	(0.0)	1	(0.1)
Erysipelas	1	(0.2)	0	(0.0)	1	(0.1)
Folliculitis	2	(0.4)	1	(0.2)	3	(0.3)
Gastroenteritis	0	(0.0)	1	(0.2)	1	(0.1)
Influenza	2	(0.4)	0	(0.0)	2	(0.2)
Lip infection	0	(0.0)	1	(0.2)	1	(0.1)
Mastitis	1	(0.2)	0	(0.0)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Oral herpes	1	(0.2)	0	(0.0)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonia	1	(0.2)	1	(0.2)	2	(0.2)
Rash pustular	4	(0.8)	1	(0.2)	5	(0.5)
Respiratory tract infection viral	0	(0.0)	2	(0.4)	2	(0.2)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
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(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**28**	**(5.5)**	**13**	**(2.6)**	**41**	**(4.1)**
Rhinitis	3	(0.6)	0	(0.0)	3	(0.3)
Sinusitis	4	(0.8)	0	(0.0)	4	(0.4)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	1	(0.2)	0	(0.0)	1	(0.1)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**5**	**(1.0)**	7	**(0.7)**
Arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Skin abrasion	0	(0.0)	1	(0.2)	1	(0.1)
Investigations	**98**	**(19.3)**	**61**	**(12.2)**	**159**	**(15.7)**
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Amylase increased	4	(0.8)	0	(0.0)	4	(0.4)
Aspartate aminotransferase increased	20	(3.9)	14	(2.8)	34	(3.4)
Blood alkaline phosphatase increased	6	(1.2)	2	(0.4)	8	(0.8)
Blood bicarbonate increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	8	(1.6)	3	(0.6)	11	(1.1)
Blood creatine phosphokinase increased	7	(1.4)	2	(0.4)	9	(0.9)
Blood creatinine increased	6	(1.2)	2	(0.4)	8	(0.8)
Blood glucose increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone decreased	7	(1.4)	1	(0.2)	8	(0.8)
Blood thyroid stimulating hormone increased	4	(0.8)	5	(1.0)	9	(0.9)
Blood urea increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
C-reactive protein increased	3	(0.6)	0	(0.0)	3	(0.3)
Cortisol decreased	0	(0.0)	2	(0.4)	2	(0.2)
Eosinophil count increased	6	(1.2)	0	(0.0)	6	(0.6)
Gamma-glutamyltransferase increased	9	(1.8)	4	(0.8)	13	(1.3)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	0	(0.0)	1	(0.2)	1	(0.1)
Haemoglobin increased	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
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(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**98**	**(19.3)**	**61**	**(12.2)**	**159**	**(15.7)**
Lipase increased	7	(1.4)	3	(0.6)	10	(1.0)
Lymphocyte count decreased	6	(1.2)	2	(0.4)	8	(0.8)
Neutrophil count decreased	2	(0.4)	7	(1.4)	9	(0.9)
Platelet count decreased	2	(0.4)	3	(0.6)	5	(0.5)
Protein total increased	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Weight decreased	13	(2.6)	11	(2.2)	24	(2.4)
Weight increased	16	(3.1)	4	(0.8)	20	(2.0)
White blood cell count decreased	0	(0.0)	5	(1.0)	5	(0.5)
White blood cell count increased	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**47**	**(9.2)**	**18**	**(3.6)**	**65**	**(6.4)**
Decreased appetite	25	(4.9)	8	(1.6)	33	(3.3)
Dehydration	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Gout	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	5	(1.0)	3	(0.6)	8	(0.8)
Hyperkalaemia	1	(0.2)	3	(0.6)	4	(0.4)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypocalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypoglycaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	2	(0.4)	3	(0.6)	5	(0.5)
Hypophosphataemia	5	(1.0)	1	(0.2)	6	(0.6)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Arthritis	6	(1.2)	0	(0.0)	6	(0.6)
Back pain	4	(0.8)	6	(1.2)	10	(1.0)
Bursitis	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**
Joint effusion	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	2	(0.4)	2	(0.2)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Muscle spasms	5	(1.0)	1	(0.2)	6	(0.6)
Muscular weakness	2	(0.4)	2	(0.4)	4	(0.4)
Musculoskeletal chest pain	1	(0.2)	2	(0.4)	3	(0.3)
Musculoskeletal discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal pain	5	(1.0)	3	(0.6)	8	(0.8)
Musculoskeletal stiffness	1	(0.2)	1	(0.2)	2	(0.2)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Neck pain	2	(0.4)	0	(0.0)	2	(0.2)
Osteoarthritis	0	(0.0)	1	(0.2)	1	(0.1)
Pain in extremity	7	(1.4)	3	(0.6)	10	(1.0)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Synovitis	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.4)**
Dysplastic naevus	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	2	(0.4)	0	(0.0)	2	(0.2)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**75**	**(14.7)**	**67**	**(13.3)**	**142**	**(14.0)**
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	2	(0.4)	0	(0.0)	2	(0.2)
Balance disorder	1	(0.2)	0	(0.0)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**75**	**(14.7)**	**67**	**(13.3)**	**142**	**(14.0)**
Disturbance in attention	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness	10	(2.0)	13	(2.6)	23	(2.3)
Dizziness postural	0	(0.0)	1	(0.2)	1	(0.1)
Dysaesthesia	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	7	(1.4)	8	(1.6)	15	(1.5)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Lethargy	4	(0.8)	6	(1.2)	10	(1.0)
Memory impairment	4	(0.8)	3	(0.6)	7	(0.7)
Migraine	0	(0.0)	2	(0.4)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Neuropathy peripheral	0	(0.0)	2	(0.4)	2	(0.2)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	4	(0.8)	4	(0.8)	8	(0.8)
Peripheral sensory neuropathy	4	(0.8)	1	(0.2)	5	(0.5)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Taste disorder	2	(0.4)	2	(0.4)	4	(0.4)
Tremor	1	(0.2)	2	(0.4)	3	(0.3)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**11**	**(2.2)**	**12**	**(2.4)**	**23**	**(2.3)**
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Agitation	1	(0.2)	1	(0.2)	2	(0.2)
Confusional state	0	(0.0)	1	(0.2)	1	(0.1)
Depressed mood	0	(0.0)	1	(0.2)	1	(0.1)
Depression	1	(0.2)	2	(0.4)	3	(0.3)
Insomnia	3	(0.6)	7	(1.4)	10	(1.0)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Libido decreased	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**3**	**(0.6)**	**1**	**(0.2)**	**4**	**(0.4)**
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Pollakiuria	0	(0.0)	1	(0.2)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**8**	**(1.6)**	**4**	**(0.8)**	**12**	**(1.2)**
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Erectile dysfunction	3	(0.6)	0	(0.0)	3	(0.3)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	1	(0.2)	1	(0.1)
Pelvic pain	0	(0.0)	1	(0.2)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**57**	**(11.2)**	**36**	**(7.2)**	**93**	**(9.2)**
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	0	(0.0)	1	(0.1)
Cough	18	(3.5)	16	(3.2)	34	(3.4)
Dysphonia	2	(0.4)	1	(0.2)	3	(0.3)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Dyspnoea exertional	3	(0.6)	1	(0.2)	4	(0.4)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonitis	17	(3.3)	3	(0.6)	20	(2.0)
Productive cough	3	(0.6)	0	(0.0)	3	(0.3)
Pulmonary embolism	2	(0.4)	1	(0.2)	3	(0.3)
Rhinitis allergic	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**57**	**(11.2)**	**36**	**(7.2)**	**93**	**(9.2)**
Rhinorrhoea	2	(0.4)	0	(0.0)	2	(0.2)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Wheezing	0	(0.0)	1	(0.2)	1	(0.1)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Acne	1	(0.2)	0	(0.0)	1	(0.1)
Actinic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Alopecia	9	(1.8)	8	(1.6)	17	(1.7)
Dermatitis	2	(0.4)	4	(0.8)	6	(0.6)
Dermatitis acneiform	7	(1.4)	6	(1.2)	13	(1.3)
Dermatitis atopic	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis contact	0	(0.0)	1	(0.2)	1	(0.1)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Dry skin	20	(3.9)	8	(1.6)	28	(2.8)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Eczema	13	(2.6)	3	(0.6)	16	(1.6)
Erythema	7	(1.4)	3	(0.6)	10	(1.0)
Hair disorder	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Hyperhidrosis	0	(0.0)	2	(0.4)	2	(0.2)
Lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Lichenoid keratosis	4	(0.8)	0	(0.0)	4	(0.4)
Macule	1	(0.2)	0	(0.0)	1	(0.1)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Night sweats	1	(0.2)	0	(0.0)	1	(0.1)
Onycholysis	1	(0.2)	0	(0.0)	1	(0.1)
Pain of skin	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Papule	2	(0.4)	0	(0.0)	2	(0.2)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Photosensitivity reaction	3	(0.6)	2	(0.4)	5	(0.5)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Psoriasis	4	(0.8)	0	(0.0)	4	(0.4)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Rash erythematous	4	(0.8)	2	(0.4)	6	(0.6)
Rash macular	1	(0.2)	1	(0.2)	2	(0.2)
Rash maculo-papular	24	(4.7)	20	(4.0)	44	(4.4)
Rash papular	3	(0.6)	1	(0.2)	4	(0.4)
Rash pruritic	4	(0.8)	1	(0.2)	5	(0.5)
Rash vesicular	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Skin exfoliation	1	(0.2)	0	(0.0)	1	(0.1)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Skin induration	1	(0.2)	0	(0.0)	1	(0.1)
Skin lesion	2	(0.4)	2	(0.4)	4	(0.4)
Skin ulcer	1	(0.2)	1	(0.2)	2	(0.2)
Stasis dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	0	(0.0)	1	(0.1)
Vitiligo	24	(4.7)	7	(1.4)	31	(3.1)
Vascular disorders	**12**	**(2.4)**	**12**	**(2.4)**	**24**	**(2.4)**
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Flushing	2	(0.4)	1	(0.2)	3	(0.3)
Hot flush	2	(0.4)	4	(0.8)	6	(0.6)
Hypertension	4	(0.8)	5	(1.0)	9	(0.9)
Hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Lymphoedema	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Drug-related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

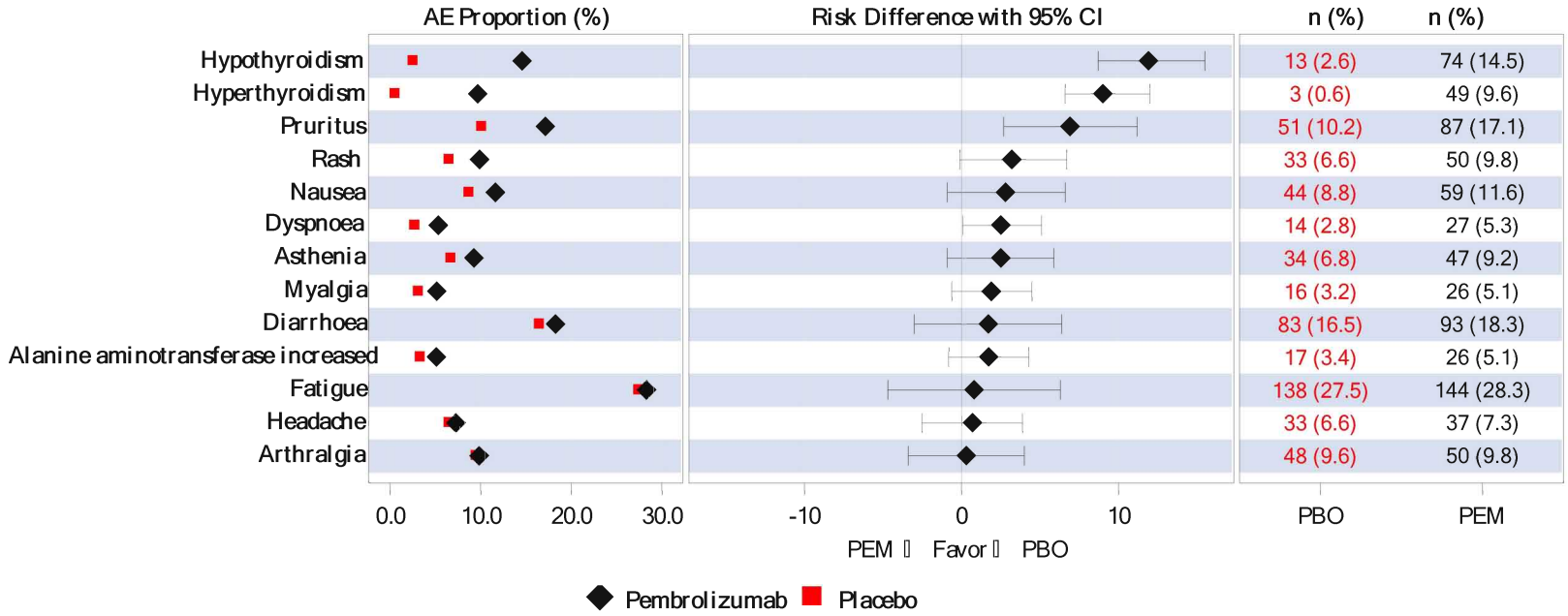
	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**12**	**(2.4)**	**12**	**(2.4)**	**24**	**(2.4)**
Thrombophlebitis superficial	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Figure 14.3-2

Between-Treatment Comparisons in Drug-Related Adverse Events
Selected Adverse Events (≥5% Incidence) and Sorted by Risk Difference
(ASaT Population)
Pembrolizumab (N=509) vs. Placebo (N=502)



PEM: Pembrolizumab
PBO: Placebo
Database Cutoff Date: 03APR2020
Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-15

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence ≥ 10% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
Grade 1	129	(25.3)	220	(43.8)	349	(34.5)
Grade 2	195	(38.3)	96	(19.1)	291	(28.8)
Grade 3	67	(13.2)	17	(3.4)	84	(8.3)
Grade 4	7	(1.4)	0	(0.0)	7	(0.7)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Endocrine disorders	**116**	**(22.8)**	**19**	**(3.8)**	**135**	**(13.4)**
Grade 1	33	(6.5)	11	(2.2)	44	(4.4)
Grade 2	80	(15.7)	8	(1.6)	88	(8.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Grade 1	13	(2.6)	7	(1.4)	20	(2.0)
Grade 2	61	(12.0)	6	(1.2)	67	(6.6)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Grade 1	110	(21.6)	120	(23.9)	230	(22.7)
Grade 2	55	(10.8)	19	(3.8)	74	(7.3)
Grade 3	18	(3.5)	5	(1.0)	23	(2.3)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Grade 1	66	(13.0)	68	(13.5)	134	(13.3)
Grade 2	23	(4.5)	12	(2.4)	35	(3.5)
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Grade 1	50	(9.8)	42	(8.4)	92	(9.1)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**
Grade 1	143	(28.1)	159	(31.7)	302	(29.9)
Grade 2	55	(10.8)	22	(4.4)	77	(7.6)
Grade 3	7	(1.4)	2	(0.4)	9	(0.9)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence ≥ 10% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Grade 1	102	(20.0)	123	(24.5)	225	(22.3)
Grade 2	38	(7.5)	13	(2.6)	51	(5.0)
Grade 3	4	(0.8)	2	(0.4)	6	(0.6)
Investigations	**98**	**(19.3)**	**61**	**(12.2)**	**159**	**(15.7)**
Grade 1	63	(12.4)	36	(7.2)	99	(9.8)
Grade 2	25	(4.9)	20	(4.0)	45	(4.5)
Grade 3	8	(1.6)	5	(1.0)	13	(1.3)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**
Grade 1	59	(11.6)	57	(11.4)	116	(11.5)
Grade 2	23	(4.5)	18	(3.6)	41	(4.1)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**75**	**(14.7)**	**67**	**(13.3)**	**142**	**(14.0)**
Grade 1	57	(11.2)	55	(11.0)	112	(11.1)
Grade 2	17	(3.3)	11	(2.2)	28	(2.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Respiratory, thoracic and mediastinal disorders	**57**	**(11.2)**	**36**	**(7.2)**	**93**	**(9.2)**
Grade 1	30	(5.9)	31	(6.2)	61	(6.0)
Grade 2	22	(4.3)	5	(1.0)	27	(2.7)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Grade 1	150	(29.5)	114	(22.7)	264	(26.1)
Grade 2	51	(10.0)	10	(2.0)	61	(6.0)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence ≥ 10% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Grade 1	71	(13.9)	48	(9.6)	119	(11.8)
Grade 2	16	(3.1)	3	(0.6)	19	(1.9)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-16

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
Grade 1	129	(25.3)	220	(43.8)	349	(34.5)
Grade 2	195	(38.3)	96	(19.1)	291	(28.8)
Grade 3	67	(13.2)	17	(3.4)	84	(8.3)
Grade 4	7	(1.4)	0	(0.0)	7	(0.7)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Blood and lymphatic system disorders	**18**	**(3.5)**	**8**	**(1.6)**	**26**	**(2.6)**
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophilia	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac disorders	**6**	**(1.2)**	**1**	**(0.2)**	7	**(0.7)**

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cardiac disorders	**6**	**(1.2)**	**1**	**(0.2)**	**7**	**(0.7)**
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Angina pectoris	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Palpitations	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Congenital, familial and genetic disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**6**	**(1.2)**	**3**	**(0.6)**	**9**	**(0.9)**
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Ear pain	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tinnitus	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Vertigo	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Vestibular disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Endocrine disorders	**116**	**(22.8)**	**19**	**(3.8)**	**135**	**(13.4)**
Grade 1	33	(6.5)	11	(2.2)	44	(4.4)
Grade 2	80	(15.7)	8	(1.6)	88	(8.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Adrenal insufficiency	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Autoimmune thyroiditis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Grade 1	36	(7.1)	3	(0.6)	39	(3.9)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Grade 1	13	(2.6)	7	(1.4)	20	(2.0)
Grade 2	61	(12.0)	6	(1.2)	67	(6.6)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	8	(1.6)	1	(0.2)	9	(0.9)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eye disorders	**26**	**(5.1)**	**13**	**(2.6)**	**39**	**(3.9)**
Grade 1	23	(4.5)	13	(2.6)	36	(3.6)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cataract	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dry eye	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye irritation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ocular hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Photopsia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Visual acuity reduced	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Visual impairment	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Vitreous floaters	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Grade 1	110	(21.6)	120	(23.9)	230	(22.7)
Grade 2	55	(10.8)	19	(3.8)	74	(7.3)
Grade 3	18	(3.5)	5	(1.0)	23	(2.3)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal distension	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Abdominal pain	20	(3.9)	14	(2.8)	34	(3.4)
Grade 1	17	(3.3)	13	(2.6)	30	(3.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Abdominal pain upper	9	(1.8)	10	(2.0)	19	(1.9)
Grade 1	7	(1.4)	10	(2.0)	17	(1.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	13	(2.6)	1	(0.2)	14	(1.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	1	(0.2)	6	(0.6)
Grade 3	7	(1.4)	0	(0.0)	7	(0.7)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Constipation	12	(2.4)	8	(1.6)	20	(2.0)
Grade 1	8	(1.6)	8	(1.6)	16	(1.6)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Grade 1	66	(13.0)	68	(13.5)	134	(13.3)
Grade 2	23	(4.5)	12	(2.4)	35	(3.5)
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Dry mouth	23	(4.5)	10	(2.0)	33	(3.3)
Grade 1	22	(4.3)	10	(2.0)	32	(3.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	8	(1.6)	2	(0.4)	10	(1.0)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dysphagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Faeces soft	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Flatulence	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Gastritis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhoids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Grade 1	50	(9.8)	42	(8.4)	92	(9.1)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
Odynophagia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Oral discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oral disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Oral pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Stomatitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	16	(3.1)	9	(1.8)	25	(2.5)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**
Grade 1	143	(28.1)	159	(31.7)	302	(29.9)
Grade 2	55	(10.8)	22	(4.4)	77	(7.6)
Grade 3	7	(1.4)	2	(0.4)	9	(0.9)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Grade 1	32	(6.3)	29	(5.8)	61	(6.0)
Grade 2	15	(2.9)	5	(1.0)	20	(2.0)
Chest pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Chills	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Face oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Grade 1	102	(20.0)	123	(24.5)	225	(22.3)
Grade 2	38	(7.5)	13	(2.6)	51	(5.0)
Grade 3	4	(0.8)	2	(0.4)	6	(0.6)
Feeling cold	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Influenza like illness	15	(2.9)	9	(1.8)	24	(2.4)
Grade 1	13	(2.6)	8	(1.6)	21	(2.1)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Non-cardiac chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Oedema peripheral	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Peripheral swelling	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Peripheral swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pyrexia	5	(1.0)	6	(1.2)	11	(1.1)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**10**	**(2.0)**	**3**	**(0.6)**	**13**	**(1.3)**
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Cholestasis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Hyperbilirubinaemia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Immune system disorders	**6**	**(1.2)**	**2**	**(0.4)**	**8**	**(0.8)**
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Sarcoidosis	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**28**	**(5.5)**	**13**	**(2.6)**	**41**	**(4.1)**
Grade 1	14	(2.8)	8	(1.6)	22	(2.2)
Grade 2	13	(2.6)	4	(0.8)	17	(1.7)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Bronchitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Conjunctivitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Diverticulitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Erysipelas	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Folliculitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Gastroenteritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Influenza	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lip infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Mastitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Oral herpes	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonia	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pneumonia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Rash pustular	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Respiratory tract infection viral	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Rhinitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Sinusitis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**5**	**(1.0)**	7	**(0.7)**
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Skin abrasion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Investigations	**98**	**(19.3)**	**61**	**(12.2)**	**159**	**(15.7)**
Grade 1	63	(12.4)	36	(7.2)	99	(9.8)
Grade 2	25	(4.9)	20	(4.0)	45	(4.5)
Grade 3	8	(1.6)	5	(1.0)	13	(1.3)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Grade 1	18	(3.5)	14	(2.8)	32	(3.2)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Amylase increased	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	20	(3.9)	14	(2.8)	34	(3.4)
Grade 1	12	(2.4)	11	(2.2)	23	(2.3)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Blood alkaline phosphatase increased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Blood bicarbonate increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Blood creatine phosphokinase increased	7	(1.4)	2	(0.4)	9	(0.9)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatinine increased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood glucose increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone decreased	7	(1.4)	1	(0.2)	8	(0.8)
Grade 1	7	(1.4)	1	(0.2)	8	(0.8)
Blood thyroid stimulating hormone increased	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Blood urea increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
C-reactive protein increased	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cortisol decreased	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Eosinophil count increased	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Gamma-glutamyltransferase increased	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haemoglobin increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lipase increased	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocyte count decreased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Neutrophil count decreased	2	(0.4)	7	(1.4)	9	(0.9)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Platelet count decreased	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Protein total increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Weight decreased	13	(2.6)	11	(2.2)	24	(2.4)
Grade 1	10	(2.0)	8	(1.6)	18	(1.8)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Weight decreased	13	(2.6)	11	(2.2)	24	(2.4)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Weight increased	16	(3.1)	4	(0.8)	20	(2.0)
Grade 1	14	(2.8)	3	(0.6)	17	(1.7)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
White blood cell count decreased	0	(0.0)	5	(1.0)	5	(0.5)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
White blood cell count increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**47**	**(9.2)**	**18**	**(3.6)**	**65**	**(6.4)**
Grade 1	23	(4.5)	15	(3.0)	38	(3.8)
Grade 2	12	(2.4)	2	(0.4)	14	(1.4)
Grade 3	10	(2.0)	1	(0.2)	11	(1.1)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Decreased appetite	25	(4.9)	8	(1.6)	33	(3.3)
Grade 1	20	(3.9)	8	(1.6)	28	(2.8)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dehydration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gout	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hyperkalaemia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypocalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypoglycaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Hypophosphataemia	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**
Grade 1	59	(11.6)	57	(11.4)	116	(11.5)
Grade 2	23	(4.5)	18	(3.6)	41	(4.1)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Grade 1	32	(6.3)	39	(7.8)	71	(7.0)
Grade 2	15	(2.9)	9	(1.8)	24	(2.4)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Arthritis	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Back pain	4	(0.8)	6	(1.2)	10	(1.0)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Bursitis	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Bursitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Joint effusion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Muscle spasms	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Muscular weakness	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal chest pain	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal pain	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Musculoskeletal stiffness	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)
Grade 1	23	(4.5)	14	(2.8)	37	(3.7)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Osteoarthritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pain in extremity	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Synovitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.4)**
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dysplastic naevus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**75**	**(14.7)**	**67**	**(13.3)**	**142**	**(14.0)**
Grade 1	57	(11.2)	55	(11.0)	112	(11.1)
Grade 2	17	(3.3)	11	(2.2)	28	(2.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Balance disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Disturbance in attention	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness	10	(2.0)	13	(2.6)	23	(2.3)
Grade 1	9	(1.8)	11	(2.2)	20	(2.0)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Dizziness postural	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysaesthesia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	7	(1.4)	8	(1.6)	15	(1.5)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Grade 1	28	(5.5)	26	(5.2)	54	(5.3)
Grade 2	9	(1.8)	6	(1.2)	15	(1.5)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lethargy	4	(0.8)	6	(1.2)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Memory impairment	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Migraine	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neuropathy peripheral	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Peripheral sensory neuropathy	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Taste disorder	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Tremor	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**11**	**(2.2)**	**12**	**(2.4)**	**23**	**(2.3)**
Grade 1	8	(1.6)	9	(1.8)	17	(1.7)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Agitation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Confusional state	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Depressed mood	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Depression	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Insomnia	3	(0.6)	7	(1.4)	10	(1.0)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Insomnia	3	(0.6)	7	(1.4)	10	(1.0)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Libido decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**3**	**(0.6)**	**1**	**(0.2)**	**4**	**(0.4)**
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pollakiuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**8**	**(1.6)**	**4**	**(0.8)**	**12**	**(1.2)**
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erectile dysfunction	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pelvic pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**57**	**(11.2)**	**36**	**(7.2)**	**93**	**(9.2)**
Grade 1	30	(5.9)	31	(6.2)	61	(6.0)
Grade 2	22	(4.3)	5	(1.0)	27	(2.7)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Cough	18	(3.5)	16	(3.2)	34	(3.4)
Grade 1	13	(2.6)	15	(3.0)	28	(2.8)
Grade 2	5	(1.0)	1	(0.2)	6	(0.6)
Dysphonia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Grade 1	20	(3.9)	14	(2.8)	34	(3.4)
Grade 2	6	(1.2)	0	(0.0)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea exertional	3	(0.6)	1	(0.2)	4	(0.4)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dyspnoea exertional	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pneumonitis	17	(3.3)	3	(0.6)	20	(2.0)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	13	(2.6)	2	(0.4)	15	(1.5)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Productive cough	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Pulmonary embolism	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rhinorrhoea	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Wheezing	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Grade 1	150	(29.5)	114	(22.7)	264	(26.1)
Grade 2	51	(10.0)	10	(2.0)	61	(6.0)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Acne	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Acne	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Actinic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Alopecia	9	(1.8)	8	(1.6)	17	(1.7)
Grade 1	9	(1.8)	8	(1.6)	17	(1.7)
Dermatitis	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Dermatitis acneiform	7	(1.4)	6	(1.2)	13	(1.3)
Grade 1	6	(1.2)	6	(1.2)	12	(1.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis contact	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dry skin	20	(3.9)	8	(1.6)	28	(2.8)
Grade 1	17	(3.3)	6	(1.2)	23	(2.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eczema	13	(2.6)	3	(0.6)	16	(1.6)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Erythema	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Hair disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperhidrosis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Lichen planus	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lichenoid keratosis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Macule	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Night sweats	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Onycholysis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pain of skin	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Papule	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Photosensitivity reaction	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Grade 1	71	(13.9)	48	(9.6)	119	(11.8)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Grade 2	16	(3.1)	3	(0.6)	19	(1.9)
Psoriasis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Grade 1	43	(8.4)	30	(6.0)	73	(7.2)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Rash erythematous	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash macular	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Rash maculo-papular	24	(4.7)	20	(4.0)	44	(4.4)
Grade 1	16	(3.1)	18	(3.6)	34	(3.4)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rash papular	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash pruritic	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash vesicular	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin exfoliation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin induration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin lesion	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Skin ulcer	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vitiligo	24	(4.7)	7	(1.4)	31	(3.1)
Grade 1	23	(4.5)	6	(1.2)	29	(2.9)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Vascular disorders	**12**	**(2.4)**	**12**	**(2.4)**	**24**	**(2.4)**
Grade 1	7	(1.4)	9	(1.8)	16	(1.6)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Flushing	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Hot flush	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hypertension	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lymphoedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Raynaud's phenomenon	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Thrombophlebitis superficial	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Thrombophlebitis superficial	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-17

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	398	(78.2)	333	(66.3)	731	(72.3)
Grade 1	129	(25.3)	220	(43.8)	349	(34.5)
Grade 2	195	(38.3)	96	(19.1)	291	(28.8)
Grade 3	67	(13.2)	17	(3.4)	84	(8.3)
Grade 4	7	(1.4)	0	(0.0)	7	(0.7)
with no adverse events	111	(21.8)	169	(33.7)	280	(27.7)
Blood and lymphatic system disorders	**18**	**(3.5)**	**8**	**(1.6)**	**26**	**(2.6)**
Grade 1	10	(2.0)	5	(1.0)	15	(1.5)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	6	(1.2)	1	(0.2)	7	(0.7)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophilia	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Neutropenia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lymphadenopathy mediastinal	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymphadenopathy	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Cardiac disorders	**6**	**(1.2)**	**1**	**(0.2)**	**7**	**(0.7)**
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Palpitations	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Angina pectoris	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Peutz-Jeghers syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**6**	**(1.2)**	**3**	**(0.6)**	**9**	**(0.9)**
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Ear pain	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tinnitus	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Ear pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vertigo	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Vestibular disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Endocrine disorders	**116**	**(22.8)**	**19**	**(3.8)**	**135**	**(13.4)**
Grade 1	33	(6.5)	11	(2.2)	44	(4.4)
Grade 2	80	(15.7)	8	(1.6)	88	(8.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hypothyroidism	74	(14.5)	13	(2.6)	87	(8.6)
Grade 1	13	(2.6)	7	(1.4)	20	(2.0)
Grade 2	61	(12.0)	6	(1.2)	67	(6.6)
Hyperthyroidism	49	(9.6)	3	(0.6)	52	(5.1)
Grade 1	36	(7.1)	3	(0.6)	39	(3.9)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Thyroiditis	11	(2.2)	1	(0.2)	12	(1.2)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	8	(1.6)	1	(0.2)	9	(0.9)
Hypophysitis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal insufficiency	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Autoimmune thyroiditis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Glucocorticoid deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Thyroiditis subacute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Eye disorders	**26**	**(5.1)**	**13**	**(2.6)**	**39**	**(3.9)**
Grade 1	23	(4.5)	13	(2.6)	36	(3.6)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Dry eye	7	(1.4)	4	(0.8)	11	(1.1)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Photophobia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Photopsia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Vision blurred	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Visual impairment	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Cataract	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eczema eyelids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye irritation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Eye pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lacrimation increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Ocular hyperaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Periorbital swelling	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Uveitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vitreous floaters	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Accommodation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Eye swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Foreign body sensation in eyes	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Visual acuity reduced	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal disorders	**184**	**(36.1)**	**144**	**(28.7)**	**328**	**(32.4)**
Grade 1	110	(21.6)	120	(23.9)	230	(22.7)
Grade 2	55	(10.8)	19	(3.8)	74	(7.3)
Grade 3	18	(3.5)	5	(1.0)	23	(2.3)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	93	(18.3)	83	(16.5)	176	(17.4)
Grade 1	66	(13.0)	68	(13.5)	134	(13.3)
Grade 2	23	(4.5)	12	(2.4)	35	(3.5)
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	59	(11.6)	44	(8.8)	103	(10.2)
Grade 1	50	(9.8)	42	(8.4)	92	(9.1)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
Dry mouth	23	(4.5)	10	(2.0)	33	(3.3)
Grade 1	22	(4.3)	10	(2.0)	32	(3.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	20	(3.9)	14	(2.8)	34	(3.4)
Grade 1	17	(3.3)	13	(2.6)	30	(3.0)
Grade 2	3	(0.6)	1	(0.2)	4	(0.4)
Vomiting	16	(3.1)	9	(1.8)	25	(2.5)
Grade 1	12	(2.4)	9	(1.8)	21	(2.1)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Colitis	13	(2.6)	1	(0.2)	14	(1.4)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Colitis	13	(2.6)	1	(0.2)	14	(1.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	5	(1.0)	1	(0.2)	6	(0.6)
Grade 3	7	(1.4)	0	(0.0)	7	(0.7)
Constipation	12	(2.4)	8	(1.6)	20	(2.0)
Grade 1	8	(1.6)	8	(1.6)	16	(1.6)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Abdominal pain upper	9	(1.8)	10	(2.0)	19	(1.9)
Grade 1	7	(1.4)	10	(2.0)	17	(1.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	8	(1.6)	2	(0.4)	10	(1.0)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Grade 2	2	(0.4)	2	(0.4)	4	(0.4)
Faeces soft	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Gastritis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Immune-mediated enterocolitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Stomatitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Oral lichen planus	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal discomfort	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Mouth ulceration	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Odynophagia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Abdominal distension	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Anal incontinence	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal motility disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gingival pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lip dry	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lip ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Oral discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Oral disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Oral pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Swollen tongue	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Aerophagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Bowel movement irregularity	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Chapped lips	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Defaecation disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysphagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Flatulence	0	(0.0)	3	(0.6)	3	(0.3)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Glossitis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Paraesthesia oral	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Periodontal disease	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Salivary duct inflammation	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**205**	**(40.3)**	**183**	**(36.5)**	**388**	**(38.4)**
Grade 1	143	(28.1)	159	(31.7)	302	(29.9)
Grade 2	55	(10.8)	22	(4.4)	77	(7.6)
Grade 3	7	(1.4)	2	(0.4)	9	(0.9)
Fatigue	144	(28.3)	138	(27.5)	282	(27.9)
Grade 1	102	(20.0)	123	(24.5)	225	(22.3)
Grade 2	38	(7.5)	13	(2.6)	51	(5.0)
Grade 3	4	(0.8)	2	(0.4)	6	(0.6)
Asthenia	47	(9.2)	34	(6.8)	81	(8.0)
Grade 1	32	(6.3)	29	(5.8)	61	(6.0)
Grade 2	15	(2.9)	5	(1.0)	20	(2.0)
Influenza like illness	15	(2.9)	9	(1.8)	24	(2.4)
Grade 1	13	(2.6)	8	(1.6)	21	(2.1)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Chills	6	(1.2)	4	(0.8)	10	(1.0)
Grade 1	6	(1.2)	4	(0.8)	10	(1.0)
Oedema peripheral	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Pyrexia	5	(1.0)	6	(1.2)	11	(1.1)
Grade 1	3	(0.6)	4	(0.8)	7	(0.7)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Non-cardiac chest pain	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Oedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Pain	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Chest pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Face oedema	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Feeling cold	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Infusion site reaction	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Injection site hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Localised oedema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral swelling	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hepatobiliary disorders	**10**	**(2.0)**	**3**	**(0.6)**	**13**	**(1.3)**
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hyperbilirubinaemia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cholestasis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hepatocellular injury	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Immune system disorders	**6**	**(1.2)**	**2**	**(0.4)**	**8**	**(0.8)**
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Sarcoidosis	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Allergy to arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Allergy to metals	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Infections and infestations	**28**	**(5.5)**	**13**	**(2.6)**	**41**	**(4.1)**
Grade 1	14	(2.8)	8	(1.6)	22	(2.2)
Grade 2	13	(2.6)	4	(0.8)	17	(1.7)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Conjunctivitis	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Rash pustular	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Sinusitis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Rhinitis	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Bronchitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Folliculitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Influenza	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Diverticulitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Erysipelas	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Mastitis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Mastitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Oral herpes	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Tinea infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal infection	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gastroenteritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Lip infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nail infection	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Nasopharyngitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Parotitis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**5**	**(1.0)**	**7**	**(0.7)**
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Infusion related reaction	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Arthropod bite	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Skin abrasion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**98**	**(19.3)**	**61**	**(12.2)**	**159**	**(15.7)**
Grade 1	63	(12.4)	36	(7.2)	99	(9.8)
Grade 2	25	(4.9)	20	(4.0)	45	(4.5)
Grade 3	8	(1.6)	5	(1.0)	13	(1.3)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Alanine aminotransferase increased	26	(5.1)	17	(3.4)	43	(4.3)
Grade 1	18	(3.5)	14	(2.8)	32	(3.2)
Grade 2	5	(1.0)	2	(0.4)	7	(0.7)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Aspartate aminotransferase increased	20	(3.9)	14	(2.8)	34	(3.4)
Grade 1	12	(2.4)	11	(2.2)	23	(2.3)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Weight increased	16	(3.1)	4	(0.8)	20	(2.0)
Grade 1	14	(2.8)	3	(0.6)	17	(1.7)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Weight decreased	13	(2.6)	11	(2.2)	24	(2.4)
Grade 1	10	(2.0)	8	(1.6)	18	(1.8)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Gamma-glutamyltransferase increased	9	(1.8)	4	(0.8)	13	(1.3)
Grade 1	6	(1.2)	1	(0.2)	7	(0.7)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Blood bilirubin increased	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Blood creatine phosphokinase increased	7	(1.4)	2	(0.4)	9	(0.9)
Grade 1	5	(1.0)	1	(0.2)	6	(0.6)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone decreased	7	(1.4)	1	(0.2)	8	(0.8)
Grade 1	7	(1.4)	1	(0.2)	8	(0.8)
Lipase increased	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lipase increased	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Blood creatinine increased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	5	(1.0)	2	(0.4)	7	(0.7)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count increased	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	6	(1.2)	0	(0.0)	6	(0.6)
Lymphocyte count decreased	6	(1.2)	2	(0.4)	8	(0.8)
Grade 1	4	(0.8)	2	(0.4)	6	(0.6)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Amylase increased	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Blood thyroid stimulating hormone increased	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
C-reactive protein increased	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Neutrophil count decreased	2	(0.4)	7	(1.4)	9	(0.9)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Grade 2	2	(0.4)	4	(0.8)	6	(0.6)
Platelet count decreased	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Blood gonadotrophin decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Protein total increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
White blood cell count increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Blood bicarbonate increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood glucose increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood urea increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Blood uric acid increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cortisol decreased	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Glomerular filtration rate decreased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Glomerular filtration rate increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Haemoglobin increased	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
White blood cell count decreased	0	(0.0)	5	(1.0)	5	(0.5)
Grade 1	0	(0.0)	4	(0.8)	4	(0.4)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Metabolism and nutrition disorders	**47**	**(9.2)**	**18**	**(3.6)**	**65**	**(6.4)**
Grade 1	23	(4.5)	15	(3.0)	38	(3.8)
Grade 2	12	(2.4)	2	(0.4)	14	(1.4)
Grade 3	10	(2.0)	1	(0.2)	11	(1.1)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Decreased appetite	25	(4.9)	8	(1.6)	33	(3.3)
Grade 1	20	(3.9)	8	(1.6)	28	(2.8)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hypophosphataemia	5	(1.0)	1	(0.2)	6	(0.6)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypophosphataemia	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	1	(0.2)	3	(0.3)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	2	(0.4)	3	(0.6)	5	(0.5)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	2	(0.4)	1	(0.2)	3	(0.3)
Dehydration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Food aversion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Gout	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hyperkalaemia	1	(0.2)	3	(0.6)	4	(0.4)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hypocalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Hypoglycaemia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**87**	**(17.1)**	**75**	**(14.9)**	**162**	**(16.0)**
Grade 1	59	(11.6)	57	(11.4)	116	(11.5)
Grade 2	23	(4.5)	18	(3.6)	41	(4.1)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	50	(9.8)	48	(9.6)	98	(9.7)
Grade 1	32	(6.3)	39	(7.8)	71	(7.0)
Grade 2	15	(2.9)	9	(1.8)	24	(2.4)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Myalgia	26	(5.1)	16	(3.2)	42	(4.2)
Grade 1	23	(4.5)	14	(2.8)	37	(3.7)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Pain in extremity	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	6	(1.2)	2	(0.4)	8	(0.8)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Arthritis	6	(1.2)	0	(0.0)	6	(0.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Muscle spasms	5	(1.0)	1	(0.2)	6	(0.6)
Grade 1	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal pain	5	(1.0)	3	(0.6)	8	(0.8)
Grade 1	4	(0.8)	1	(0.2)	5	(0.5)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Back pain	4	(0.8)	6	(1.2)	10	(1.0)
Grade 1	4	(0.8)	6	(1.2)	10	(1.0)
Muscular weakness	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Neck pain	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Bursitis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal chest pain	1	(0.2)	2	(0.4)	3	(0.3)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal chest pain	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal stiffness	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Sjogren's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Synovitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Joint effusion	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Muscle fatigue	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal discomfort	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia intercostal	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Osteoarthritis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.4)**

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.4)**
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dysplastic naevus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**75**	**(14.7)**	**67**	**(13.3)**	**142**	**(14.0)**
Grade 1	57	(11.2)	55	(11.0)	112	(11.1)
Grade 2	17	(3.3)	11	(2.2)	28	(2.8)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Headache	37	(7.3)	33	(6.6)	70	(6.9)
Grade 1	28	(5.5)	26	(5.2)	54	(5.3)
Grade 2	9	(1.8)	6	(1.2)	15	(1.5)
Grade 3	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness	10	(2.0)	13	(2.6)	23	(2.3)
Grade 1	9	(1.8)	11	(2.2)	20	(2.0)
Grade 2	1	(0.2)	2	(0.4)	3	(0.3)
Dysgeusia	7	(1.4)	8	(1.6)	15	(1.5)
Grade 1	6	(1.2)	8	(1.6)	14	(1.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lethargy	4	(0.8)	6	(1.2)	10	(1.0)
Grade 1	3	(0.6)	5	(1.0)	8	(0.8)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Memory impairment	4	(0.8)	3	(0.6)	7	(0.7)
Grade 1	3	(0.6)	3	(0.6)	6	(0.6)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	4	(0.8)	4	(0.8)	8	(0.8)
Grade 1	4	(0.8)	4	(0.8)	8	(0.8)
Peripheral sensory neuropathy	4	(0.8)	1	(0.2)	5	(0.5)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Peripheral sensory neuropathy	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Taste disorder	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Balance disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hypogeusia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hyposmia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Somnolence	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Tremor	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	1	(0.2)	2	(0.4)	3	(0.3)
Vibratory sense increased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Clumsiness	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Disturbance in attention	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness postural	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Dysaesthesia	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dysaesthesia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Migraine	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Neuropathy peripheral	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Psychiatric disorders	**11**	**(2.2)**	**12**	**(2.4)**	**23**	**(2.3)**
Grade 1	8	(1.6)	9	(1.8)	17	(1.7)
Grade 2	3	(0.6)	3	(0.6)	6	(0.6)
Insomnia	3	(0.6)	7	(1.4)	10	(1.0)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Grade 2	1	(0.2)	3	(0.6)	4	(0.4)
Irritability	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Affective disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Agitation	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Depression	1	(0.2)	2	(0.4)	3	(0.3)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Libido decreased	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Nervousness	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Confusional state	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Depressed mood	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Sleep disorder	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**3**	**(0.6)**	**1**	**(0.2)**	**4**	**(0.4)**
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pollakiuria	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Reproductive system and breast disorders	**8**	**(1.6)**	**4**	**(0.8)**	**12**	**(1.2)**
Grade 1	4	(0.8)	3	(0.6)	7	(0.7)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Erectile dysfunction	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Ejaculation disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Menometrorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menorrhagia	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Menstruation irregular	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pelvic pain	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pelvic pain	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**57**	**(11.2)**	**36**	**(7.2)**	**93**	**(9.2)**
Grade 1	30	(5.9)	31	(6.2)	61	(6.0)
Grade 2	22	(4.3)	5	(1.0)	27	(2.7)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	27	(5.3)	14	(2.8)	41	(4.1)
Grade 1	20	(3.9)	14	(2.8)	34	(3.4)
Grade 2	6	(1.2)	0	(0.0)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Cough	18	(3.5)	16	(3.2)	34	(3.4)
Grade 1	13	(2.6)	15	(3.0)	28	(2.8)
Grade 2	5	(1.0)	1	(0.2)	6	(0.6)
Pneumonitis	17	(3.3)	3	(0.6)	20	(2.0)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	13	(2.6)	2	(0.4)	15	(1.5)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Dyspnoea exertional	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Productive cough	3	(0.6)	0	(0.0)	3	(0.3)
Grade 1	3	(0.6)	0	(0.0)	3	(0.3)
Dysphonia	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Pulmonary embolism	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Rhinorrhoea	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Bronchospasm	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Chronic obstructive pulmonary disease	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Lung disorder	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Sinus congestion	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Haemoptysis	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Laryngeal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Nasal oedema	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Pleural thickening	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Wheezing	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Skin and subcutaneous tissue disorders	**205**	**(40.3)**	**124**	**(24.7)**	**329**	**(32.5)**
Grade 1	150	(29.5)	114	(22.7)	264	(26.1)
Grade 2	51	(10.0)	10	(2.0)	61	(6.0)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Pruritus	87	(17.1)	51	(10.2)	138	(13.6)
Grade 1	71	(13.9)	48	(9.6)	119	(11.8)
Grade 2	16	(3.1)	3	(0.6)	19	(1.9)
Rash	50	(9.8)	33	(6.6)	83	(8.2)
Grade 1	43	(8.4)	30	(6.0)	73	(7.2)
Grade 2	7	(1.4)	3	(0.6)	10	(1.0)
Rash maculo-papular	24	(4.7)	20	(4.0)	44	(4.4)
Grade 1	16	(3.1)	18	(3.6)	34	(3.4)
Grade 2	7	(1.4)	2	(0.4)	9	(0.9)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Vitiligo	24	(4.7)	7	(1.4)	31	(3.1)
Grade 1	23	(4.5)	6	(1.2)	29	(2.9)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vitiligo	24	(4.7)	7	(1.4)	31	(3.1)
Grade 2	1	(0.2)	1	(0.2)	2	(0.2)
Dry skin	20	(3.9)	8	(1.6)	28	(2.8)
Grade 1	17	(3.3)	6	(1.2)	23	(2.3)
Grade 2	3	(0.6)	2	(0.4)	5	(0.5)
Eczema	13	(2.6)	3	(0.6)	16	(1.6)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	8	(1.6)	0	(0.0)	8	(0.8)
Alopecia	9	(1.8)	8	(1.6)	17	(1.7)
Grade 1	9	(1.8)	8	(1.6)	17	(1.7)
Skin hypopigmentation	8	(1.6)	3	(0.6)	11	(1.1)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis acneiform	7	(1.4)	6	(1.2)	13	(1.3)
Grade 1	6	(1.2)	6	(1.2)	12	(1.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Erythema	7	(1.4)	3	(0.6)	10	(1.0)
Grade 1	5	(1.0)	3	(0.6)	8	(0.8)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Lichenoid keratosis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Psoriasis	4	(0.8)	0	(0.0)	4	(0.4)
Grade 2	4	(0.8)	0	(0.0)	4	(0.4)
Rash erythematous	4	(0.8)	2	(0.4)	6	(0.6)
Grade 1	3	(0.6)	2	(0.4)	5	(0.5)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash pruritic	4	(0.8)	1	(0.2)	5	(0.5)
Grade 1	3	(0.6)	1	(0.2)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Photosensitivity reaction	3	(0.6)	2	(0.4)	5	(0.5)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rash papular	3	(0.6)	1	(0.2)	4	(0.4)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis	2	(0.4)	4	(0.8)	6	(0.6)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dermatitis	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	4	(0.8)	6	(0.6)
Dyshidrotic eczema	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Pain of skin	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Palmar-plantar erythrodysaesthesia syndrome	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Papule	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Seborrhoeic dermatitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Skin lesion	2	(0.4)	2	(0.4)	4	(0.4)
Grade 1	2	(0.4)	2	(0.4)	4	(0.4)
Acne	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Actinic keratosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis atopic	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Dermatosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Hair disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Macule	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nail disorder	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Nail dystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Night sweats	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Onycholysis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Panniculitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Petechiae	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Purpura	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Rash macular	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Rash vesicular	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin exfoliation	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin induration	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Skin ulcer	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Stasis dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	0	(0.0)	1	(0.1)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Dermatitis contact	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Hyperhidrosis	0	(0.0)	2	(0.4)	2	(0.2)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Nail ridging	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Vascular disorders	**12**	**(2.4)**	**12**	**(2.4)**	**24**	**(2.4)**
Grade 1	7	(1.4)	9	(1.8)	16	(1.6)
Grade 2	4	(0.8)	1	(0.2)	5	(0.5)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Hypertension	4	(0.8)	5	(1.0)	9	(0.9)
Grade 1	0	(0.0)	3	(0.6)	3	(0.3)
Grade 2	3	(0.6)	0	(0.0)	3	(0.3)
Grade 3	1	(0.2)	2	(0.4)	3	(0.3)
Flushing	2	(0.4)	1	(0.2)	3	(0.3)
Grade 1	2	(0.4)	1	(0.2)	3	(0.3)
Hot flush	2	(0.4)	4	(0.8)	6	(0.6)
Grade 1	2	(0.4)	3	(0.6)	5	(0.5)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Lymphoedema	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	2	(0.4)	0	(0.0)	2	(0.2)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Raynaud's phenomenon	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Thrombophlebitis superficial	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Drug-Related Adverse Events by Decreasing Incidence by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypotension	0	(0.0)	1	(0.2)	1	(0.1)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.1.4 Grade 3 to 5 Adverse Events

Table 14.3-18

Subjects With Grade 3-5 Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	162	(31.8)	96	(19.1)	258	(25.5)
with no adverse events	347	(68.2)	406	(80.9)	753	(74.5)
Hypertension	28	(5.5)	18	(3.6)	46	(4.5)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Arthralgia	6	(1.2)	0	(0.0)	6	(0.6)
Blood creatine phosphokinase increased	6	(1.2)	1	(0.2)	7	(0.7)
Diarrhoea	6	(1.2)	6	(1.2)	12	(1.2)
Lipase increased	6	(1.2)	5	(1.0)	11	(1.1)
Basal cell carcinoma	5	(1.0)	3	(0.6)	8	(0.8)
Hyponatraemia	5	(1.0)	2	(0.4)	7	(0.7)
Pulmonary embolism	5	(1.0)	1	(0.2)	6	(0.6)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Fatigue	4	(0.8)	3	(0.6)	7	(0.7)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Cellulitis	3	(0.6)	6	(1.2)	9	(0.9)
Gamma-glutamyltransferase increased	3	(0.6)	2	(0.4)	5	(0.5)
Hyperglycaemia	3	(0.6)	1	(0.2)	4	(0.4)
Hypokalaemia	3	(0.6)	1	(0.2)	4	(0.4)
Immune-mediated enterocolitis	3	(0.6)	1	(0.2)	4	(0.4)
Pneumonitis	3	(0.6)	0	(0.0)	3	(0.3)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Erysipelas	2	(0.4)	4	(0.8)	6	(0.6)
Lymphopenia	2	(0.4)	0	(0.0)	2	(0.2)
Pneumonia	2	(0.4)	0	(0.0)	2	(0.2)
Pyrexia	2	(0.4)	0	(0.0)	2	(0.2)
Rash	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Animal bite	1	(0.2)	0	(0.0)	1	(0.1)
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Asthenia	1	(0.2)	0	(0.0)	1	(0.1)
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Blood lactate dehydrogenase increased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cataract	1	(0.2)	1	(0.2)	2	(0.2)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Constipation	1	(0.2)	0	(0.0)	1	(0.1)
Contrast media allergy	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	1	(0.2)	2	(0.2)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Gastroenteritis viral	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypophosphataemia	1	(0.2)	2	(0.4)	3	(0.3)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Intervertebral disc protrusion	1	(0.2)	2	(0.4)	3	(0.3)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Lymphoedema	1	(0.2)	0	(0.0)	1	(0.1)
Malignant melanoma	1	(0.2)	2	(0.4)	3	(0.3)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Meniscus injury	1	(0.2)	1	(0.2)	2	(0.2)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Musculoskeletal pain	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	1	(0.2)	0	(0.0)	1	(0.1)
Nephrolithiasis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Pain in extremity	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Skin infection	1	(0.2)	1	(0.2)	2	(0.2)
Soft tissue infection	1	(0.2)	0	(0.0)	1	(0.1)
Squamous cell carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Synovial rupture	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	0	(0.0)	1	(0.1)
Tooth infection	1	(0.2)	1	(0.2)	2	(0.2)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Vertigo	1	(0.2)	0	(0.0)	1	(0.1)
Viral infection	1	(0.2)	0	(0.0)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	0	(0.0)	1	(0.2)	1	(0.1)
Anxiety	0	(0.0)	1	(0.2)	1	(0.1)
Back pain	0	(0.0)	2	(0.4)	2	(0.2)
Benign prostatic hyperplasia	0	(0.0)	1	(0.2)	1	(0.1)
Blood alkaline phosphatase increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)
Colon adenoma	0	(0.0)	1	(0.2)	1	(0.1)
Diverticulitis	0	(0.0)	1	(0.2)	1	(0.1)
Fall	0	(0.0)	1	(0.2)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhoids	0	(0.0)	1	(0.2)	1	(0.1)
Headache	0	(0.0)	1	(0.2)	1	(0.1)
Hypercalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hyperhidrosis	0	(0.0)	1	(0.2)	1	(0.1)
Hyperlipasaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Infected dermal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Infected seroma	0	(0.0)	2	(0.4)	2	(0.2)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Lymphocyte count decreased	0	(0.0)	2	(0.4)	2	(0.2)
Neutrophil count decreased	0	(0.0)	2	(0.4)	2	(0.2)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Procedural pain	0	(0.0)	1	(0.2)	1	(0.1)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Renal colic	0	(0.0)	1	(0.2)	1	(0.1)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Suicidal ideation	0	(0.0)	1	(0.2)	1	(0.1)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Upper respiratory tract infection	0	(0.0)	1	(0.2)	1	(0.1)
Vomiting	0	(0.0)	1	(0.2)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-19

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	162	(31.8)	96	(19.1)	258	(25.5)
with no adverse events	347	(68.2)	406	(80.9)	753	(74.5)
Blood and lymphatic system disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Lymphopenia	2	(0.4)	0	(0.0)	2	(0.2)
Cardiac disorders	**4**	**(0.8)**	**1**	**(0.2)**	**5**	**(0.5)**
Atrial fibrillation	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Hypertrophic cardiomyopathy	0	(0.0)	1	(0.2)	1	(0.1)
Ear and labyrinth disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Vertigo	1	(0.2)	0	(0.0)	1	(0.1)
Endocrine disorders	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.3)**
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Cataract	1	(0.2)	1	(0.2)	2	(0.2)
Gastrointestinal disorders	**28**	**(5.5)**	**10**	**(2.0)**	**38**	**(3.8)**
Abdominal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	0	(0.0)	1	(0.2)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**28**	**(5.5)**	**10**	**(2.0)**	**38**	**(3.8)**
Constipation	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	6	(1.2)	6	(1.2)	12	(1.2)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	0	(0.0)	1	(0.2)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	3	(0.6)	1	(0.2)	4	(0.4)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	1	(0.2)	0	(0.0)	1	(0.1)
Umbilical hernia	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	0	(0.0)	1	(0.2)	1	(0.1)
General disorders and administration site conditions	**9**	**(1.8)**	**3**	**(0.6)**	**12**	**(1.2)**
Asthenia	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	4	(0.8)	3	(0.6)	7	(0.7)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	2	(0.4)	0	(0.0)	2	(0.2)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**8**	**(1.6)**	**2**	**(0.4)**	**10**	**(1.0)**
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Hepatitis	4	(0.8)	1	(0.2)	5	(0.5)
Immune system disorders	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.3)**
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Contrast media allergy	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**18**	**(3.5)**	**19**	**(3.8)**	**37**	**(3.7)**
Anorectal infection	1	(0.2)	0	(0.0)	1	(0.1)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	3	(0.6)	6	(1.2)	9	(0.9)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	0	(0.0)	1	(0.2)	1	(0.1)
Erysipelas	2	(0.4)	4	(0.8)	6	(0.6)
Gastroenteritis viral	1	(0.2)	0	(0.0)	1	(0.1)
Infected dermal cyst	0	(0.0)	1	(0.2)	1	(0.1)
Infected seroma	0	(0.0)	2	(0.4)	2	(0.2)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	2	(0.4)	0	(0.0)	2	(0.2)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Pyelonephritis	0	(0.0)	1	(0.2)	1	(0.1)
Skin infection	1	(0.2)	1	(0.2)	2	(0.2)
Soft tissue infection	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Tooth infection	1	(0.2)	1	(0.2)	2	(0.2)
Upper respiratory tract infection	0	(0.0)	1	(0.2)	1	(0.1)
Viral infection	1	(0.2)	0	(0.0)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**3**	**(0.6)**	**6**	**(1.2)**	**9**	**(0.9)**
Animal bite	1	(0.2)	0	(0.0)	1	(0.1)
Fall	0	(0.0)	1	(0.2)	1	(0.1)
Meniscus injury	1	(0.2)	1	(0.2)	2	(0.2)
Post procedural haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Procedural pain	0	(0.0)	1	(0.2)	1	(0.1)
Road traffic accident	0	(0.0)	1	(0.2)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Synovial rupture	1	(0.2)	0	(0.0)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**18**	**(3.5)**	**15**	**(3.0)**	**33**	**(3.3)**
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Blood alkaline phosphatase increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	0	(0.0)	1	(0.2)	1	(0.1)
Blood creatine phosphokinase increased	6	(1.2)	1	(0.2)	7	(0.7)
Blood lactate dehydrogenase increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood triglycerides increased	0	(0.0)	1	(0.2)	1	(0.1)
Gamma-glutamyltransferase increased	3	(0.6)	2	(0.4)	5	(0.5)
Lipase increased	6	(1.2)	5	(1.0)	11	(1.1)
Lymphocyte count decreased	0	(0.0)	2	(0.4)	2	(0.2)
Neutrophil count decreased	0	(0.0)	2	(0.4)	2	(0.2)
Metabolism and nutrition disorders	**19**	**(3.7)**	**10**	**(2.0)**	**29**	**(2.9)**
Decreased appetite	1	(0.2)	1	(0.2)	2	(0.2)
Diabetes mellitus	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypercalcaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hyperglycaemia	3	(0.6)	1	(0.2)	4	(0.4)
Hyperlipasaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypokalaemia	3	(0.6)	1	(0.2)	4	(0.4)
Hyponatraemia	5	(1.0)	2	(0.4)	7	(0.7)
Hypophosphataemia	1	(0.2)	2	(0.4)	3	(0.3)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Musculoskeletal and connective tissue disorders	**11**	**(2.2)**	**5**	**(1.0)**	**16**	**(1.6)**
Arthralgia	6	(1.2)	0	(0.0)	6	(0.6)
Back pain	0	(0.0)	2	(0.4)	2	(0.2)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Intervertebral disc protrusion	1	(0.2)	2	(0.4)	3	(0.3)
Musculoskeletal pain	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**11**	**(2.2)**	**5**	**(1.0)**	**16**	**(1.6)**
Neck pain	1	(0.2)	0	(0.0)	1	(0.1)
Pain in extremity	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Rotator cuff syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**15**	**(2.9)**	**13**	**(2.6)**	**28**	**(2.8)**
Basal cell carcinoma	5	(1.0)	3	(0.6)	8	(0.8)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Colon adenoma	0	(0.0)	1	(0.2)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Malignant melanoma	1	(0.2)	2	(0.4)	3	(0.3)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Squamous cell carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorders	**6**	**(1.2)**	**9**	**(1.8)**	**15**	**(1.5)**
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Cognitive disorder	0	(0.0)	1	(0.2)	1	(0.1)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Headache	0	(0.0)	1	(0.2)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**6**	**(1.2)**	**9**	**(1.8)**	**15**	**(1.5)**
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Syncope	1	(0.2)	4	(0.8)	5	(0.5)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Psychiatric disorders	**0**	**(0.0)**	**2**	**(0.4)**	**2**	**(0.2)**
Anxiety	0	(0.0)	1	(0.2)	1	(0.1)
Suicidal ideation	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**4**	**(0.8)**	**2**	**(0.4)**	**6**	**(0.6)**
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Nephrolithiasis	1	(0.2)	0	(0.0)	1	(0.1)
Renal colic	0	(0.0)	1	(0.2)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**0**	**(0.0)**	**2**	**(0.4)**	**2**	**(0.2)**
Benign prostatic hyperplasia	0	(0.0)	1	(0.2)	1	(0.1)
Prostatic obstruction	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**10**	**(2.0)**	**2**	**(0.4)**	**12**	**(1.2)**
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)	1	(0.1)
Dyspnoea	1	(0.2)	0	(0.0)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonitis	3	(0.6)	0	(0.0)	3	(0.3)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary embolism	5	(1.0)	1	(0.2)	6	(0.6)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**1**	**(0.2)**	**8**	**(0.8)**
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**7**	**(1.4)**	**1**	**(0.2)**	**8**	**(0.8)**
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Hyperhidrosis	0	(0.0)	1	(0.2)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Rash	2	(0.4)	0	(0.0)	2	(0.2)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**31**	**(6.1)**	**19**	**(3.8)**	**50**	**(4.9)**
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Hypertension	28	(5.5)	18	(3.6)	46	(4.5)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Lymphoedema	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.1.5 Grade 3 to 5 Adverse Events Related to Study Intervention

Table 14.3-20

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with no adverse events	435	(85.5)	485	(96.6)	920	(91.0)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Diarrhoea	4	(0.8)	3	(0.6)	7	(0.7)
Fatigue	4	(0.8)	2	(0.4)	6	(0.6)
Lipase increased	4	(0.8)	3	(0.6)	7	(0.7)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Arthralgia	3	(0.6)	0	(0.0)	3	(0.3)
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Immune-mediated enterocolitis	3	(0.6)	1	(0.2)	4	(0.4)
Pneumonitis	3	(0.6)	0	(0.0)	3	(0.3)
Blood creatine phosphokinase increased	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Hyponatraemia	2	(0.4)	1	(0.2)	3	(0.3)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypertension	1	(0.2)	2	(0.4)	3	(0.3)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)

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

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hypophosphataemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Lymphopenia	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	1	(0.2)	1	(0.1)
Headache	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)

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

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-21

Subjects With Grade 3-5 Drug-Related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	74	(14.5)	17	(3.4)	91	(9.0)
with no adverse events	435	(85.5)	485	(96.6)	920	(91.0)
Blood and lymphatic system disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Lymphopenia	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Endocrine disorders	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.3)**
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**19**	**(3.7)**	**5**	**(1.0)**	**24**	**(2.4)**
Abdominal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	4	(0.8)	3	(0.6)	7	(0.7)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Immune-mediated enterocolitis	3	(0.6)	1	(0.2)	4	(0.4)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
General disorders and administration site conditions	**7**	**(1.4)**	**2**	**(0.4)**	**9**	**(0.9)**
Fatigue	4	(0.8)	2	(0.4)	6	(0.6)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Drug-Related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**7**	**(1.4)**	**2**	**(0.4)**	**9**	**(0.9)**
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**6**	**(1.2)**	**1**	**(0.2)**	**7**	**(0.7)**
Autoimmune hepatitis	3	(0.6)	0	(0.0)	3	(0.3)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Infections and infestations	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	1	(0.2)	1	(0.1)
Investigations	**10**	**(2.0)**	**5**	**(1.0)**	**15**	**(1.5)**
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Blood creatine phosphokinase increased	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Lipase increased	4	(0.8)	3	(0.6)	7	(0.7)
Metabolism and nutrition disorders	**12**	**(2.4)**	**1**	**(0.2)**	**13**	**(1.3)**
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Hyperamylasaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypokalaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	2	(0.4)	1	(0.2)	3	(0.3)
Hypophosphataemia	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 diabetes mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Musculoskeletal and connective tissue disorders	**5**	**(1.0)**	**0**	**(0.0)**	**5**	**(0.5)**
Arthralgia	3	(0.6)	0	(0.0)	3	(0.3)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Grade 3-5 Drug-Related Adverse Events by Body System or Organ Class and Preferred Term
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Headache	0	(0.0)	1	(0.2)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**5**	**(1.0)**	**0**	**(0.0)**	**5**	**(0.5)**
Dyspnoea	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonitis	3	(0.6)	0	(0.0)	3	(0.3)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Skin and subcutaneous tissue disorders	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.4)**
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**1**	**(0.2)**	**2**	**(0.4)**	**3**	**(0.3)**
Hypertension	1	(0.2)	2	(0.4)	3	(0.3)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.1.6 Adverse Events by Demographic Subgroups

Table 14.3-22

Adverse Event Summary by Age Category
(ASaT Population)

	<50				50-64				≥65				Total			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	192		185		193		193		124		124		509		502	
with one or more adverse events	180	(93.8)	170	(91.9)	182	(94.3)	177	(91.7)	118	(95.2)	107	(86.3)	480	(94.3)	454	(90.4)
with no adverse event	12	(6.3)	15	(8.1)	11	(5.7)	16	(8.3)	6	(4.8)	17	(13.7)	29	(5.7)	48	(9.6)
with drug-related† adverse events	148	(77.1)	125	(67.6)	154	(79.8)	137	(71.0)	96	(77.4)	71	(57.3)	398	(78.2)	333	(66.3)
with toxicity grade 3-5 adverse events	45	(23.4)	33	(17.8)	64	(33.2)	39	(20.2)	53	(42.7)	24	(19.4)	162	(31.8)	96	(19.1)
with toxicity grade 3-5 drug-related adverse events	23	(12.0)	8	(4.3)	28	(14.5)	6	(3.1)	23	(18.5)	3	(2.4)	74	(14.5)	17	(3.4)
with serious adverse events	39	(20.3)	25	(13.5)	45	(23.3)	35	(18.1)	43	(34.7)	23	(18.5)	127	(25.0)	83	(16.5)
with serious drug-related adverse events	23	(12.0)	1	(0.5)	23	(11.9)	4	(2.1)	16	(12.9)	1	(0.8)	62	(12.2)	6	(1.2)
who died	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	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)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	27	(14.1)	7	(3.8)	28	(14.5)	7	(3.6)	16	(12.9)	4	(3.2)	71	(13.9)	18	(3.6)
discontinued drug due to a drug-related adverse event	26	(13.5)	5	(2.7)	23	(11.9)	2	(1.0)	13	(10.5)	1	(0.8)	62	(12.2)	8	(1.6)
discontinued drug due to a serious adverse event	13	(6.8)	2	(1.1)	9	(4.7)	5	(2.6)	7	(5.6)	4	(3.2)	29	(5.7)	11	(2.2)

Adverse Event Summary by Age Category
(ASaT Population)

	<50				50-64				≥65				Total			
	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	12	(6.3)	0	(0.0)	6	(3.1)	1	(0.5)	4	(3.2)	1	(0.8)	22	(4.3)	2	(0.4)

† Determined by the investigator to be related to the drug.

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

AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-23

Adverse Event Summary by Europe Age Category
(ASaT Population)

	< 65				65 to 74				75 to 84				≥ 85			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	385		378		96		97		26		27		2		0	
with one or more adverse events	362	(94.0)	347	(91.8)	92	(95.8)	84	(86.6)	24	(92.3)	23	(85.2)	2	(100.0)	0	(0.0)
with no adverse event	23	(6.0)	31	(8.2)	4	(4.2)	13	(13.4)	2	(7.7)	4	(14.8)	0	(0.0)	0	(0.0)
with drug-related† adverse events	302	(78.4)	262	(69.3)	75	(78.1)	56	(57.7)	19	(73.1)	15	(55.6)	2	(100.0)	0	(0.0)
with toxicity grade 3-5 adverse events	109	(28.3)	72	(19.0)	37	(38.5)	18	(18.6)	15	(57.7)	6	(22.2)	1	(50.0)	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	51	(13.2)	14	(3.7)	15	(15.6)	2	(2.1)	7	(26.9)	1	(3.7)	1	(50.0)	0	(0.0)
with serious adverse events	84	(21.8)	60	(15.9)	29	(30.2)	18	(18.6)	12	(46.2)	5	(18.5)	2	(100.0)	0	(0.0)
with serious drug-related adverse events	46	(11.9)	5	(1.3)	10	(10.4)	1	(1.0)	4	(15.4)	0	(0.0)	2	(100.0)	0	(0.0)
who died	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	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)	0	(0.0)	0	(0.0)
discontinued drug due to an adverse event	55	(14.3)	14	(3.7)	9	(9.4)	3	(3.1)	6	(23.1)	1	(3.7)	1	(50.0)	0	(0.0)
discontinued drug due to a drug-related adverse event	49	(12.7)	7	(1.9)	8	(8.3)	1	(1.0)	4	(15.4)	0	(0.0)	1	(50.0)	0	(0.0)
discontinued drug due to a serious adverse event	22	(5.7)	7	(1.9)	3	(3.1)	3	(3.1)	3	(11.5)	1	(3.7)	1	(50.0)	0	(0.0)

Adverse Event Summary by Europe Age Category
(ASaT Population)

	< 65				65 to 74				75 to 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	18	(4.7)	1	(0.3)	2	(2.1)	1	(1.0)	1	(3.8)	0	(0.0)	1	(50.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-24

Adverse Event Summary by Gender
(ASaT Population)

	Male				Female				Total			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	320		302		189		200		509		502	
with one or more adverse events	303	(94.7)	271	(89.7)	177	(93.7)	183	(91.5)	480	(94.3)	454	(90.4)
with no adverse event	17	(5.3)	31	(10.3)	12	(6.3)	17	(8.5)	29	(5.7)	48	(9.6)
with drug-related[†] adverse events	242	(75.6)	186	(61.6)	156	(82.5)	147	(73.5)	398	(78.2)	333	(66.3)
with toxicity grade 3-5 adverse events	103	(32.2)	55	(18.2)	59	(31.2)	41	(20.5)	162	(31.8)	96	(19.1)
with toxicity grade 3-5 drug-related adverse events	45	(14.1)	11	(3.6)	29	(15.3)	6	(3.0)	74	(14.5)	17	(3.4)
with serious adverse events	75	(23.4)	44	(14.6)	52	(27.5)	39	(19.5)	127	(25.0)	83	(16.5)
with serious drug-related adverse events	33	(10.3)	4	(1.3)	29	(15.3)	2	(1.0)	62	(12.2)	6	(1.2)
who died	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	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	38	(11.9)	12	(4.0)	33	(17.5)	6	(3.0)	71	(13.9)	18	(3.6)
discontinued drug due to a drug-related adverse event	32	(10.0)	7	(2.3)	30	(15.9)	1	(0.5)	62	(12.2)	8	(1.6)
discontinued drug due to a serious adverse event	14	(4.4)	7	(2.3)	15	(7.9)	4	(2.0)	29	(5.7)	11	(2.2)
discontinued drug due to a serious drug-related adverse event	9	(2.8)	2	(0.7)	13	(6.9)	0	(0.0)	22	(4.3)	2	(0.4)

[†] Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-25

Adverse Event Summary by Region
(ASaT Population)

	EU				Ex-EU				Total			
	Pembrolizumab		Placebo		Pembrolizumab		Placebo		Pembrolizumab		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	319		314		190		188		509		502	
with one or more adverse events	306	(95.9)	284	(90.4)	174	(91.6)	170	(90.4)	480	(94.3)	454	(90.4)
with no adverse event	13	(4.1)	30	(9.6)	16	(8.4)	18	(9.6)	29	(5.7)	48	(9.6)
with drug-related† adverse events	257	(80.6)	210	(66.9)	141	(74.2)	123	(65.4)	398	(78.2)	333	(66.3)
with toxicity grade 3-5 adverse events	98	(30.7)	54	(17.2)	64	(33.7)	42	(22.3)	162	(31.8)	96	(19.1)
with toxicity grade 3-5 drug-related adverse events	48	(15.0)	12	(3.8)	26	(13.7)	5	(2.7)	74	(14.5)	17	(3.4)
with serious adverse events	66	(20.7)	45	(14.3)	61	(32.1)	38	(20.2)	127	(25.0)	83	(16.5)
with serious drug-related adverse events	36	(11.3)	4	(1.3)	26	(13.7)	2	(1.1)	62	(12.2)	6	(1.2)
who died	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	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	45	(14.1)	13	(4.1)	26	(13.7)	5	(2.7)	71	(13.9)	18	(3.6)
discontinued drug due to a drug-related adverse event	41	(12.9)	6	(1.9)	21	(11.1)	2	(1.1)	62	(12.2)	8	(1.6)
discontinued drug due to a serious adverse event	18	(5.6)	8	(2.5)	11	(5.8)	3	(1.6)	29	(5.7)	11	(2.2)
discontinued drug due to a serious drug-related adverse event	15	(4.7)	2	(0.6)	7	(3.7)	0	(0.0)	22	(4.3)	2	(0.4)

† Determined by the investigator to be related to the drug.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
EU Classification was updated after the MK3475-054 Recurrence-Free Survival Clinical Study Report such that Russia and Serbia have been re-classified as Ex-EU countries.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.2 Serious Adverse Events, Including Deaths

14.3.1.2.1 Deaths due to Adverse Events

Table 14.3-26

Subjects With Adverse Events Resulting in Death by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	1	(0.2)	0	(0.0)	1	(0.1)
with no adverse events	508	(99.8)	502	(100.0)	1,010	(99.9)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.2.2 Other Serious Adverse Events

Table 14.3-27

Subjects With Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	127	(25.0)	83	(16.5)	210	(20.8)
with no adverse events	382	(75.0)	419	(83.5)	801	(79.2)
Basal cell carcinoma	17	(3.3)	25	(5.0)	42	(4.2)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Pneumonitis	7	(1.4)	0	(0.0)	7	(0.7)
Squamous cell carcinoma	6	(1.2)	3	(0.6)	9	(0.9)
Diarrhoea	5	(1.0)	2	(0.4)	7	(0.7)
Bowen's disease	4	(0.8)	1	(0.2)	5	(0.5)
Malignant melanoma	4	(0.8)	3	(0.6)	7	(0.7)
Pyrexia	4	(0.8)	0	(0.0)	4	(0.4)
Aspartate aminotransferase increased	3	(0.6)	0	(0.0)	3	(0.3)
Cellulitis	3	(0.6)	7	(1.4)	10	(1.0)
Immune-mediated enterocolitis	3	(0.6)	0	(0.0)	3	(0.3)
Type 1 diabetes mellitus	3	(0.6)	0	(0.0)	3	(0.3)
Alanine aminotransferase increased	2	(0.4)	0	(0.0)	2	(0.2)
Anaphylactic reaction	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Decreased appetite	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Erysipelas	2	(0.4)	4	(0.8)	6	(0.6)
Hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Hyperglycaemia	2	(0.4)	0	(0.0)	2	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)	2	(0.2)
Pneumonia	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)
Animal bite	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	1	(0.2)	1	(0.2)	2	(0.2)
Appendiceal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Benign lymph node neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Benign neoplasm of testis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac failure congestive	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	1	(0.2)	2	(0.2)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Complicated appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Constipation	1	(0.2)	0	(0.0)	1	(0.1)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Drug reaction with eosinophilia and systemic symptoms	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	1	(0.2)	0	(0.0)	1	(0.1)
Food poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Gastroenteritis viral	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Headache	1	(0.2)	0	(0.0)	1	(0.1)
Hepatocellular carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	1	(0.2)	2	(0.4)	3	(0.3)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Interstitial lung disease	1	(0.2)	0	(0.0)	1	(0.1)
Intervertebral disc protrusion	1	(0.2)	2	(0.4)	3	(0.3)
Keratoacanthoma	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Lymphoedema	1	(0.2)	0	(0.0)	1	(0.1)
Malignant melanoma in situ	1	(0.2)	6	(1.2)	7	(0.7)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Melanocytic naevus	1	(0.2)	0	(0.0)	1	(0.1)
Meningioma	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Nephrolithiasis	1	(0.2)	0	(0.0)	1	(0.1)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Pleural effusion	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Post-traumatic pain	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	1	(0.2)	1	(0.2)	2	(0.2)
Psoriasis	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Sarcoidosis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Skin infection	1	(0.2)	1	(0.2)	2	(0.2)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Soft tissue infection	1	(0.2)	0	(0.0)	1	(0.1)
Squamous cell carcinoma of skin	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	1	(0.2)	0	(0.0)	1	(0.1)
Synovial rupture	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Urinary retention	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	0	(0.0)	1	(0.1)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Vertigo	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Viral infection	1	(0.2)	0	(0.0)	1	(0.1)
Wound necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	0	(0.0)	1	(0.2)	1	(0.1)
Angiolipoma	0	(0.0)	1	(0.2)	1	(0.1)
Atrial fibrillation	0	(0.0)	1	(0.2)	1	(0.1)
Benign prostatic hyperplasia	0	(0.0)	1	(0.2)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Cholelithiasis	0	(0.0)	1	(0.2)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)	1	(0.1)
Colon adenoma	0	(0.0)	1	(0.2)	1	(0.1)
Diverticulitis	0	(0.0)	1	(0.2)	1	(0.1)
Dizziness	0	(0.0)	1	(0.2)	1	(0.1)
Fasciitis	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Haemorrhoids	0	(0.0)	1	(0.2)	1	(0.1)
Infected seroma	0	(0.0)	2	(0.4)	2	(0.2)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Invasive ductal breast carcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Oesophageal haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haematoma	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)
Renal colic	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	1	(0.2)	1	(0.1)
Sciatica	0	(0.0)	1	(0.2)	1	(0.1)
Sertoli cell testicular tumour	0	(0.0)	1	(0.2)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.2)	1	(0.1)
Superficial spreading melanoma stage unspecified	0	(0.0)	1	(0.2)	1	(0.1)
Thrombophlebitis superficial	0	(0.0)	1	(0.2)	1	(0.1)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)
Upper respiratory tract infection	0	(0.0)	1	(0.2)	1	(0.1)
Vertebrobasilar insufficiency	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vomiting	0	(0.0)	1	(0.2)	1	(0.1)
Vulvitis	0	(0.0)	1	(0.2)	1	(0.1)

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

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

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-28

Subjects With Drug-related Serious Adverse Events by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	62	(12.2)	6	(1.2)	68	(6.7)
with no adverse events	447	(87.8)	496	(98.8)	943	(93.3)
Colitis	7	(1.4)	0	(0.0)	7	(0.7)
Pneumonitis	7	(1.4)	0	(0.0)	7	(0.7)
Diarrhoea	4	(0.8)	1	(0.2)	5	(0.5)
Aspartate aminotransferase increased	3	(0.6)	0	(0.0)	3	(0.3)
Immune-mediated enterocolitis	3	(0.6)	0	(0.0)	3	(0.3)
Type 1 diabetes mellitus	3	(0.6)	0	(0.0)	3	(0.3)
Alanine aminotransferase increased	2	(0.4)	0	(0.0)	2	(0.2)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Decreased appetite	2	(0.4)	0	(0.0)	2	(0.2)
Diabetic ketoacidosis	2	(0.4)	0	(0.0)	2	(0.2)
Hypophysitis	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Arthralgia	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Drug eruption	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypercreatininaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	1	(0.2)	1	(0.2)	2	(0.2)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-related Serious Adverse Events by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Psoriasis	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Sarcoidosis	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	1	(0.2)	2	(0.2)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.3 Other Clinically Meaningful Adverse Events

14.3.1.3.1 Adverse Events Leading to Study Intervention Discontinuation

Table 14.3-29

Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	71	(13.9)	18	(3.6)	89	(8.8)
with no adverse events	438	(86.1)	484	(96.4)	922	(91.2)
Pneumonitis	8	(1.6)	1	(0.2)	9	(0.9)
Colitis	6	(1.2)	0	(0.0)	6	(0.6)
Diarrhoea	5	(1.0)	0	(0.0)	5	(0.5)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Pulmonary embolism	3	(0.6)	0	(0.0)	3	(0.3)
Sarcoidosis	3	(0.6)	0	(0.0)	3	(0.3)
Arthralgia	2	(0.4)	0	(0.0)	2	(0.2)
Aspartate aminotransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Fatigue	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Haemoglobin increased	1	(0.2)	0	(0.0)	1	(0.1)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Large intestine perforation	1	(0.2)	0	(0.0)	1	(0.1)
Mantle cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Metastases to central nervous system	1	(0.2)	1	(0.2)	2	(0.2)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myocardial necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Nodular melanoma	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Renal cell carcinoma	1	(0.2)	1	(0.2)	2	(0.2)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Choroid melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Depression	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	0	(0.0)	1	(0.2)	1	(0.1)
Glomerulosclerosis	0	(0.0)	1	(0.2)	1	(0.1)
Immune-mediated enterocolitis	0	(0.0)	1	(0.2)	1	(0.1)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)	1	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Lentigo maligna	0	(0.0)	1	(0.2)	1	(0.1)
Malignant melanoma	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Rectal adenocarcinoma	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Secondary adrenocortical insufficiency	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-30

Subjects With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	62	(12.2)	8	(1.6)	70	(6.9)
with no adverse events	447	(87.8)	494	(98.4)	941	(93.1)
Pneumonitis	8	(1.6)	1	(0.2)	9	(0.9)
Colitis	6	(1.2)	0	(0.0)	6	(0.6)
Diarrhoea	5	(1.0)	0	(0.0)	5	(0.5)
Alanine aminotransferase increased	3	(0.6)	1	(0.2)	4	(0.4)
Hepatitis	3	(0.6)	1	(0.2)	4	(0.4)
Sarcoidosis	3	(0.6)	0	(0.0)	3	(0.3)
Arthralgia	2	(0.4)	0	(0.0)	2	(0.2)
Aspartate aminotransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Autoimmune hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Fatigue	2	(0.4)	0	(0.0)	2	(0.2)
Pulmonary embolism	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Aptyalism	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Colitis microscopic	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Diabetic ketoacidosis	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	1	(0.2)	1	(0.2)	2	(0.2)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Hypopituitarism	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Iridocyclitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Oral lichen planus	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events Resulting in Treatment Discontinuation by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Polymyalgia rheumatica	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Rheumatoid arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Small intestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Systemic inflammatory response syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	1	(0.2)	0	(0.0)	1	(0.1)
Depression	0	(0.0)	1	(0.2)	1	(0.1)
Dysgeusia	0	(0.0)	1	(0.2)	1	(0.1)
Immune-mediated enterocolitis	0	(0.0)	1	(0.2)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.2)	1	(0.1)
Secondary adrenocortical insufficiency	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.3.2 Adverse Events Leading to Study Intervention Interruption

Table 14.3-31

Subjects With Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	98	(19.3)	46	(9.2)	144	(14.2)
with no adverse events	411	(80.7)	456	(90.8)	867	(85.8)
Diarrhoea	11	(2.2)	4	(0.8)	15	(1.5)
Pneumonitis	11	(2.2)	2	(0.4)	13	(1.3)
Alanine aminotransferase increased	7	(1.4)	2	(0.4)	9	(0.9)
Arthralgia	7	(1.4)	0	(0.0)	7	(0.7)
Aspartate aminotransferase increased	7	(1.4)	3	(0.6)	10	(1.0)
Colitis	5	(1.0)	1	(0.2)	6	(0.6)
Fatigue	5	(1.0)	1	(0.2)	6	(0.6)
Cough	4	(0.8)	2	(0.4)	6	(0.6)
Dyspnoea	4	(0.8)	0	(0.0)	4	(0.4)
Lipase increased	3	(0.6)	2	(0.4)	5	(0.5)
Nausea	3	(0.6)	0	(0.0)	3	(0.3)
Pneumonia	3	(0.6)	2	(0.4)	5	(0.5)
Vomiting	3	(0.6)	0	(0.0)	3	(0.3)
Amylase increased	2	(0.4)	0	(0.0)	2	(0.2)
Blood alkaline phosphatase increased	2	(0.4)	1	(0.2)	3	(0.3)
Blood creatine phosphokinase increased	2	(0.4)	1	(0.2)	3	(0.3)
Blood creatinine increased	2	(0.4)	0	(0.0)	2	(0.2)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	3	(0.6)	5	(0.5)
Hepatitis	2	(0.4)	0	(0.0)	2	(0.2)
Hyperthyroidism	2	(0.4)	0	(0.0)	2	(0.2)
Hypopituitarism	2	(0.4)	0	(0.0)	2	(0.2)
Influenza like illness	2	(0.4)	4	(0.8)	6	(0.6)
Nasopharyngitis	2	(0.4)	0	(0.0)	2	(0.2)
Oral lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Pyrexia	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Anaphylactic reaction	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Back pain	1	(0.2)	0	(0.0)	1	(0.1)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	1	(0.2)	1	(0.2)	2	(0.2)
Dyspnoea exertional	1	(0.2)	1	(0.2)	2	(0.2)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Facial paralysis	1	(0.2)	0	(0.0)	1	(0.1)
Gastroenteritis viral	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal infection	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Headache	1	(0.2)	1	(0.2)	2	(0.2)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyponatraemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Ileus	1	(0.2)	0	(0.0)	1	(0.1)
Intervertebral disc protrusion	1	(0.2)	0	(0.0)	1	(0.1)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Ligament injury	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Meniscus injury	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Petit mal epilepsy	1	(0.2)	0	(0.0)	1	(0.1)
Pleural effusion	1	(0.2)	0	(0.0)	1	(0.1)
Post procedural cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Rash pustular	1	(0.2)	0	(0.0)	1	(0.1)
Renal failure	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Sinusitis	1	(0.2)	0	(0.0)	1	(0.1)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.1)
Trigeminal nerve disorder	1	(0.2)	0	(0.0)	1	(0.1)
Upper respiratory tract infection	1	(0.2)	0	(0.0)	1	(0.1)
Wound infection	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	0	(0.0)	2	(0.4)	2	(0.2)
Asthenia	0	(0.0)	1	(0.2)	1	(0.1)
Atrial fibrillation	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	0	(0.0)	1	(0.2)	1	(0.1)
Carotid artery aneurysm	0	(0.0)	1	(0.2)	1	(0.1)
Cataract	0	(0.0)	1	(0.2)	1	(0.1)
Cellulitis	0	(0.0)	2	(0.4)	2	(0.2)
Cholecystitis	0	(0.0)	1	(0.2)	1	(0.1)
Conjunctivitis viral	0	(0.0)	1	(0.2)	1	(0.1)
Diverticulitis	0	(0.0)	1	(0.2)	1	(0.1)
Gilbert's syndrome	0	(0.0)	1	(0.2)	1	(0.1)
Hyperlipasaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypertension	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.2)	1	(0.1)
Hypothyroidism	0	(0.0)	1	(0.2)	1	(0.1)
Infected seroma	0	(0.0)	1	(0.2)	1	(0.1)
Influenza	0	(0.0)	1	(0.2)	1	(0.1)
Insomnia	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	1	(0.2)	1	(0.1)
Lymph node pain	0	(0.0)	1	(0.2)	1	(0.1)
Musculoskeletal chest pain	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia	0	(0.0)	1	(0.2)	1	(0.1)
Nephritis	0	(0.0)	1	(0.2)	1	(0.1)
Platelet count decreased	0	(0.0)	1	(0.2)	1	(0.1)
Post procedural haemorrhage	0	(0.0)	1	(0.2)	1	(0.1)
Rash maculo-papular	0	(0.0)	1	(0.2)	1	(0.1)
Thrombocytopenia	0	(0.0)	1	(0.2)	1	(0.1)
Transient ischaemic attack	0	(0.0)	1	(0.2)	1	(0.1)

Subjects With Adverse Events Resulting in Treatment Interruption by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Vision blurred	0	(0.0)	3	(0.6)	3	(0.3)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-32

Subjects With Drug-Related Adverse Events Resulting in Treatment Interruption by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	74	(14.5)	18	(3.6)	92	(9.1)
with no adverse events	435	(85.5)	484	(96.4)	919	(90.9)
Diarrhoea	10	(2.0)	3	(0.6)	13	(1.3)
Pneumonitis	10	(2.0)	2	(0.4)	12	(1.2)
Arthralgia	7	(1.4)	0	(0.0)	7	(0.7)
Alanine aminotransferase increased	5	(1.0)	1	(0.2)	6	(0.6)
Aspartate aminotransferase increased	5	(1.0)	1	(0.2)	6	(0.6)
Colitis	5	(1.0)	1	(0.2)	6	(0.6)
Fatigue	4	(0.8)	0	(0.0)	4	(0.4)
Colitis microscopic	2	(0.4)	0	(0.0)	2	(0.2)
Cough	2	(0.4)	1	(0.2)	3	(0.3)
Dyspnoea	2	(0.4)	0	(0.0)	2	(0.2)
Gamma-glutamyltransferase increased	2	(0.4)	1	(0.2)	3	(0.3)
Hyperthyroidism	2	(0.4)	0	(0.0)	2	(0.2)
Hypopituitarism	2	(0.4)	0	(0.0)	2	(0.2)
Lipase increased	2	(0.4)	2	(0.4)	4	(0.4)
Nausea	2	(0.4)	0	(0.0)	2	(0.2)
Oral lichen planus	2	(0.4)	0	(0.0)	2	(0.2)
Thyroiditis	2	(0.4)	0	(0.0)	2	(0.2)
Type 1 diabetes mellitus	2	(0.4)	0	(0.0)	2	(0.2)
Vomiting	2	(0.4)	0	(0.0)	2	(0.2)
Abdominal pain	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Amnesia	1	(0.2)	0	(0.0)	1	(0.1)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Asthmatic crisis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune colitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	1	(0.2)	2	(0.2)
Blood creatinine increased	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Granuloma	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Adverse Events Resulting in Treatment Interruption by Decreasing Incidence (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Headache	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hidradenitis	1	(0.2)	0	(0.0)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Influenza like illness	1	(0.2)	1	(0.2)	2	(0.2)
Lichen planus	1	(0.2)	0	(0.0)	1	(0.1)
Lymphocytic hypophysitis	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenia gravis	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Oedema	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral sensory neuropathy	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Secondary adrenocortical insufficiency	1	(0.2)	0	(0.0)	1	(0.1)
Sinusitis	1	(0.2)	0	(0.0)	1	(0.1)
Asthenia	0	(0.0)	1	(0.2)	1	(0.1)
Hypothyroidism	0	(0.0)	1	(0.2)	1	(0.1)
Joint range of motion decreased	0	(0.0)	1	(0.2)	1	(0.1)
Myalgia	0	(0.0)	1	(0.2)	1	(0.1)
Rash maculo-papular	0	(0.0)	1	(0.2)	1	(0.1)
Thrombocytopenia	0	(0.0)	1	(0.2)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression" and "Disease progression" not related to the drug are excluded.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.3.1.4 Adverse Events of Special Interest

14.3.1.4.1 Summary of AEOSI

Table 14.3-33

Adverse Event Summary
AEOSI
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
with no adverse event	330	(64.8)	463	(92.2)	793	(78.4)
with drug-related† adverse events	165	(32.4)	30	(6.0)	195	(19.3)
with toxicity grade 3-5 adverse events	39	(7.7)	3	(0.6)	42	(4.2)
with toxicity grade 3-5 drug-related adverse events	34	(6.7)	3	(0.6)	37	(3.7)
with serious adverse events	40	(7.9)	3	(0.6)	43	(4.3)
with serious drug-related adverse events	36	(7.1)	2	(0.4)	38	(3.8)
who died	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)
discontinued drug due to an adverse event	34	(6.7)	6	(1.2)	40	(4.0)
discontinued drug due to a drug-related adverse event	34	(6.7)	5	(1.0)	39	(3.9)
discontinued drug due to a serious adverse event	12	(2.4)	3	(0.6)	15	(1.5)
discontinued drug due to a serious drug-related adverse event	12	(2.4)	2	(0.4)	14	(1.4)

† Determined by the investigator to be related to the drug.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-34

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence ≥ 5% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
Grade 1	43	(8.4)	21	(4.2)	64	(6.3)
Grade 2	97	(19.1)	15	(3.0)	112	(11.1)
Grade 3	34	(6.7)	3	(0.6)	37	(3.7)
Grade 4	5	(1.0)	0	(0.0)	5	(0.5)
with no adverse events	330	(64.8)	463	(92.2)	793	(78.4)
Hyperthyroidism	**53**	**(10.4)**	**6**	**(1.2)**	**59**	**(5.8)**
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypothyroidism	**76**	**(14.9)**	**13**	**(2.6)**	**89**	**(8.8)**
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 1.

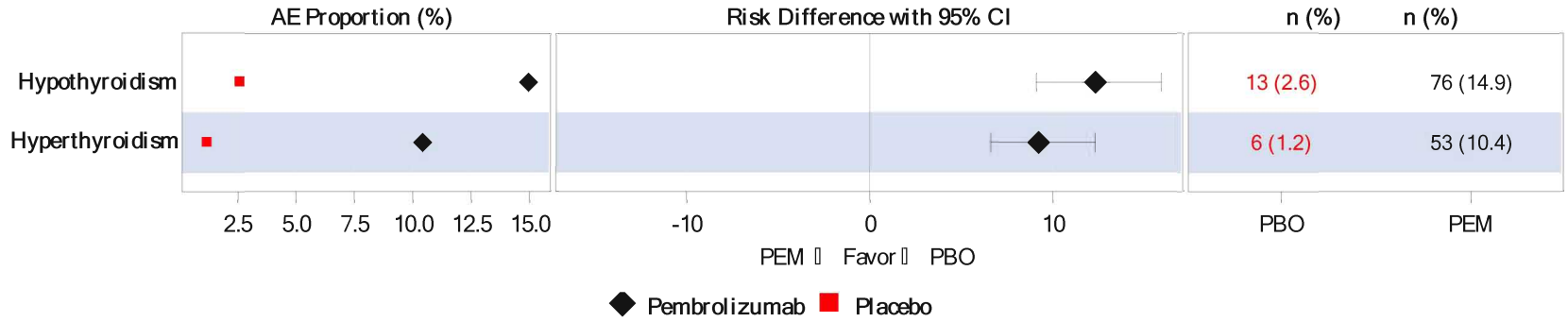
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Figure 14.3-3

Between-Treatment Comparisons in Adverse Events of Special Interest
Selected Adverse Events (≥5% Incidence) and Sorted by Risk Difference
(ASaT Population)
Pembrolizumab (N=509) vs. Placebo (N=502)



PEM: Pembrolizumab
PBO: Placebo
Database Cutoff Date: 03APR2020
Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-35

Adverse Event Summary
AEOSI
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	45	(26.5)
with no adverse event	125	(73.5)
with drug-related† adverse events	43	(25.3)
with toxicity grade 3-5 adverse events	11	(6.5)
with toxicity grade 3-5 drug-related adverse events	9	(5.3)
with serious adverse events	8	(4.7)
with serious drug-related adverse events	7	(4.1)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued drug due to an adverse event	7	(4.1)
discontinued drug due to a drug-related adverse event	7	(4.1)
discontinued drug due to a serious adverse event	3	(1.8)
discontinued drug due to a serious drug-related adverse event	3	(1.8)

† 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 and AEOSIs were followed 90 days after last dose of study treatment in Part 2.
AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-36

Subjects With Adverse Events of Special Interest (AEOSI) by Decreasing Incidence
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
with no adverse events	330	(64.8)	463	(92.2)	793	(78.4)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Colitis	20	(3.9)	3	(0.6)	23	(2.3)
Pneumonitis	19	(3.7)	3	(0.6)	22	(2.2)
Thyroiditis	14	(2.8)	2	(0.4)	16	(1.6)
Hypophysitis	11	(2.2)	1	(0.2)	12	(1.2)
Infusion Reactions	11	(2.2)	3	(0.6)	14	(1.4)
Hepatitis	9	(1.8)	1	(0.2)	10	(1.0)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Adrenal Insufficiency	5	(1.0)	4	(0.8)	9	(0.9)
Skin-A	5	(1.0)	0	(0.0)	5	(0.5)
Type 1 Diabetes Mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Nephritis	2	(0.4)	1	(0.2)	3	(0.3)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Uveitis	2	(0.4)	0	(0.0)	2	(0.2)
Myasthenic Syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)

Every subject is counted a single time for each applicable row and column.
AEs were followed 30 days after last dose of study treatment in Part 1.
SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-37

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	179	(35.2)	39	(7.8)	218	(21.6)
Grade 1	43	(8.4)	21	(4.2)	64	(6.3)
Grade 2	97	(19.1)	15	(3.0)	112	(11.1)
Grade 3	34	(6.7)	3	(0.6)	37	(3.7)
Grade 4	5	(1.0)	0	(0.0)	5	(0.5)
with no adverse events	330	(64.8)	463	(92.2)	793	(78.4)
Adrenal Insufficiency	**5**	**(1.0)**	**4**	**(0.8)**	**9**	**(0.9)**
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Adrenal Insufficiency	5	(1.0)	4	(0.8)	9	(0.9)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	**20**	**(3.9)**	**3**	**(0.6)**	**23**	**(2.3)**
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	8	(1.6)	2	(0.4)	10	(1.0)
Grade 3	11	(2.2)	1	(0.2)	12	(1.2)
Colitis	20	(3.9)	3	(0.6)	23	(2.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	8	(1.6)	2	(0.4)	10	(1.0)
Grade 3	11	(2.2)	1	(0.2)	12	(1.2)
Hepatitis	**9**	**(1.8)**	**1**	**(0.2)**	**10**	**(1.0)**
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	9	(1.8)	1	(0.2)	10	(1.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Hyperthyroidism	**53**	**(10.4)**	**6**	**(1.2)**	**59**	**(5.8)**
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hyperthyroidism	53	(10.4)	6	(1.2)	59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Hypophysitis	**11**	**(2.2)**	**1**	**(0.2)**	**12**	**(1.2)**
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	7	(1.4)	0	(0.0)	7	(0.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hypophysitis	11	(2.2)	1	(0.2)	12	(1.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	7	(1.4)	0	(0.0)	7	(0.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Hypothyroidism	**76**	**(14.9)**	**13**	**(2.6)**	**89**	**(8.8)**
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Hypothyroidism	76	(14.9)	13	(2.6)	89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Infusion Reactions	**11**	**(2.2)**	**3**	**(0.6)**	**14**	**(1.4)**
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Infusion Reactions	11	(2.2)	3	(0.6)	14	(1.4)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Myasthenic Syndrome	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Myasthenic Syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Myocarditis	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	1	(0.2)	2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Nephritis	**2**	**(0.4)**	**1**	**(0.2)**	**3**	**(0.3)**
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Nephritis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Pancreatitis	**2**	**(0.4)**	**1**	**(0.2)**	**3**	**(0.3)**
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Pancreatitis	2	(0.4)	1	(0.2)	3	(0.3)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0% in One or More Treatment Groups)
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Pneumonitis	**19**	**(3.7)**	**3**	**(0.6)**	**22**	**(2.2)**
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	14	(2.8)	2	(0.4)	16	(1.6)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Pneumonitis	19	(3.7)	3	(0.6)	22	(2.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	14	(2.8)	2	(0.4)	16	(1.6)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Sarcoidosis	7	**(1.4)**	**0**	**(0.0)**	7	**(0.7)**
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Sarcoidosis	7	(1.4)	0	(0.0)	7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Severe Skin Reactions	**5**	**(1.0)**	**0**	**(0.0)**	**5**	**(0.5)**
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Skin-A	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Thyroiditis	**14**	**(2.8)**	**2**	**(0.4)**	**16**	**(1.6)**
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
Thyroiditis	14	(2.8)	2	(0.4)	16	(1.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
Type 1 Diabetes Mellitus	**5**	**(1.0)**	**0**	**(0.0)**	**5**	**(0.5)**
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Type 1 Diabetes Mellitus	5	(1.0)	0	(0.0)	5	(0.5)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade (Incidence > 0% in One or More Treatment Groups) (ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Uveitis	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.2)**
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Uveitis	2	(0.4)	0	(0.0)	2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 subject.

Grades are based on NCI CTCAE version 4.03.

AEs were followed 30 days after last dose of study treatment in Part 1.

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-38

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0%)
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Subjects in population	170	
with one or more adverse events	45	(26.5)
Grade 1	6	(3.5)
Grade 2	28	(16.5)
Grade 3	9	(5.3)
Grade 4	2	(1.2)
with no adverse events	125	(73.5)
Adrenal Insufficiency	**1**	**(0.6)**
Grade 2	1	(0.6)
Adrenal Insufficiency	1	(0.6)
Grade 2	1	(0.6)
Colitis	**3**	**(1.8)**
Grade 1	1	(0.6)
Grade 2	1	(0.6)
Grade 3	1	(0.6)
Colitis	3	(1.8)
Grade 1	1	(0.6)
Grade 2	1	(0.6)
Grade 3	1	(0.6)
Hepatitis	**1**	**(0.6)**
Grade 2	1	(0.6)
Hepatitis	1	(0.6)
Grade 2	1	(0.6)
Hyperthyroidism	**17**	**(10.0)**
Grade 1	10	(5.9)
Grade 2	6	(3.5)
Grade 3	1	(0.6)
Hyperthyroidism	17	(10.0)
Grade 1	10	(5.9)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0%)
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Hyperthyroidism	17	(10.0)
Grade 2	6	(3.5)
Grade 3	1	(0.6)
Hypophysitis	**3**	**(1.8)**
Grade 2	2	(1.2)
Grade 3	1	(0.6)
Hypophysitis	3	(1.8)
Grade 2	2	(1.2)
Grade 3	1	(0.6)
Hypothyroidism	**24**	**(14.1)**
Grade 1	3	(1.8)
Grade 2	21	(12.4)
Hypothyroidism	24	(14.1)
Grade 1	3	(1.8)
Grade 2	21	(12.4)
Infusion Reactions	**2**	**(1.2)**
Grade 1	1	(0.6)
Grade 2	1	(0.6)
Infusion Reactions	2	(1.2)
Grade 1	1	(0.6)
Grade 2	1	(0.6)
Myositis	**1**	**(0.6)**
Grade 2	1	(0.6)
Myositis	1	(0.6)
Grade 2	1	(0.6)
Pancreatitis	**2**	**(1.2)**
Grade 2	1	(0.6)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade
(Incidence > 0%)
(ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Pancreatitis	**2**	**(1.2)**
Grade 3	1	(0.6)
Pancreatitis	2	(1.2)
Grade 2	1	(0.6)
Grade 3	1	(0.6)
Pneumonitis	**3**	**(1.8)**
Grade 2	1	(0.6)
Grade 3	2	(1.2)
Pneumonitis	3	(1.8)
Grade 2	1	(0.6)
Grade 3	2	(1.2)
Severe Skin Reactions	**5**	**(2.9)**
Grade 3	5	(2.9)
Skin-A	4	(2.4)
Grade 3	4	(2.4)
Skin-B	1	(0.6)
Grade 3	1	(0.6)
Type 1 Diabetes Mellitus	**3**	**(1.8)**
Grade 3	1	(0.6)
Grade 4	2	(1.2)
Type 1 Diabetes Mellitus	3	(1.8)
Grade 3	1	(0.6)

Subjects With Adverse Events of Special Interest (AEOSI) by Maximum Toxicity Grade (Incidence > 0%) (ASaT Population - Part 2)

	Pembrolizumab	
	n	(%)
Type 1 Diabetes Mellitus	3	(1.8)
Grade 4	2	(1.2)

Every subject is counted a single time for each applicable specific adverse event. A subject 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 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 subject.

Grades are based on NCI CTCAE version 4.03.

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

SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 2.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-39

Subjects with AEOSI with and without Systemic Corticosteroid Use
(Incidence > 0% in One or More Treatment Groups)
ASaT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1011	
Subjects with one or more events	179		39		218	
Treated with systemic corticosteroid	58	(32.4)	8	(20.5)	66	(30.3)
Not treated with systemic corticosteroid	121	(67.6)	31	(79.5)	152	(69.7)
Adrenal Insufficiency						
Subjects with one or more events	5		4		9	
Treated with systemic corticosteroid	1	(20.0)	1	(25.0)	2	(22.2)
Not treated with systemic corticosteroid	4	(80.0)	3	(75.0)	7	(77.8)
Colitis						
Subjects with one or more events	20		3		23	
Treated with systemic corticosteroid	19	(95.0)	3	(100.0)	22	(95.7)
Not treated with systemic corticosteroid	1	(5.0)	0	(0.0)	1	(4.3)
Hepatitis						
Subjects with one or more events	9		1		10	
Treated with systemic corticosteroid	6	(66.7)	1	(100.0)	7	(70.0)
Not treated with systemic corticosteroid	3	(33.3)	0	(0.0)	3	(30.0)
Hyperthyroidism						
Subjects with one or more events	53		6		59	
Treated with systemic corticosteroid	4	(7.5)	0	(0.0)	4	(6.8)
Not treated with systemic corticosteroid	49	(92.5)	6	(100.0)	55	(93.2)
Hypophysitis						
Subjects with one or more events	11		1		12	
Treated with systemic corticosteroid	4	(36.4)	0	(0.0)	4	(33.3)
Not treated with systemic corticosteroid	7	(63.6)	1	(100.0)	8	(66.7)
Hypothyroidism						
Subjects with one or more events	76		13		89	
Treated with systemic corticosteroid	1	(1.3)	0	(0.0)	1	(1.1)
Not treated with systemic corticosteroid	75	(98.7)	13	(100.0)	88	(98.9)
Infusion Reactions						

The number of subjects with one or more events is used as the denominator for the percentage calculation.
(Database Cutoff Date: 03APR2020).

Subjects with AEOSI with and without Systemic Corticosteroid Use (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects with one or more events	11		3		14	
Treated with systemic corticosteroid	2	(18.2)	0	(0.0)	2	(14.3)
Not treated with systemic corticosteroid	9	(81.8)	3	(100.0)	12	(85.7)
Myasthenic Syndrome						
Subjects with one or more events	1		0		1	
Treated with systemic corticosteroid	1	(100.0)	0	(0.0)	1	(100.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Myocarditis						
Subjects with one or more events	1		0		1	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	1	(100.0)	0	(0.0)	1	(100.0)
Myositis						
Subjects with one or more events	1		1		2	
Treated with systemic corticosteroid	1	(100.0)	0	(0.0)	1	(50.0)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)	1	(50.0)
Nephritis						
Subjects with one or more events	2		1		3	
Treated with systemic corticosteroid	2	(100.0)	1	(100.0)	3	(100.0)
Not treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Pancreatitis						
Subjects with one or more events	2		1		3	
Treated with systemic corticosteroid	2	(100.0)	0	(0.0)	2	(66.7)
Not treated with systemic corticosteroid	0	(0.0)	1	(100.0)	1	(33.3)
Pneumonitis						
Subjects with one or more events	19		3		22	
Treated with systemic corticosteroid	17	(89.5)	2	(66.7)	19	(86.4)
Not treated with systemic corticosteroid	2	(10.5)	1	(33.3)	3	(13.6)
Sarcoidosis						
Subjects with one or more events	7		0		7	

The number of subjects with one or more events is used as the denominator for the percentage calculation.
(Database Cutoff Date: 03APR2020).

Subjects with AEOSI with and without Systemic Corticosteroid Use (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	7	(100.0)	0	(0.0)	7	(100.0)
Severe Skin Reactions						
Subjects with one or more events	5		0		5	
Treated with systemic corticosteroid	3	(60.0)	0	(0.0)	3	(60.0)
Not treated with systemic corticosteroid	2	(40.0)	0	(0.0)	2	(40.0)
Thyroiditis						
Subjects with one or more events	14		2		16	
Treated with systemic corticosteroid	3	(21.4)	0	(0.0)	3	(18.8)
Not treated with systemic corticosteroid	11	(78.6)	2	(100.0)	13	(81.3)
Type 1 Diabetes Mellitus						
Subjects with one or more events	5		0		5	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	5	(100.0)	0	(0.0)	5	(100.0)
Uveitis						
Subjects with one or more events	2		0		2	
Treated with systemic corticosteroid	0	(0.0)	0	(0.0)	0	(0.0)
Not treated with systemic corticosteroid	2	(100.0)	0	(0.0)	2	(100.0)

The number of subjects with one or more events is used as the denominator for the percentage calculation.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-40

Time to Onset and Duration of AEOSI
(Incidence > 0% in One or More Treatment Groups)
ASaT Population

	Pembrolizumab	Placebo	Total
Subjects in population	**509**	**502**	**1011**
Subjects with AEOSI (%)	179 (35.2)	39 (7.8)	218 (21.6)
Time to Onset of First AEOSI (days)†			
Mean (SD)	126.4 (103.4)	129.8 (92.4)	127.0 (101.3)
Median	86.0	104.0	90.0
Range	1 to 441	1 to 344	1 to 441
Total number of episodes of AEOSI	364	53	417
Average number of episodes of AEOSI per subject	2.0	1.4	1.9
Episode Durations (days)‡			
Median	43.0	36.0	43.0
Range	1 to 1548+	1 to 1454+	1 to 1548+
Adrenal Insufficiency			
Subjects with AEOSI (%)	5 (1.0)	4 (0.8)	9 (0.9)
Time to Onset of First AEOSI (days)†			
Mean (SD)	319.2 (83.8)	152.3 (79.4)	245.0 (116.7)
Median	341.0	146.5	252.0
Range	207 to 423	64 to 252	64 to 423
Total number of episodes of AEOSI	5	4	9
Average number of episodes of AEOSI per subject	1.0	1.0	1.0
Episode Durations (days)‡			
Median	152.0	49.0	90.0
Range	12 to 1159+	3 to 230	3 to 1159+
Colitis			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Colitis			
Subjects with AEOSI (%)	20 (3.9)	3 (0.6)	23 (2.3)
Time to Onset of First AEOSI (days)†			
Mean (SD)	201.4 (122.6)	144.3 (126.1)	193.9 (121.7)
Median	177.0	86.0	175.0
Range	47 to 416	58 to 289	47 to 416
Total number of episodes of AEOSI	53	3	56
Average number of episodes of AEOSI per subject	2.7	1.0	2.4
Episode Durations (days)‡			
Median	10.0	21.0	10.0
Range	1 to 1376+	10 to 36	1 to 1376+
Hepatitis			
Subjects with AEOSI (%)	9 (1.8)	1 (0.2)	10 (1.0)
Time to Onset of First AEOSI (days)†			
Mean (SD)	217.3 (97.6)	43.0 (--)	199.9 (107.3)
Median	200.0	43.0	189.5
Range	84 to 358	43 to 43	43 to 358
Total number of episodes of AEOSI	24	3	27
Average number of episodes of AEOSI per subject	2.7	3.0	2.7
Episode Durations (days)‡			
Median	9.5	1.0	9.0
Range	1 to 201	1 to 23	1 to 201
Hyperthyroidism			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Hyperthyroidism			
Subjects with AEOSI (%)	53 (10.4)	6 (1.2)	59 (5.8)
Time to Onset of First AEOSI (days)†			
Mean (SD)	65.1 (67.9)	186.5 (76.2)	77.4 (77.5)
Median	43.0	211.5	43.0
Range	15 to 377	64 to 254	15 to 377
Total number of episodes of AEOSI	63	6	69
Average number of episodes of AEOSI per subject	1.2	1.0	1.2
Episode Durations (days)‡			
Median	43.0	64.5	43.0
Range	4 to 1311+	20 to 441	4 to 1311+
Hypophysitis			
Subjects with AEOSI (%)	11 (2.2)	1 (0.2)	12 (1.2)
Time to Onset of First AEOSI (days)†			
Mean (SD)	216.4 (79.9)	42.0 (--)	201.8 (91.3)
Median	210.0	42.0	209.0
Range	93 to 358	42 to 42	42 to 358
Total number of episodes of AEOSI	17	1	18
Average number of episodes of AEOSI per subject	1.5	1.0	1.5
Episode Durations (days)‡			
Median	43.0	316.0	43.5
Range	3 to 1464+	316 to 316	3 to 1464+
Hypothyroidism			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Hypothyroidism			
Subjects with AEOSI (%)	76 (14.9)	13 (2.6)	89 (8.8)
Time to Onset of First AEOSI (days)†			
Mean (SD)	126.6 (81.6)	125.7 (75.2)	126.4 (80.3)
Median	104.0	106.0	106.0
Range	42 to 432	43 to 272	42 to 432
Total number of episodes of AEOSI	94	13	107
Average number of episodes of AEOSI per subject	1.2	1.0	1.2
Episode Durations (days)‡			
Median	Not reached	281.0	Not reached
Range	3 to 1480+	22 to 1454+	3 to 1480+
Infusion Reactions			
Subjects with AEOSI (%)	11 (2.2)	3 (0.6)	14 (1.4)
Time to Onset of First AEOSI (days)†			
Mean (SD)	171.4 (145.4)	1.0 (0.0)	134.9 (146.7)
Median	128.0	1.0	81.5
Range	1 to 441	1 to 1	1 to 441
Total number of episodes of AEOSI	11	4	15
Average number of episodes of AEOSI per subject	1.0	1.3	1.1
Episode Durations (days)‡			
Median	7.0	1.5	2.0
Range	1 to 64	1 to 391	1 to 391
Myasthenic Syndrome			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Myasthenic Syndrome			
Subjects with AEOSI (%)	1 (0.2)	0 (0.0)	1 (0.1)
Time to Onset of First AEOSI (days)†			
Mean (SD)	36.0 (--)		36.0 (--)
Median	36.0		36.0
Range	36 to 36		36 to 36
Total number of episodes of AEOSI	3		3
Average number of episodes of AEOSI per subject	3.0		3.0
Episode Durations (days)‡			
Median	10.0		10.0
Range	8 to 1249+		8 to 1249+
Myocarditis			
Subjects with AEOSI (%)	1 (0.2)	0 (0.0)	1 (0.1)
Time to Onset of First AEOSI (days)†			
Mean (SD)	138.0 (--)		138.0 (--)
Median	138.0		138.0
Range	138 to 138		138 to 138
Total number of episodes of AEOSI	2		2
Average number of episodes of AEOSI per subject	2.0		2.0
Episode Durations (days)‡			
Median	34.0		34.0
Range	5 to 63		5 to 63
Myositis			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Myositis			
Subjects with AEOSI (%)	1 (0.2)	1 (0.2)	2 (0.2)
Time to Onset of First AEOSI (days)†			
Mean (SD)	183.0 (--)	104.0 (--)	143.5 (55.9)
Median	183.0	104.0	143.5
Range	183 to 183	104 to 104	104 to 183
Total number of episodes of AEOSI	2	1	3
Average number of episodes of AEOSI per subject	2.0	1.0	1.5
Episode Durations (days)‡			
Median	40.5	27.0	39.0
Range	39 to 42	27 to 27	27 to 42
Nephritis			
Subjects with AEOSI (%)	2 (0.4)	1 (0.2)	3 (0.3)
Time to Onset of First AEOSI (days)†			
Mean (SD)	396.0 (39.6)	344.0 (--)	378.7 (41.1)
Median	396.0	344.0	368.0
Range	368 to 424	344 to 344	344 to 424
Total number of episodes of AEOSI	3	9	12
Average number of episodes of AEOSI per subject	1.5	9.0	4.0
Episode Durations (days)‡			
Median	13.0	5.0	6.0
Range	6 to 138	2 to 1035+	2 to 1035+
Pancreatitis			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Pancreatitis			
Subjects with AEOSI (%)	2 (0.4)	1 (0.2)	3 (0.3)
Time to Onset of First AEOSI (days)†			
Mean (SD)	354.0 (63.6)	81.0 (--)	263.0 (163.9)
Median	354.0	81.0	309.0
Range	309 to 399	81 to 81	81 to 399
Total number of episodes of AEOSI	3	2	5
Average number of episodes of AEOSI per subject	1.5	2.0	1.7
Episode Durations (days)‡			
Median	21.0	5.5	10.0
Range	10 to 72	5 to 6	5 to 72
Pneumonitis			
Subjects with AEOSI (%)	19 (3.7)	3 (0.6)	22 (2.2)
Time to Onset of First AEOSI (days)†			
Mean (SD)	164.6 (123.1)	90.7 (59.4)	154.5 (118.3)
Median	121.0	79.0	117.0
Range	24 to 431	38 to 155	24 to 431
Total number of episodes of AEOSI	37	5	42
Average number of episodes of AEOSI per subject	1.9	1.7	1.9
Episode Durations (days)‡			
Median	29.0	64.0	34.5
Range	2 to 1175+	10 to 146	2 to 1175+
Sarcoidosis			

Time to Onset and Duration of AEOSI
(Incidence > 0% in One or More Treatment Groups)
ASaT Population

	Pembrolizumab	Placebo	Total
Sarcoidosis			
Subjects with AEOSI (%)	7 (1.4)	0 (0.0)	7 (0.7)
Time to Onset of First AEOSI (days)†			
Mean (SD)	107.0 (52.4)		107.0 (52.4)
Median	86.0		86.0
Range	37 to 186		37 to 186
Total number of episodes of AEOSI	9		9
Average number of episodes of AEOSI per subject	1.3		1.3
Episode Durations (days)‡			
Median	124.0		124.0
Range	2 to 1548+		2 to 1548+
Severe Skin Reactions			
Subjects with AEOSI (%)	5 (1.0)	0 (0.0)	5 (0.5)
Time to Onset of First AEOSI (days)†			
Mean (SD)	163.4 (60.0)		163.4 (60.0)
Median	148.0		148.0
Range	106 to 232		106 to 232
Total number of episodes of AEOSI	7		7
Average number of episodes of AEOSI per subject	1.4		1.4
Episode Durations (days)‡			
Median	21.0		21.0
Range	1 to 50		1 to 50
Thyroiditis			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Thyroiditis			
Subjects with AEOSI (%)	14 (2.8)	2 (0.4)	16 (1.6)
Time to Onset of First AEOSI (days)†			
Mean (SD)	59.0 (33.3)	190.0 (147.1)	75.4 (66.4)
Median	45.0	190.0	55.5
Range	7 to 128	86 to 294	7 to 294
Total number of episodes of AEOSI	16	2	18
Average number of episodes of AEOSI per subject	1.1	1.0	1.1
Episode Durations (days)‡			
Median	85.0	Not reached	86.0
Range	2 to 1450+	528+ to 1103+	2 to 1450+
Type 1 Diabetes Mellitus			
Subjects with AEOSI (%)	5 (1.0)	0 (0.0)	5 (0.5)
Time to Onset of First AEOSI (days)†			
Mean (SD)	115.6 (113.8)		115.6 (113.8)
Median	64.0		64.0
Range	43 to 315		43 to 315
Total number of episodes of AEOSI	12		12
Average number of episodes of AEOSI per subject	2.4		2.4
Episode Durations (days)‡			
Median	10.5		10.5
Range	2 to 1359+		2 to 1359+
Uveitis			

Time to Onset and Duration of AEOSI (Incidence > 0% in One or More Treatment Groups) ASaT Population

	Pembrolizumab	Placebo	Total
Uveitis			
Subjects with AEOSI (%)	2 (0.4)	0 (0.0)	2 (0.2)
Time to Onset of First AEOSI (days)†			
Mean (SD)	313.5 (17.7)		313.5 (17.7)
Median	313.5		313.5
Range	301 to 326		301 to 326
Total number of episodes of AEOSI	3		3
Average number of episodes of AEOSI per subject	1.5		1.5
Episode Durations (days)‡			
Median	38.0		38.0
Range	34 to 40		34 to 40

(%) = Number of subjects with AEOSI / Number of subjects in population.

† Time to onset statistics are based on number of subjects with AEOSI.

‡ From product-limit (Kaplan-Meier) method for censored data. If an adverse event is not resolved at the time of analysis or the subject 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.

(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-41

Adverse Event of Special Interest Summary
AEOSI - Adrenal Insufficiency
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	5	(1.0)	4	(0.8)	9	(0.9)
with adverse event with maximum toxicity grade:					9	(0.9)
Grade 1	0	(0.0)	2	(0.4)	2	(0.2)
Grade 2	4	(0.8)	2	(0.4)	6	(0.6)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	3	(0.6)	4	(0.8)	7	(0.7)
who needed steroids to treat/resolve the adverse event	1	(0.2)	1	(0.2)	2	(0.2)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-42

Adverse Event of Special Interest Summary
AEOSI - Colitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	20	(3.9)	3	(0.6)	23	(2.3)
with adverse event with maximum toxicity grade:					23	(2.3)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	8	(1.6)	2	(0.4)	10	(1.0)
Grade 3	11	(2.2)	1	(0.2)	12	(1.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	18	(3.5)	3	(0.6)	21	(2.1)
who needed steroids to treat/resolve the adverse event	19	(3.7)	3	(0.6)	22	(2.2)
who needed an additional immune modulating drug to treat/resolve the adverse event	3	(0.6)	1	(0.2)	4	(0.4)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-43

Adverse Event of Special Interest Summary
AEOSI - Hepatitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	9	(1.8)	1	(0.2)	10	(1.0)
with adverse event with maximum toxicity grade:					10	(1.0)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	6	(1.2)	1	(0.2)	7	(0.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	8	(1.6)	1	(0.2)	9	(0.9)
who needed steroids to treat/resolve the adverse event	6	(1.2)	1	(0.2)	7	(0.7)
who needed an additional immune modulating drug to treat/resolve the adverse event	1	(0.2)	0	(0.0)	1	(0.1)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-44

Adverse Event of Special Interest Summary
AEOSI - Hyperthyroidism
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	53	(10.4)	6	(1.2)	59	(5.8)
with adverse event with maximum toxicity grade:					59	(5.8)
Grade 1	40	(7.9)	6	(1.2)	46	(4.5)
Grade 2	13	(2.6)	0	(0.0)	13	(1.3)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	52	(10.2)	5	(1.0)	57	(5.6)
who needed steroids to treat/resolve the adverse event	4	(0.8)	0	(0.0)	4	(0.4)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-45

Adverse Event of Special Interest Summary
AEOSI - Hypophysitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	11	(2.2)	1	(0.2)	12	(1.2)
with adverse event with maximum toxicity grade:					12	(1.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	7	(1.4)	0	(0.0)	7	(0.7)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	6	(1.2)	0	(0.0)	6	(0.6)
who needed steroids to treat/resolve the adverse event	4	(0.8)	0	(0.0)	4	(0.4)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-46

Adverse Event of Special Interest Summary
AEOSI - Hypothyroidism
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	76	(14.9)	13	(2.6)	89	(8.8)
with adverse event with maximum toxicity grade:					89	(8.8)
Grade 1	14	(2.8)	7	(1.4)	21	(2.1)
Grade 2	62	(12.2)	6	(1.2)	68	(6.7)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	20	(3.9)	8	(1.6)	28	(2.8)
who needed steroids to treat/resolve the adverse event	1	(0.2)	0	(0.0)	1	(0.1)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-47

Adverse Event of Special Interest Summary
AEOSI - Infusion Reactions
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	11	(2.2)	3	(0.6)	14	(1.4)
with adverse event with maximum toxicity grade:					14	(1.4)
Grade 1	7	(1.4)	3	(0.6)	10	(1.0)
Grade 2	2	(0.4)	0	(0.0)	2	(0.2)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	2	(0.4)	0	(0.0)	2	(0.2)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	11	(2.2)	3	(0.6)	14	(1.4)
who needed steroids to treat/resolve the adverse event	2	(0.4)	0	(0.0)	2	(0.2)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-48

Adverse Event of Special Interest Summary
AEOSI - Myasthenic Syndrome
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	1	(0.2)	0	(0.0)	1	(0.1)
with adverse event with maximum toxicity grade:					1	(0.1)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	0	(0.0)	0	(0.0)	0	(0.0)
who needed steroids to treat/resolve the adverse event	1	(0.2)	0	(0.0)	1	(0.1)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-49

Adverse Event of Special Interest Summary
AEOSI - Myocarditis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	1	(0.2)	0	(0.0)	1	(0.1)
with adverse event with maximum toxicity grade:					1	(0.1)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	1	(0.2)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	1	(0.2)	0	(0.0)	1	(0.1)
who needed steroids to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-50

Adverse Event of Special Interest Summary
AEOSI - Myositis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	1	(0.2)	1	(0.2)	2	(0.2)
with adverse event with maximum toxicity grade:					2	(0.2)
Grade 1	0	(0.0)	1	(0.2)	1	(0.1)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	0	(0.0)	1	(0.2)	1	(0.1)
who needed steroids to treat/resolve the adverse event	1	(0.2)	0	(0.0)	1	(0.1)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-51

Adverse Event of Special Interest Summary
AEOSI - Nephritis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	2	(0.4)	1	(0.2)	3	(0.3)
with adverse event with maximum toxicity grade:					3	(0.3)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3	2	(0.4)	0	(0.0)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	2	(0.4)	0	(0.0)	2	(0.2)
who needed steroids to treat/resolve the adverse event	2	(0.4)	1	(0.2)	3	(0.3)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-52

Adverse Event of Special Interest Summary
AEOSI - Pancreatitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	2	(0.4)	1	(0.2)	3	(0.3)
with adverse event with maximum toxicity grade:					3	(0.3)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	2	(0.4)	1	(0.2)	3	(0.3)
who needed steroids to treat/resolve the adverse event	2	(0.4)	0	(0.0)	2	(0.2)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-53

Adverse Event of Special Interest Summary
AEOSI - Pneumonitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	19	(3.7)	3	(0.6)	22	(2.2)
with adverse event with maximum toxicity grade:					22	(2.2)
Grade 1	1	(0.2)	1	(0.2)	2	(0.2)
Grade 2	14	(2.8)	2	(0.4)	16	(1.6)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	16	(3.1)	3	(0.6)	19	(1.9)
who needed steroids to treat/resolve the adverse event	17	(3.3)	2	(0.4)	19	(1.9)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-54

Adverse Event of Special Interest Summary
AEOSI - Sarcoidosis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	7	(1.4)	0	(0.0)	7	(0.7)
with adverse event with maximum toxicity grade:					7	(0.7)
Grade 1	7	(1.4)	0	(0.0)	7	(0.7)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	4	(0.8)	0	(0.0)	4	(0.4)
who needed steroids to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-55

Adverse Event of Special Interest Summary
AEOSI - Severe Skin Reactions
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	5	(1.0)	0	(0.0)	5	(0.5)
with adverse event with maximum toxicity grade:					5	(0.5)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	5	(1.0)	0	(0.0)	5	(0.5)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	2	(0.4)	0	(0.0)	2	(0.2)
who needed steroids to treat/resolve the adverse event	3	(0.6)	0	(0.0)	3	(0.3)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-56

Adverse Event of Special Interest Summary
AEOSI - Thyroiditis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	14	(2.8)	2	(0.4)	16	(1.6)
with adverse event with maximum toxicity grade:					16	(1.6)
Grade 1	5	(1.0)	0	(0.0)	5	(0.5)
Grade 2	9	(1.8)	2	(0.4)	11	(1.1)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	12	(2.4)	0	(0.0)	12	(1.2)
who needed steroids to treat/resolve the adverse event	3	(0.6)	0	(0.0)	3	(0.3)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-57

Adverse Event of Special Interest Summary
AEOSI - Type 1 Diabetes Mellitus
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	5	(1.0)	0	(0.0)	5	(0.5)
with adverse event with maximum toxicity grade:					5	(0.5)
Grade 1	0	(0.0)	0	(0.0)	0	(0.0)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	4	(0.8)	0	(0.0)	4	(0.4)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	3	(0.6)	0	(0.0)	3	(0.3)
who needed steroids to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

Table 14.3-58

Adverse Event of Special Interest Summary
AEOSI - Uveitis
(ASaT Population)

	Pembrolizumab		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	509		502		1,011	
with one or more adverse events	2	(0.4)	0	(0.0)	2	(0.2)
with adverse event with maximum toxicity grade:					2	(0.2)
Grade 1	1	(0.2)	0	(0.0)	1	(0.1)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 5	0	(0.0)	0	(0.0)	0	(0.0)
with adverse event resolved/resolved with sequelae	2	(0.4)	0	(0.0)	2	(0.2)
who needed steroids to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)
who needed an additional immune modulating drug to treat/resolve the adverse event	0	(0.0)	0	(0.0)	0	(0.0)

Only the highest reported grade of a given adverse event is counted for the individual subject.
AEs were followed 30 days after last dose of study treatment in Part 1; SAEs and AEOSIs were followed 90 days after last dose of study treatment in Part 1. AEs of special interest per ECI guidance.
(Database Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adae]

14.4 Clinical Laboratory Evaluation

14.4.1 Laboratory Values Over Time

Table 14.4-1

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Alanine Aminotransferase (IU/L)								
Cycle 2	Pembrolizumab	52	25.5 (12.6)	[4.0, 69.0]	26.8 (12.4)	[7.0, 61.0]	1.3 (12.2)	[-35.0, 40.0]
	Placebo	52	25.9 (14.3)	[9.0, 72.0]	29.9 (22.4)	[9.0, 118.0]	4.0 (19.0)	[-28.0, 78.0]
Cycle 3	Pembrolizumab	478	26.2 (14.3)	[4.0, 114.0]	28.1 (22.2)	[5.0, 223.0]	1.9 (21.6)	[-81.0, 200.0]
	Placebo	483	25.1 (13.7)	[5.0, 120.0]	24.1 (12.6)	[5.0, 117.0]	-1.1 (10.2)	[-62.0, 61.0]
Cycle 4	Pembrolizumab	48	24.6 (10.7)	[10.0, 69.0]	28.0 (15.0)	[10.0, 76.0]	3.4 (10.7)	[-14.0, 34.0]
	Placebo	41	25.1 (13.4)	[10.0, 72.0]	26.3 (20.1)	[7.0, 126.0]	1.2 (16.3)	[-32.0, 73.0]
Cycle 5	Pembrolizumab	442	26.3 (14.2)	[4.0, 114.0]	27.6 (31.7)	[5.0, 430.0]	1.3 (29.2)	[-88.0, 380.0]
	Placebo	423	24.8 (13.5)	[5.0, 120.0]	23.7 (12.4)	[5.0, 111.0]	-1.1 (10.3)	[-49.0, 73.0]
Cycle 6	Pembrolizumab	55	25.5 (12.3)	[10.0, 86.0]	26.5 (14.6)	[10.0, 90.0]	1.1 (10.5)	[-17.0, 46.0]
	Placebo	31	21.5 (10.8)	[10.0, 60.0]	19.8 (7.6)	[8.0, 42.0]	-1.7 (9.2)	[-38.0, 13.0]
Cycle 7	Pembrolizumab	411	26.0 (14.1)	[4.0, 114.0]	25.1 (15.6)	[4.0, 159.0]	-0.9 (16.1)	[-97.0, 139.0]
	Placebo	394	24.6 (13.2)	[5.0, 120.0]	23.5 (14.0)	[5.0, 170.0]	-1.1 (12.5)	[-52.0, 153.0]
Cycle 8	Pembrolizumab	42	24.2 (8.5)	[10.0, 50.0]	26.4 (13.1)	[12.0, 66.0]	2.3 (12.4)	[-18.0, 42.0]
	Placebo	41	27.8 (15.7)	[6.0, 72.0]	28.6 (18.7)	[9.0, 95.0]	0.9 (19.0)	[-32.0, 78.0]
Cycle 9	Pembrolizumab	382	26.0 (14.0)	[4.0, 114.0]	24.3 (12.4)	[7.0, 95.0]	-1.6 (12.7)	[-88.0, 47.0]
	Placebo	363	25.1 (13.8)	[5.0, 120.0]	23.5 (12.5)	[6.0, 123.0]	-1.6 (11.6)	[-60.0, 106.0]
Cycle 10	Pembrolizumab	41	27.3 (13.2)	[13.0, 86.0]	27.7 (15.1)	[9.0, 78.0]	0.4 (11.3)	[-22.0, 33.0]
	Placebo	33	24.8 (14.0)	[10.0, 72.0]	27.2 (24.9)	[11.0, 153.0]	2.3 (25.2)	[-28.0, 136.0]
Cycle 11	Pembrolizumab	363	26.0 (14.1)	[4.0, 114.0]	25.0 (13.9)	[3.0, 129.0]	-1.0 (13.9)	[-86.0, 65.0]
	Placebo	343	25.0 (13.6)	[5.0, 120.0]	24.6 (15.8)	[5.0, 163.0]	-0.4 (14.8)	[-50.0, 146.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 12	Pembrolizumab	33	25.0 (8.5)	[13.0, 51.0]	29.0 (18.4)	[10.0, 111.0]	4.0 (20.2)	[-21.0, 97.0]
	Placebo	29	24.3 (11.7)	[12.0, 67.0]	26.5 (19.8)	[15.0, 120.0]	2.2 (21.7)	[-36.0, 103.0]
Cycle 13	Pembrolizumab	338	26.0 (13.9)	[4.0, 114.0]	25.1 (14.0)	[2.0, 111.0]	-0.9 (14.8)	[-95.0, 94.0]
	Placebo	318	24.9 (13.5)	[5.0, 120.0]	23.8 (13.3)	[5.0, 106.0]	-1.1 (12.3)	[-54.0, 89.0]
Cycle 14	Pembrolizumab	39	27.3 (10.3)	[13.0, 51.0]	25.9 (10.2)	[8.0, 48.0]	-1.4 (10.6)	[-26.0, 25.0]
	Placebo	27	23.1 (9.3)	[10.0, 51.0]	25.0 (11.8)	[14.0, 68.0]	1.9 (12.2)	[-17.0, 51.0]
Cycle 15	Pembrolizumab	328	25.8 (13.8)	[4.0, 114.0]	24.2 (12.6)	[4.0, 109.0]	-1.6 (12.5)	[-93.0, 38.0]
	Placebo	317	24.9 (13.6)	[5.0, 120.0]	23.9 (13.2)	[5.0, 130.0]	-1.0 (11.3)	[-50.0, 60.0]
Cycle 16	Pembrolizumab	39	27.9 (14.5)	[7.0, 87.0]	32.4 (26.1)	[6.0, 144.0]	4.5 (17.8)	[-21.0, 57.0]
	Placebo	21	24.9 (13.9)	[10.0, 72.0]	30.3 (30.7)	[8.0, 154.0]	5.4 (28.4)	[-22.0, 121.0]
Cycle 17	Pembrolizumab	307	25.9 (14.2)	[4.0, 114.0]	25.6 (16.8)	[7.0, 151.0]	-0.3 (16.4)	[-86.0, 100.0]
	Placebo	305	24.9 (13.7)	[5.0, 120.0]	23.6 (11.5)	[4.0, 90.0]	-1.4 (10.8)	[-58.0, 38.0]
Cycle 18	Pembrolizumab	46	27.0 (16.1)	[7.0, 87.0]	32.2 (29.2)	[9.0, 181.0]	5.2 (26.0)	[-50.0, 127.0]
	Placebo	36	25.9 (14.7)	[7.0, 72.0]	22.4 (8.1)	[10.0, 37.0]	-3.5 (11.7)	[-38.0, 18.0]
Cycle 19	Pembrolizumab	43	23.6 (8.6)	[10.0, 51.0]	26.0 (20.7)	[10.0, 125.0]	2.4 (19.4)	[-22.0, 97.0]
	Placebo	38	27.1 (20.9)	[6.0, 120.0]	24.6 (13.6)	[7.0, 77.0]	-2.5 (11.4)	[-44.0, 13.0]
Cycle 20	Pembrolizumab	8	22.4 (10.0)	[10.0, 42.0]	23.9 (13.0)	[12.0, 52.0]	1.5 (13.4)	[-14.0, 24.0]
	Placebo	2	26.0 (9.9)	[19.0, 33.0]	24.0 (12.7)	[15.0, 33.0]	-2.0 (2.8)	[-4.0, 0.0]
Cycle 21	Pembrolizumab	4	25.8 (12.1)	[14.0, 42.0]	35.3 (35.4)	[13.0, 88.0]	9.5 (24.4)	[-5.0, 46.0]
	Placebo	2	14.5 (12.0)	[6.0, 23.0]	16.5 (14.8)	[6.0, 27.0]	2.0 (2.8)	[0.0, 4.0]
Cycle 22	Pembrolizumab	2	11.5 (2.1)	[10.0, 13.0]	16.0 (1.4)	[15.0, 17.0]	4.5 (0.7)	[4.0, 5.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 23	Pembrolizumab	1	13.0 (-)	[13.0, 13.0]	21.0 (-)	[21.0, 21.0]	8.0 (-)	[8.0, 8.0]
Missing	Pembrolizumab	27	27.3 (11.9)	[13.0, 52.0]	30.6 (19.8)	[13.0, 82.0]	3.3 (18.0)	[-35.0, 57.0]
	Placebo	18	24.2 (10.4)	[10.0, 48.0]	34.5 (24.3)	[13.0, 116.0]	10.3 (23.5)	[-12.0, 97.0]
Unscheduled	Pembrolizumab	31	27.9 (8.5)	[13.0, 54.0]	29.5 (25.4)	[14.0, 154.0]	1.6 (20.5)	[-15.0, 100.0]
	Placebo	17	25.6 (10.1)	[10.0, 41.0]	27.5 (15.4)	[9.0, 64.0]	1.9 (13.0)	[-21.0, 37.0]
End of Treatment	Pembrolizumab	1	13.0 (-)	[13.0, 13.0]	16.0 (-)	[16.0, 16.0]	3.0 (-)	[3.0, 3.0]
	Placebo	7	26.1 (15.0)	[9.0, 55.0]	36.1 (50.1)	[8.0, 149.0]	10.0 (37.2)	[-7.0, 94.0]
Albumin (g/dL)								
Cycle 2	Pembrolizumab	45	4.2 (0.4)	[2.8, 4.9]	4.1 (0.4)	[2.9, 4.9]	-0.1 (0.3)	[-1.1, 0.4]
	Placebo	45	4.3 (0.4)	[3.6, 5.0]	4.2 (0.5)	[2.7, 5.1]	-0.1 (0.5)	[-1.7, 0.7]
Cycle 3	Pembrolizumab	455	4.3 (0.4)	[2.8, 5.5]	4.2 (0.4)	[2.9, 5.0]	-0.1 (0.3)	[-1.5, 1.6]
	Placebo	464	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.3, 6.7]	-0.0 (0.3)	[-0.7, 2.6]
Cycle 4	Pembrolizumab	47	4.2 (0.4)	[2.8, 4.9]	4.1 (0.4)	[3.0, 5.0]	-0.1 (0.3)	[-0.7, 0.8]
	Placebo	37	4.3 (0.4)	[3.8, 5.1]	4.2 (0.4)	[2.9, 4.9]	-0.1 (0.4)	[-1.7, 0.4]
Cycle 5	Pembrolizumab	431	4.3 (0.4)	[2.8, 5.5]	4.2 (0.4)	[3.1, 5.3]	-0.0 (0.3)	[-1.4, 1.2]
	Placebo	405	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.1, 5.2]	-0.0 (0.3)	[-0.9, 1.1]
Cycle 6	Pembrolizumab	52	4.2 (0.3)	[3.6, 4.9]	4.2 (0.4)	[3.3, 4.9]	-0.0 (0.3)	[-0.8, 0.7]
	Placebo	31	4.3 (0.4)	[3.6, 5.2]	4.2 (0.4)	[3.5, 5.2]	-0.1 (0.3)	[-0.9, 0.6]
Cycle 7	Pembrolizumab	394	4.3 (0.4)	[2.8, 5.5]	4.2 (0.4)	[3.1, 5.3]	-0.0 (0.3)	[-1.4, 1.5]
	Placebo	376	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.0, 5.2]	-0.0 (0.3)	[-1.2, 1.3]
Cycle 8	Pembrolizumab	40	4.2 (0.4)	[3.6, 4.9]	4.1 (0.4)	[3.2, 4.7]	-0.1 (0.3)	[-0.9, 0.9]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	39	4.2 (0.4)	[3.4, 5.2]	4.1 (0.4)	[3.2, 5.0]	-0.1 (0.3)	[-0.9, 0.7]
Cycle 9	Pembrolizumab	370	4.3 (0.4)	[2.8, 5.5]	4.2 (0.4)	[3.0, 5.3]	-0.0 (0.3)	[-1.4, 1.4]
	Placebo	344	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.4, 5.1]	-0.0 (0.3)	[-1.0, 1.3]
Cycle 10	Pembrolizumab	40	4.2 (0.3)	[3.6, 4.9]	4.2 (0.4)	[3.2, 4.9]	-0.0 (0.3)	[-0.6, 1.0]
	Placebo	31	4.3 (0.3)	[3.6, 5.0]	4.2 (0.4)	[3.4, 4.9]	-0.0 (0.3)	[-0.5, 0.8]
Cycle 11	Pembrolizumab	346	4.3 (0.4)	[3.0, 5.5]	4.2 (0.4)	[3.3, 5.2]	-0.1 (0.3)	[-1.3, 1.4]
	Placebo	332	4.3 (0.4)	[2.9, 5.4]	4.3 (0.3)	[3.3, 5.2]	-0.0 (0.3)	[-1.0, 1.2]
Cycle 12	Pembrolizumab	30	4.2 (0.3)	[3.6, 4.9]	4.1 (0.4)	[3.4, 4.8]	-0.1 (0.3)	[-1.0, 0.5]
	Placebo	26	4.3 (0.3)	[3.9, 4.9]	4.2 (0.3)	[3.6, 4.7]	-0.1 (0.3)	[-0.6, 0.6]
Cycle 13	Pembrolizumab	329	4.3 (0.3)	[3.0, 5.5]	4.2 (0.4)	[3.3, 5.1]	-0.0 (0.3)	[-1.2, 1.5]
	Placebo	306	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.2, 5.3]	-0.0 (0.3)	[-0.8, 1.3]
Cycle 14	Pembrolizumab	38	4.2 (0.3)	[3.6, 4.9]	4.2 (0.4)	[3.0, 5.0]	-0.0 (0.3)	[-0.7, 0.6]
	Placebo	27	4.4 (0.3)	[3.6, 5.0]	4.3 (0.3)	[3.5, 5.0]	-0.1 (0.3)	[-0.8, 0.4]
Cycle 15	Pembrolizumab	318	4.3 (0.3)	[3.0, 5.5]	4.2 (0.4)	[3.4, 7.0]	-0.0 (0.3)	[-1.2, 2.0]
	Placebo	307	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.3, 5.3]	-0.0 (0.3)	[-1.4, 1.1]
Cycle 16	Pembrolizumab	36	4.2 (0.3)	[3.6, 5.0]	4.1 (0.4)	[3.4, 4.8]	-0.1 (0.4)	[-1.2, 0.5]
	Placebo	21	4.3 (0.4)	[3.6, 5.0]	4.1 (0.4)	[3.6, 5.0]	-0.1 (0.4)	[-0.9, 0.7]
Cycle 17	Pembrolizumab	299	4.3 (0.3)	[3.0, 5.5]	4.2 (0.4)	[3.3, 5.2]	-0.1 (0.3)	[-1.3, 1.5]
	Placebo	298	4.3 (0.4)	[2.9, 5.4]	4.3 (0.4)	[3.5, 5.3]	-0.0 (0.3)	[-1.1, 1.2]
Cycle 18	Pembrolizumab	40	4.3 (0.3)	[3.6, 5.0]	4.2 (0.4)	[3.5, 4.9]	-0.1 (0.3)	[-1.0, 0.5]
	Placebo	33	4.3 (0.4)	[3.5, 5.2]	4.3 (0.4)	[3.3, 5.1]	-0.0 (0.3)	[-0.7, 0.5]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 19	Pembrolizumab	41	4.2 (0.4)	[3.4, 5.0]	4.1 (0.4)	[2.6, 4.9]	-0.1 (0.4)	[-1.2, 0.7]
	Placebo	37	4.3 (0.4)	[3.6, 5.1]	4.2 (0.3)	[3.5, 4.8]	-0.1 (0.3)	[-1.2, 0.7]
Cycle 20	Pembrolizumab	7	4.4 (0.3)	[3.8, 4.6]	4.3 (0.5)	[3.4, 4.8]	-0.0 (0.2)	[-0.4, 0.2]
	Placebo	2	3.9 (0.4)	[3.6, 4.2]	4.1 (0.3)	[3.9, 4.3]	0.2 (0.1)	[0.1, 0.3]
Cycle 21	Pembrolizumab	3	4.0 (0.3)	[3.8, 4.4]	4.1 (0.3)	[3.8, 4.4]	0.1 (0.2)	[0.0, 0.3]
	Placebo	2	4.0 (0.6)	[3.6, 4.4]	4.2 (0.4)	[3.9, 4.4]	0.1 (0.9)	[-0.5, 0.8]
Cycle 22	Pembrolizumab	2	4.3 (0.3)	[4.1, 4.6]	4.5 (0.3)	[4.3, 4.7]	0.2 (0.0)	[0.2, 0.2]
Cycle 23	Pembrolizumab	1	4.1 (-)	[4.1, 4.1]	4.3 (-)	[4.3, 4.3]	0.2 (-)	[0.2, 0.2]
Missing	Pembrolizumab	24	4.3 (0.4)	[3.7, 5.0]	4.2 (0.4)	[3.1, 4.7]	-0.1 (0.3)	[-0.7, 0.3]
	Placebo	16	4.3 (0.2)	[3.9, 4.8]	4.2 (0.4)	[3.3, 4.9]	-0.1 (0.4)	[-1.1, 0.5]
Unscheduled	Pembrolizumab	24	4.2 (0.4)	[3.8, 5.0]	3.8 (0.6)	[2.5, 4.6]	-0.4 (0.4)	[-1.3, 0.3]
	Placebo	14	4.3 (0.4)	[3.6, 5.0]	4.3 (0.3)	[3.7, 4.6]	-0.1 (0.2)	[-0.4, 0.2]
End of Treatment	Pembrolizumab	1	4.1 (-)	[4.1, 4.1]	4.4 (-)	[4.4, 4.4]	0.3 (-)	[0.3, 0.3]
	Placebo	6	4.2 (0.3)	[3.7, 4.6]	3.9 (0.3)	[3.5, 4.4]	-0.3 (0.5)	[-1.1, 0.3]
Alkaline Phosphatase (IU/L)								
Cycle 2	Pembrolizumab	50	72.1 (17.5)	[41.0, 142.0]	71.3 (15.8)	[47.0, 131.0]	-0.8 (10.1)	[-33.0, 18.0]
	Placebo	50	73.2 (20.8)	[28.0, 159.0]	86.1 (82.4)	[27.0, 621.0]	12.9 (78.8)	[-25.0, 540.0]
Cycle 3	Pembrolizumab	471	78.3 (37.6)	[13.0, 400.0]	77.8 (37.4)	[20.0, 352.0]	-0.5 (17.1)	[-98.0, 115.0]
	Placebo	471	78.0 (34.1)	[25.0, 301.0]	75.6 (32.5)	[27.0, 282.0]	-2.5 (12.1)	[-104.0, 39.0]
Cycle 4	Pembrolizumab	47	75.3 (19.6)	[41.0, 142.0]	75.1 (23.9)	[48.0, 173.0]	-0.2 (15.3)	[-36.0, 71.0]
	Placebo	39	71.3 (18.4)	[28.0, 117.0]	72.8 (23.9)	[29.0, 146.0]	1.4 (12.0)	[-19.0, 50.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 5	Pembrolizumab	432	77.6 (36.7)	[13.0, 400.0]	76.9 (40.9)	[20.0, 439.0]	-0.7 (24.8)	[-126.0, 303.0]
	Placebo	414	77.2 (32.6)	[28.0, 301.0]	74.7 (31.1)	[26.0, 267.0]	-2.6 (14.8)	[-98.0, 92.0]
Cycle 6	Pembrolizumab	52	76.9 (24.1)	[40.0, 185.0]	77.2 (29.2)	[41.0, 191.0]	0.3 (15.3)	[-30.0, 82.0]
	Placebo	31	77.4 (30.5)	[36.0, 208.0]	74.7 (25.7)	[40.0, 171.0]	-2.7 (12.7)	[-37.0, 23.0]
Cycle 7	Pembrolizumab	403	77.4 (36.6)	[13.0, 400.0]	75.3 (34.2)	[19.0, 311.0]	-2.1 (21.4)	[-178.0, 116.0]
	Placebo	378	77.4 (32.4)	[28.0, 301.0]	74.4 (30.8)	[28.0, 274.0]	-3.0 (14.5)	[-106.0, 66.0]
Cycle 8	Pembrolizumab	40	74.5 (25.7)	[30.0, 185.0]	74.9 (27.3)	[45.0, 180.0]	0.4 (18.4)	[-24.0, 85.0]
	Placebo	39	76.6 (28.2)	[44.0, 208.0]	75.2 (27.4)	[42.0, 173.0]	-1.4 (16.3)	[-35.0, 59.0]
Cycle 9	Pembrolizumab	368	77.6 (37.0)	[13.0, 400.0]	74.7 (34.0)	[5.0, 311.0]	-2.9 (17.6)	[-124.0, 72.0]
	Placebo	352	76.9 (32.1)	[28.0, 301.0]	74.9 (31.5)	[27.0, 287.0]	-2.1 (14.3)	[-98.0, 59.0]
Cycle 10	Pembrolizumab	40	73.6 (16.1)	[41.0, 114.0]	76.5 (24.1)	[37.0, 170.0]	3.0 (20.6)	[-21.0, 106.0]
	Placebo	31	80.6 (30.3)	[48.0, 208.0]	77.7 (22.4)	[50.0, 168.0]	-2.9 (13.2)	[-40.0, 20.0]
Cycle 11	Pembrolizumab	353	77.8 (37.4)	[13.0, 400.0]	74.3 (33.6)	[19.0, 284.0]	-3.5 (20.3)	[-174.0, 107.0]
	Placebo	334	77.1 (32.4)	[28.0, 301.0]	74.2 (31.8)	[26.0, 276.0]	-2.8 (14.7)	[-103.0, 46.0]
Cycle 12	Pembrolizumab	33	78.1 (59.3)	[40.0, 400.0]	76.4 (42.4)	[41.0, 240.0]	-1.7 (43.1)	[-173.0, 164.0]
	Placebo	29	81.7 (31.5)	[43.0, 208.0]	75.7 (24.3)	[47.0, 174.0]	-6.0 (12.0)	[-34.0, 13.0]
Cycle 13	Pembrolizumab	327	77.6 (37.1)	[13.0, 400.0]	75.4 (37.2)	[19.0, 329.0]	-2.2 (24.5)	[-154.0, 253.0]
	Placebo	311	77.0 (30.8)	[28.0, 269.0]	74.1 (31.0)	[27.0, 251.0]	-2.9 (15.1)	[-102.0, 59.0]
Cycle 14	Pembrolizumab	38	72.5 (22.6)	[13.0, 131.0]	69.7 (20.3)	[23.0, 128.0]	-2.8 (16.6)	[-65.0, 42.0]
	Placebo	27	77.9 (19.8)	[43.0, 116.0]	75.8 (18.3)	[41.0, 129.0]	-2.0 (13.1)	[-32.0, 37.0]
Cycle 15	Pembrolizumab	321	75.8 (33.7)	[13.0, 400.0]	72.8 (29.2)	[21.0, 269.0]	-3.0 (18.2)	[-161.0, 90.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	308	77.1 (30.9)	[28.0, 269.0]	75.0 (33.1)	[30.0, 250.0]	-2.1 (17.6)	[-101.0, 118.0]
Cycle 16	Pembrolizumab	37	79.2 (26.9)	[40.0, 185.0]	79.7 (28.7)	[49.0, 176.0]	0.5 (24.3)	[-51.0, 112.0]
	Placebo	21	72.7 (17.5)	[43.0, 116.0]	87.0 (91.5)	[41.0, 482.0]	14.3 (86.3)	[-18.0, 390.0]
Cycle 17	Pembrolizumab	303	75.1 (32.3)	[13.0, 400.0]	72.9 (31.5)	[18.0, 256.0]	-2.2 (20.3)	[-169.0, 152.0]
	Placebo	297	76.8 (30.8)	[29.0, 269.0]	73.2 (30.3)	[30.0, 255.0]	-3.6 (15.8)	[-115.0, 67.0]
Cycle 18	Pembrolizumab	42	72.3 (26.5)	[29.0, 202.0]	69.1 (21.8)	[31.0, 151.0]	-3.2 (14.5)	[-51.0, 39.0]
	Placebo	35	70.2 (17.1)	[35.0, 116.0]	69.7 (14.9)	[50.0, 116.0]	-0.5 (11.9)	[-39.0, 24.0]
Cycle 19	Pembrolizumab	42	75.8 (33.4)	[41.0, 242.0]	78.1 (66.9)	[37.0, 486.0]	2.3 (41.7)	[-49.0, 244.0]
	Placebo	36	72.1 (26.3)	[35.0, 176.0]	65.5 (17.5)	[34.0, 102.0]	-6.5 (19.6)	[-109.0, 19.0]
Cycle 20	Pembrolizumab	8	76.1 (18.7)	[48.0, 99.0]	92.1 (67.4)	[48.0, 256.0]	16.0 (58.5)	[-26.0, 157.0]
	Placebo	2	87.5 (6.4)	[83.0, 92.0]	97.5 (16.3)	[86.0, 109.0]	10.0 (9.9)	[3.0, 17.0]
Cycle 21	Pembrolizumab	4	63.5 (12.9)	[48.0, 76.0]	66.3 (14.3)	[49.0, 79.0]	2.8 (9.0)	[-9.0, 12.0]
	Placebo	2	80.5 (4.9)	[77.0, 84.0]	74.0 (1.4)	[73.0, 75.0]	-6.5 (3.5)	[-9.0, -4.0]
Cycle 22	Pembrolizumab	2	72.5 (37.5)	[46.0, 99.0]	123.5 (105.4)	[49.0, 198.0]	51.0 (67.9)	[3.0, 99.0]
Cycle 23	Pembrolizumab	1	46.0 (-)	[46.0, 46.0]	39.0 (-)	[39.0, 39.0]	-7.0 (-)	[-7.0, -7.0]
Missing	Pembrolizumab	27	77.2 (18.9)	[48.0, 129.0]	75.1 (20.3)	[44.0, 131.0]	-2.1 (17.6)	[-50.0, 34.0]
	Placebo	18	74.3 (15.6)	[46.0, 100.0]	77.4 (18.9)	[45.0, 132.0]	3.1 (15.6)	[-24.0, 51.0]
Unscheduled	Pembrolizumab	26	79.8 (21.6)	[49.0, 142.0]	76.6 (20.6)	[52.0, 133.0]	-3.2 (19.5)	[-31.0, 45.0]
	Placebo	16	83.3 (30.9)	[28.0, 116.0]	81.1 (28.2)	[31.0, 120.0]	-2.2 (13.7)	[-21.0, 25.0]
End of Treatment	Pembrolizumab	1	59.0 (-)	[59.0, 59.0]	63.0 (-)	[63.0, 63.0]	4.0 (-)	[4.0, 4.0]
	Placebo	7	74.4 (9.4)	[61.0, 88.0]	82.4 (21.9)	[62.0, 125.0]	8.0 (17.9)	[-7.0, 47.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Aspartate Aminotransferase (IU/L)								
Cycle 2	Pembrolizumab	53	21.8 (8.7)	[6.0, 60.0]	24.6 (9.3)	[13.0, 57.0]	2.8 (8.9)	[-17.0, 38.0]
	Placebo	52	23.1 (8.9)	[10.0, 60.0]	26.7 (15.7)	[10.0, 97.0]	3.6 (12.5)	[-14.0, 52.0]
Cycle 3	Pembrolizumab	474	23.1 (8.1)	[6.0, 73.0]	25.4 (14.2)	[6.0, 163.0]	2.3 (13.3)	[-32.0, 135.0]
	Placebo	473	22.9 (8.0)	[8.0, 74.0]	23.0 (10.1)	[7.0, 169.0]	0.2 (9.6)	[-38.0, 148.0]
Cycle 4	Pembrolizumab	46	22.8 (9.4)	[14.0, 60.0]	25.6 (11.5)	[13.0, 59.0]	2.8 (7.7)	[-12.0, 26.0]
	Placebo	40	21.3 (7.1)	[11.0, 42.0]	23.4 (10.5)	[9.0, 69.0]	2.1 (10.5)	[-14.0, 44.0]
Cycle 5	Pembrolizumab	435	23.0 (7.8)	[6.0, 73.0]	24.9 (14.8)	[8.0, 160.0]	2.0 (13.8)	[-44.0, 134.0]
	Placebo	419	22.7 (8.1)	[8.0, 74.0]	22.6 (7.7)	[7.0, 58.0]	-0.1 (6.9)	[-35.0, 39.0]
Cycle 6	Pembrolizumab	52	23.4 (8.4)	[14.0, 53.0]	24.3 (10.8)	[12.0, 65.0]	0.9 (9.0)	[-27.0, 43.0]
	Placebo	31	20.4 (6.3)	[11.0, 34.0]	18.8 (5.7)	[8.0, 29.0]	-1.6 (5.9)	[-16.0, 10.0]
Cycle 7	Pembrolizumab	405	23.0 (8.1)	[6.0, 73.0]	24.0 (10.1)	[6.0, 100.0]	0.9 (9.3)	[-38.0, 60.0]
	Placebo	388	22.7 (7.9)	[10.0, 74.0]	23.0 (8.7)	[9.0, 111.0]	0.2 (8.6)	[-36.0, 99.0]
Cycle 8	Pembrolizumab	42	23.3 (8.4)	[14.0, 53.0]	25.7 (11.2)	[14.0, 61.0]	2.4 (10.4)	[-25.0, 39.0]
	Placebo	39	24.0 (7.8)	[12.0, 42.0]	23.9 (9.7)	[10.0, 59.0]	-0.2 (11.4)	[-22.0, 47.0]
Cycle 9	Pembrolizumab	376	23.1 (8.2)	[6.0, 73.0]	23.6 (8.8)	[9.0, 79.0]	0.5 (8.7)	[-39.0, 57.0]
	Placebo	356	22.9 (8.2)	[10.0, 74.0]	22.6 (7.5)	[9.0, 87.0]	-0.2 (7.9)	[-34.0, 75.0]
Cycle 10	Pembrolizumab	40	25.0 (9.7)	[14.0, 53.0]	27.2 (13.0)	[11.0, 70.0]	2.2 (11.0)	[-23.0, 43.0]
	Placebo	32	22.0 (7.4)	[11.0, 42.0]	23.9 (15.7)	[11.0, 101.0]	1.8 (16.8)	[-16.0, 89.0]
Cycle 11	Pembrolizumab	361	23.1 (8.3)	[6.0, 73.0]	23.7 (9.2)	[8.0, 102.0]	0.6 (8.7)	[-44.0, 58.0]
	Placebo	339	22.8 (8.4)	[10.0, 74.0]	23.3 (9.3)	[7.0, 101.0]	0.5 (9.8)	[-39.0, 89.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 12	Pembrolizumab	31	24.2 (7.9)	[12.0, 53.0]	27.2 (10.7)	[14.0, 52.0]	3.0 (11.8)	[-22.0, 40.0]
	Placebo	27	21.3 (6.8)	[11.0, 42.0]	23.4 (14.8)	[14.0, 92.0]	2.1 (17.2)	[-25.0, 80.0]
Cycle 13	Pembrolizumab	333	22.8 (7.8)	[6.0, 57.0]	23.5 (8.9)	[8.0, 74.0]	0.7 (8.8)	[-34.0, 45.0]
	Placebo	314	22.7 (8.5)	[10.0, 74.0]	23.0 (8.8)	[8.0, 83.0]	0.2 (9.2)	[-36.0, 67.0]
Cycle 14	Pembrolizumab	39	26.0 (9.3)	[12.0, 53.0]	26.7 (10.2)	[13.0, 61.0]	0.7 (10.4)	[-22.0, 45.0]
	Placebo	27	21.8 (6.3)	[11.0, 35.0]	27.5 (14.0)	[12.0, 78.0]	5.7 (14.6)	[-6.0, 59.0]
Cycle 15	Pembrolizumab	322	22.7 (7.6)	[6.0, 57.0]	23.3 (10.3)	[6.0, 137.0]	0.7 (9.3)	[-27.0, 104.0]
	Placebo	315	22.8 (8.5)	[10.0, 74.0]	22.9 (9.1)	[8.0, 114.0]	0.0 (8.7)	[-39.0, 87.0]
Cycle 16	Pembrolizumab	36	25.2 (10.0)	[12.0, 53.0]	28.3 (18.9)	[11.0, 120.0]	3.0 (14.1)	[-15.0, 68.0]
	Placebo	18	21.9 (7.6)	[11.0, 42.0]	27.5 (18.8)	[13.0, 92.0]	5.6 (17.4)	[-9.0, 59.0]
Cycle 17	Pembrolizumab	303	22.8 (7.7)	[6.0, 57.0]	23.9 (11.9)	[9.0, 151.0]	1.1 (11.6)	[-35.0, 126.0]
	Placebo	303	22.6 (8.2)	[10.0, 74.0]	22.6 (6.9)	[8.0, 51.0]	-0.1 (7.2)	[-38.0, 23.0]
Cycle 18	Pembrolizumab	44	24.5 (9.6)	[11.0, 57.0]	31.7 (25.2)	[13.0, 143.0]	7.3 (24.5)	[-35.0, 118.0]
	Placebo	35	24.1 (9.7)	[11.0, 50.0]	22.8 (9.0)	[10.0, 57.0]	-1.3 (11.2)	[-23.0, 39.0]
Cycle 19	Pembrolizumab	40	21.8 (6.9)	[12.0, 53.0]	22.9 (7.9)	[11.0, 51.0]	1.1 (7.4)	[-12.0, 28.0]
	Placebo	37	24.5 (12.0)	[12.0, 74.0]	21.9 (6.5)	[7.0, 42.0]	-2.6 (8.1)	[-32.0, 10.0]
Cycle 20	Pembrolizumab	7	23.4 (13.7)	[12.0, 53.0]	26.0 (13.1)	[17.0, 54.0]	2.6 (4.2)	[-3.0, 10.0]
	Placebo	2	30.5 (3.5)	[28.0, 33.0]	32.5 (4.9)	[29.0, 36.0]	2.0 (1.4)	[1.0, 3.0]
Cycle 21	Pembrolizumab	4	21.0 (8.8)	[12.0, 33.0]	22.0 (6.4)	[17.0, 31.0]	1.0 (9.2)	[-11.0, 10.0]
	Placebo	2	15.0 (4.2)	[12.0, 18.0]	17.0 (0.0)	[17.0, 17.0]	2.0 (4.2)	[-1.0, 5.0]
Cycle 22	Pembrolizumab	2	22.5 (3.5)	[20.0, 25.0]	23.0 (1.4)	[22.0, 24.0]	0.5 (4.9)	[-3.0, 4.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 23	Pembrolizumab	1	20.0 (-)	[20.0, 20.0]	21.0 (-)	[21.0, 21.0]	1.0 (-)	[1.0, 1.0]
Missing	Pembrolizumab	27	22.9 (7.0)	[12.0, 44.0]	33.4 (48.1)	[9.0, 267.0]	10.6 (48.7)	[-22.0, 246.0]
	Placebo	18	22.5 (4.6)	[12.0, 29.0]	31.7 (21.5)	[13.0, 110.0]	9.2 (23.0)	[-12.0, 96.0]
Unscheduled	Pembrolizumab	32	21.8 (9.3)	[15.0, 48.0]	22.9 (14.9)	[8.0, 85.0]	1.0 (10.4)	[-18.0, 39.0]
	Placebo	15	24.0 (4.8)	[15.0, 33.0]	33.5 (20.9)	[13.0, 89.0]	9.5 (20.8)	[-7.0, 68.0]
End of Treatment	Pembrolizumab	1	12.0 (-)	[12.0, 12.0]	14.0 (-)	[14.0, 14.0]	2.0 (-)	[2.0, 2.0]
	Placebo	7	21.1 (4.5)	[15.0, 28.0]	25.1 (14.8)	[16.0, 58.0]	4.0 (12.0)	[-6.0, 30.0]
Bilirubin (mg/dL)								
Cycle 2	Pembrolizumab	53	0.6 (0.3)	[0.2, 1.8]	0.5 (0.3)	[0.2, 1.4]	-0.0 (0.2)	[-0.6, 0.6]
	Placebo	49	0.5 (0.2)	[0.2, 1.2]	0.6 (0.3)	[0.2, 1.5]	0.0 (0.2)	[-0.5, 0.8]
Cycle 3	Pembrolizumab	476	0.6 (0.3)	[0.2, 2.0]	0.6 (0.4)	[0.1, 5.1]	0.0 (0.3)	[-1.0, 4.7]
	Placebo	478	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.2]	0.0 (0.2)	[-0.8, 1.2]
Cycle 4	Pembrolizumab	48	0.6 (0.3)	[0.2, 1.8]	0.6 (0.3)	[0.1, 1.5]	-0.0 (0.2)	[-1.0, 0.5]
	Placebo	38	0.6 (0.3)	[0.2, 1.2]	0.6 (0.3)	[0.2, 1.9]	-0.0 (0.3)	[-0.5, 1.2]
Cycle 5	Pembrolizumab	436	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.1, 2.5]	0.0 (0.2)	[-0.8, 1.6]
	Placebo	418	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.2]	0.0 (0.2)	[-0.9, 1.1]
Cycle 6	Pembrolizumab	53	0.6 (0.3)	[0.2, 1.8]	0.6 (0.3)	[0.2, 2.0]	0.0 (0.3)	[-0.6, 1.4]
	Placebo	31	0.6 (0.3)	[0.2, 1.2]	0.5 (0.3)	[0.2, 1.2]	-0.0 (0.2)	[-0.5, 0.5]
Cycle 7	Pembrolizumab	409	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.1, 2.2]	0.0 (0.2)	[-1.2, 1.3]
	Placebo	389	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.9]	0.0 (0.2)	[-1.1, 1.3]
Cycle 8	Pembrolizumab	41	0.6 (0.4)	[0.2, 1.8]	0.6 (0.3)	[0.2, 1.5]	-0.0 (0.2)	[-0.8, 0.5]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	40	0.6 (0.3)	[0.2, 1.6]	0.7 (0.6)	[0.2, 4.0]	0.1 (0.6)	[-0.8, 3.5]
Cycle 9	Pembrolizumab	377	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.2, 2.2]	0.0 (0.2)	[-1.0, 0.9]
	Placebo	360	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 1.8]	-0.0 (0.2)	[-1.0, 0.9]
Cycle 10	Pembrolizumab	42	0.6 (0.4)	[0.2, 1.8]	0.7 (0.5)	[0.2, 2.6]	0.0 (0.3)	[-0.5, 1.6]
	Placebo	33	0.6 (0.3)	[0.2, 1.6]	0.6 (0.3)	[0.1, 1.5]	0.0 (0.2)	[-0.4, 0.5]
Cycle 11	Pembrolizumab	361	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.2, 2.3]	-0.0 (0.2)	[-1.0, 0.9]
	Placebo	342	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.3]	0.0 (0.2)	[-0.9, 1.3]
Cycle 12	Pembrolizumab	33	0.5 (0.3)	[0.2, 1.8]	0.5 (0.3)	[0.2, 1.3]	-0.0 (0.2)	[-0.6, 0.6]
	Placebo	29	0.5 (0.2)	[0.2, 1.1]	0.5 (0.3)	[0.2, 1.7]	0.0 (0.2)	[-0.4, 0.7]
Cycle 13	Pembrolizumab	336	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.2, 2.8]	0.0 (0.2)	[-0.9, 1.3]
	Placebo	314	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.3]	0.0 (0.2)	[-0.8, 1.4]
Cycle 14	Pembrolizumab	38	0.5 (0.3)	[0.2, 1.8]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.3)	[-1.2, 0.4]
	Placebo	27	0.6 (0.3)	[0.2, 1.2]	0.6 (0.4)	[0.2, 1.9]	0.0 (0.3)	[-0.5, 0.9]
Cycle 15	Pembrolizumab	327	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.2, 3.6]	0.0 (0.3)	[-1.1, 2.0]
	Placebo	314	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.2]	0.0 (0.2)	[-1.3, 1.3]
Cycle 16	Pembrolizumab	37	0.5 (0.3)	[0.2, 1.4]	0.6 (0.3)	[0.2, 1.4]	0.0 (0.2)	[-0.4, 0.4]
	Placebo	21	0.6 (0.3)	[0.2, 1.2]	0.6 (0.4)	[0.1, 1.5]	-0.0 (0.2)	[-0.5, 0.5]
Cycle 17	Pembrolizumab	308	0.6 (0.3)	[0.2, 2.0]	0.6 (0.3)	[0.2, 2.5]	-0.0 (0.2)	[-0.8, 0.9]
	Placebo	303	0.6 (0.3)	[0.1, 2.4]	0.6 (0.3)	[0.1, 2.4]	0.0 (0.2)	[-0.7, 1.2]
Cycle 18	Pembrolizumab	44	0.6 (0.4)	[0.2, 1.9]	0.7 (0.4)	[0.3, 1.7]	0.0 (0.3)	[-0.5, 1.0]
	Placebo	34	0.6 (0.3)	[0.2, 1.4]	0.6 (0.4)	[0.2, 1.9]	0.0 (0.2)	[-0.4, 0.9]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 19	Pembrolizumab	43	0.5 (0.3)	[0.2, 1.9]	0.5 (0.2)	[0.2, 1.3]	-0.0 (0.3)	[-0.9, 0.5]
	Placebo	38	0.6 (0.3)	[0.2, 1.2]	0.6 (0.3)	[0.2, 2.0]	0.0 (0.3)	[-0.8, 1.0]
Cycle 20	Pembrolizumab	8	0.5 (0.2)	[0.3, 1.0]	0.5 (0.2)	[0.3, 1.0]	0.1 (0.3)	[-0.4, 0.6]
	Placebo	2	0.4 (0.2)	[0.3, 0.5]	0.6 (0.2)	[0.4, 0.8]	0.2 (0.1)	[0.1, 0.2]
Cycle 21	Pembrolizumab	4	0.4 (0.2)	[0.3, 0.6]	0.5 (0.1)	[0.4, 0.6]	0.1 (0.2)	[-0.2, 0.3]
	Placebo	2	0.6 (0.0)	[0.6, 0.6]	0.7 (0.1)	[0.6, 0.8]	0.1 (0.1)	[0.0, 0.2]
Cycle 22	Pembrolizumab	2	0.9 (0.2)	[0.8, 1.0]	0.6 (0.0)	[0.5, 0.6]	-0.3 (0.2)	[-0.5, -0.2]
Cycle 23	Pembrolizumab	1	0.8 (-)	[0.8, 0.8]	0.6 (-)	[0.6, 0.6]	-0.2 (-)	[-0.2, -0.2]
Missing	Pembrolizumab	26	0.6 (0.4)	[0.2, 1.8]	0.7 (0.5)	[0.3, 2.4]	0.1 (0.3)	[-0.4, 0.9]
	Placebo	17	0.7 (0.3)	[0.4, 1.6]	0.8 (0.3)	[0.4, 1.5]	0.1 (0.3)	[-0.3, 0.7]
Unscheduled	Pembrolizumab	34	0.5 (0.3)	[0.2, 1.8]	0.6 (0.4)	[0.2, 1.8]	0.1 (0.3)	[-0.3, 1.1]
	Placebo	22	0.8 (0.2)	[0.4, 1.2]	1.2 (0.8)	[0.4, 3.2]	0.4 (0.7)	[-0.5, 2.3]
End of Treatment	Pembrolizumab	1	0.4 (-)	[0.4, 0.4]	0.3 (-)	[0.3, 0.3]	-0.1 (-)	[-0.1, -0.1]
	Placebo	7	0.5 (0.2)	[0.2, 0.7]	0.5 (0.3)	[0.2, 1.1]	0.1 (0.2)	[-0.2, 0.4]
Calcium (mg/dL)								
Cycle 2	Pembrolizumab	48	9.3 (0.4)	[8.8, 10.4]	9.3 (0.4)	[8.4, 10.0]	-0.0 (0.3)	[-0.8, 0.8]
	Placebo	51	9.4 (0.4)	[8.8, 10.4]	9.4 (0.4)	[8.0, 10.1]	-0.1 (0.4)	[-1.6, 0.8]
Cycle 3	Pembrolizumab	467	9.4 (0.4)	[8.0, 11.2]	9.3 (0.4)	[8.0, 10.4]	-0.0 (0.4)	[-2.0, 1.2]
	Placebo	472	9.4 (0.4)	[8.0, 11.1]	9.4 (0.4)	[8.4, 10.8]	0.0 (0.4)	[-1.2, 1.6]
Cycle 4	Pembrolizumab	48	9.3 (0.3)	[8.8, 10.0]	9.3 (0.4)	[8.0, 10.4]	-0.1 (0.4)	[-0.8, 0.8]
	Placebo	36	9.6 (0.4)	[8.8, 10.4]	9.4 (0.5)	[8.4, 10.8]	-0.2 (0.5)	[-1.2, 0.8]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 5	Pembrolizumab	435	9.4 (0.4)	[8.0, 11.2]	9.3 (0.4)	[7.6, 10.8]	-0.0 (0.4)	[-1.6, 1.2]
	Placebo	410	9.4 (0.4)	[8.0, 11.1]	9.4 (0.5)	[7.2, 10.8]	-0.0 (0.5)	[-1.6, 1.2]
Cycle 6	Pembrolizumab	54	9.4 (0.3)	[8.8, 10.0]	9.3 (0.3)	[8.4, 10.0]	-0.1 (0.4)	[-1.2, 0.4]
	Placebo	30	9.5 (0.4)	[8.8, 10.4]	9.3 (0.4)	[8.4, 10.0]	-0.2 (0.4)	[-0.8, 0.4]
Cycle 7	Pembrolizumab	402	9.4 (0.4)	[8.0, 11.2]	9.3 (0.4)	[7.6, 10.4]	-0.0 (0.5)	[-1.6, 1.2]
	Placebo	380	9.4 (0.4)	[8.0, 11.1]	9.4 (0.4)	[7.6, 10.9]	-0.0 (0.4)	[-1.2, 1.2]
Cycle 8	Pembrolizumab	41	9.4 (0.4)	[8.4, 10.0]	9.3 (0.5)	[8.4, 10.1]	-0.1 (0.6)	[-1.2, 1.2]
	Placebo	37	9.4 (0.4)	[8.8, 10.4]	9.4 (0.5)	[8.4, 11.6]	-0.0 (0.6)	[-0.8, 2.8]
Cycle 9	Pembrolizumab	376	9.4 (0.4)	[8.0, 11.2]	9.3 (0.4)	[8.4, 10.8]	-0.0 (0.5)	[-1.6, 1.3]
	Placebo	352	9.4 (0.4)	[8.0, 10.4]	9.4 (0.4)	[7.6, 10.4]	-0.0 (0.4)	[-1.2, 1.6]
Cycle 10	Pembrolizumab	39	9.5 (0.3)	[8.4, 10.0]	9.3 (0.3)	[8.4, 10.0]	-0.2 (0.4)	[-0.8, 0.8]
	Placebo	31	9.5 (0.4)	[8.8, 10.4]	9.4 (0.4)	[8.8, 10.0]	-0.1 (0.3)	[-0.5, 0.8]
Cycle 11	Pembrolizumab	352	9.4 (0.4)	[8.0, 11.2]	9.3 (0.4)	[7.9, 10.8]	-0.1 (0.5)	[-2.4, 1.6]
	Placebo	335	9.4 (0.4)	[8.0, 10.4]	9.4 (0.4)	[8.0, 10.8]	-0.0 (0.4)	[-1.6, 1.2]
Cycle 12	Pembrolizumab	32	9.5 (0.4)	[8.7, 10.4]	9.4 (0.4)	[8.4, 10.4]	-0.1 (0.4)	[-0.8, 0.5]
	Placebo	27	9.4 (0.5)	[8.4, 10.4]	9.4 (0.4)	[8.4, 10.0]	-0.1 (0.3)	[-0.8, 0.4]
Cycle 13	Pembrolizumab	333	9.4 (0.4)	[8.0, 10.8]	9.3 (0.4)	[8.0, 11.2]	-0.0 (0.4)	[-1.9, 1.2]
	Placebo	311	9.4 (0.4)	[8.0, 10.4]	9.3 (0.4)	[7.6, 10.4]	-0.1 (0.4)	[-1.3, 1.2]
Cycle 14	Pembrolizumab	38	9.5 (0.4)	[8.8, 10.4]	9.4 (0.5)	[8.2, 10.8]	-0.1 (0.5)	[-1.2, 0.8]
	Placebo	24	9.5 (0.5)	[8.8, 10.4]	9.4 (0.4)	[8.8, 10.4]	-0.1 (0.4)	[-1.2, 0.4]
Cycle 15	Pembrolizumab	322	9.4 (0.4)	[8.0, 10.8]	9.4 (0.4)	[8.4, 10.4]	-0.0 (0.4)	[-1.6, 1.2]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	311	9.4 (0.4)	[8.0, 10.4]	9.4 (0.4)	[7.9, 11.1]	-0.0 (0.4)	[-1.6, 1.2]
Cycle 16	Pembrolizumab	37	9.4 (0.4)	[8.8, 10.4]	9.4 (0.4)	[8.4, 10.3]	-0.1 (0.4)	[-1.2, 0.8]
	Placebo	20	9.5 (0.5)	[8.8, 10.4]	9.3 (0.4)	[8.8, 10.0]	-0.2 (0.4)	[-1.2, 0.5]
Cycle 17	Pembrolizumab	305	9.4 (0.4)	[8.0, 10.8]	9.3 (0.4)	[8.0, 10.8]	-0.0 (0.4)	[-1.2, 1.6]
	Placebo	295	9.4 (0.4)	[8.0, 10.4]	9.4 (0.4)	[8.3, 10.4]	-0.1 (0.4)	[-1.3, 0.8]
Cycle 18	Pembrolizumab	42	9.4 (0.4)	[8.8, 10.3]	9.3 (0.4)	[8.4, 10.3]	-0.0 (0.4)	[-1.2, 0.4]
	Placebo	35	9.5 (0.4)	[8.8, 10.4]	9.4 (0.4)	[8.4, 10.0]	-0.1 (0.3)	[-0.8, 0.4]
Cycle 19	Pembrolizumab	42	9.3 (0.4)	[8.8, 10.0]	9.3 (0.4)	[8.4, 10.0]	0.0 (0.4)	[-0.9, 0.8]
	Placebo	37	9.5 (0.4)	[8.8, 10.4]	9.4 (0.4)	[8.8, 10.0]	-0.1 (0.4)	[-0.9, 0.4]
Cycle 20	Pembrolizumab	8	9.3 (0.4)	[8.8, 10.0]	9.4 (0.2)	[9.1, 9.6]	0.1 (0.5)	[-0.4, 0.8]
	Placebo	2	9.2 (0.6)	[8.8, 9.6]	9.2 (0.6)	[8.8, 9.6]	0.0 (0.0)	[0.0, 0.0]
Cycle 21	Pembrolizumab	4	9.1 (0.3)	[8.8, 9.5]	9.7 (0.4)	[9.2, 10.1]	0.7 (0.5)	[0.0, 1.2]
	Placebo	2	9.6 (0.0)	[9.6, 9.6]	9.0 (0.3)	[8.8, 9.2]	-0.6 (0.3)	[-0.8, -0.4]
Cycle 22	Pembrolizumab	1	10.0 (-)	[10.0, 10.0]	9.2 (-)	[9.2, 9.2]	-0.8 (-)	[-0.8, -0.8]
Missing	Pembrolizumab	26	9.5 (0.6)	[8.4, 10.5]	9.4 (0.3)	[8.8, 10.4]	-0.2 (0.7)	[-1.4, 1.2]
	Placebo	17	9.5 (0.3)	[8.8, 10.0]	9.4 (0.5)	[8.4, 10.4]	-0.2 (0.5)	[-1.2, 0.8]
Unscheduled	Pembrolizumab	30	9.5 (0.2)	[8.8, 9.6]	9.4 (0.5)	[8.4, 10.0]	-0.1 (0.5)	[-1.2, 0.8]
	Placebo	16	9.4 (0.5)	[8.8, 10.4]	9.2 (0.4)	[8.8, 10.0]	-0.2 (0.5)	[-1.2, 0.8]
End of Treatment	Pembrolizumab	1	8.8 (-)	[8.8, 8.8]	9.6 (-)	[9.6, 9.6]	0.8 (-)	[0.8, 0.8]
	Placebo	6	9.5 (0.3)	[9.1, 10.0]	9.3 (0.7)	[8.4, 10.0]	-0.2 (0.8)	[-1.6, 0.4]
Creatinine (mg/dL)								

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 2	Pembrolizumab	54	0.8 (0.2)	[0.5, 1.7]	0.8 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.2, 0.2]
	Placebo	52	0.8 (0.2)	[0.6, 1.4]	0.8 (0.2)	[0.6, 1.3]	0.0 (0.1)	[-0.2, 0.2]
Cycle 3	Pembrolizumab	480	0.9 (0.2)	[0.4, 1.7]	0.9 (0.5)	[0.5, 11.8]	0.0 (0.5)	[-0.3, 10.5]
	Placebo	484	0.9 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.5, 1.8]	0.0 (0.1)	[-0.3, 0.6]
Cycle 4	Pembrolizumab	49	0.9 (0.1)	[0.6, 1.3]	1.0 (0.3)	[0.6, 1.9]	0.1 (0.2)	[-0.2, 0.8]
	Placebo	41	0.8 (0.2)	[0.4, 1.2]	0.8 (0.2)	[0.5, 1.4]	-0.0 (0.1)	[-0.4, 0.2]
Cycle 5	Pembrolizumab	445	0.9 (0.2)	[0.4, 1.6]	0.9 (0.4)	[0.5, 8.9]	0.1 (0.4)	[-0.4, 8.0]
	Placebo	424	0.9 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.4, 1.8]	0.0 (0.1)	[-0.3, 0.4]
Cycle 6	Pembrolizumab	54	0.8 (0.1)	[0.6, 1.3]	0.9 (0.1)	[0.6, 1.4]	0.0 (0.1)	[-0.2, 0.3]
	Placebo	31	0.8 (0.2)	[0.5, 1.2]	0.8 (0.2)	[0.6, 1.1]	0.0 (0.1)	[-0.3, 0.2]
Cycle 7	Pembrolizumab	413	0.8 (0.2)	[0.4, 1.4]	0.9 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.4, 0.6]
	Placebo	395	0.9 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.4, 1.9]	0.0 (0.1)	[-0.3, 0.5]
Cycle 8	Pembrolizumab	41	0.9 (0.2)	[0.6, 1.3]	0.9 (0.2)	[0.6, 1.6]	0.1 (0.2)	[-0.2, 0.9]
	Placebo	44	0.8 (0.2)	[0.5, 1.2]	0.9 (0.2)	[0.6, 1.6]	0.0 (0.1)	[-0.3, 0.5]
Cycle 9	Pembrolizumab	382	0.8 (0.2)	[0.4, 1.4]	0.9 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.3, 0.4]
	Placebo	364	0.8 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.5, 1.7]	0.0 (0.1)	[-0.2, 0.4]
Cycle 10	Pembrolizumab	40	0.8 (0.2)	[0.5, 1.2]	0.9 (0.2)	[0.5, 1.2]	0.0 (0.1)	[-0.3, 0.2]
	Placebo	34	0.8 (0.2)	[0.4, 1.2]	0.8 (0.2)	[0.5, 1.5]	0.0 (0.1)	[-0.1, 0.4]
Cycle 11	Pembrolizumab	364	0.8 (0.2)	[0.4, 1.4]	0.9 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.5, 0.7]
	Placebo	344	0.9 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.4, 1.8]	0.0 (0.1)	[-0.3, 0.4]
Cycle 12	Pembrolizumab	33	0.9 (0.2)	[0.5, 1.3]	0.9 (0.2)	[0.6, 1.4]	0.0 (0.1)	[-0.2, 0.1]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	28	0.8 (0.1)	[0.6, 1.2]	0.8 (0.2)	[0.6, 1.4]	0.0 (0.1)	[-0.2, 0.3]
Cycle 13	Pembrolizumab	340	0.8 (0.2)	[0.4, 1.3]	0.9 (0.2)	[0.5, 1.9]	0.0 (0.1)	[-0.3, 0.8]
	Placebo	318	0.8 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.5, 1.5]	0.0 (0.1)	[-0.3, 0.4]
Cycle 14	Pembrolizumab	38	0.9 (0.2)	[0.5, 1.2]	1.0 (0.5)	[0.6, 3.9]	0.1 (0.5)	[-0.2, 3.2]
	Placebo	27	0.8 (0.2)	[0.6, 1.2]	0.8 (0.2)	[0.6, 1.4]	0.0 (0.1)	[-0.2, 0.2]
Cycle 15	Pembrolizumab	329	0.8 (0.2)	[0.4, 1.3]	0.9 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.3, 0.5]
	Placebo	316	0.8 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.5, 1.5]	0.0 (0.1)	[-0.2, 0.4]
Cycle 16	Pembrolizumab	38	0.8 (0.1)	[0.5, 1.1]	0.8 (0.1)	[0.5, 1.2]	0.0 (0.1)	[-0.2, 0.3]
	Placebo	22	0.8 (0.2)	[0.6, 1.2]	0.9 (0.2)	[0.6, 1.4]	0.1 (0.1)	[-0.2, 0.3]
Cycle 17	Pembrolizumab	307	0.8 (0.2)	[0.4, 1.3]	0.9 (0.2)	[0.5, 1.9]	0.0 (0.1)	[-0.4, 1.0]
	Placebo	305	0.8 (0.2)	[0.4, 1.7]	0.9 (0.2)	[0.5, 1.6]	0.0 (0.1)	[-0.2, 0.4]
Cycle 18	Pembrolizumab	45	0.8 (0.1)	[0.6, 1.2]	0.9 (0.2)	[0.6, 1.4]	0.0 (0.1)	[-0.2, 0.4]
	Placebo	36	0.9 (0.2)	[0.6, 1.7]	0.9 (0.2)	[0.6, 1.7]	0.0 (0.1)	[-0.2, 0.2]
Cycle 19	Pembrolizumab	43	0.9 (0.2)	[0.6, 1.3]	0.9 (0.2)	[0.6, 1.4]	0.0 (0.1)	[-0.4, 0.3]
	Placebo	38	0.8 (0.2)	[0.6, 1.3]	0.8 (0.2)	[0.6, 1.3]	0.0 (0.1)	[-0.2, 0.3]
Cycle 20	Pembrolizumab	8	0.9 (0.2)	[0.8, 1.3]	1.0 (0.3)	[0.8, 1.5]	0.1 (0.1)	[-0.1, 0.4]
	Placebo	2	0.8 (0.3)	[0.7, 1.0]	0.9 (0.2)	[0.7, 1.1]	0.1 (0.0)	[0.1, 0.1]
Cycle 21	Pembrolizumab	4	1.0 (0.3)	[0.7, 1.3]	1.1 (0.2)	[1.0, 1.4]	0.1 (0.1)	[0.0, 0.3]
	Placebo	2	0.8 (0.2)	[0.7, 1.0]	0.8 (0.1)	[0.7, 0.8]	-0.1 (0.1)	[-0.1, 0.0]
Cycle 22	Pembrolizumab	2	0.8 (0.2)	[0.7, 0.9]	0.9 (0.2)	[0.7, 1.0]	0.1 (0.1)	[0.1, 0.1]
Cycle 23	Pembrolizumab	1	0.7 (-)	[0.7, 0.7]	0.7 (-)	[0.7, 0.7]	0.0 (-)	[0.0, 0.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Missing	Pembrolizumab	26	0.8 (0.2)	[0.6, 1.3]	0.8 (0.2)	[0.5, 1.4]	-0.0 (0.1)	[-0.5, 0.3]
	Placebo	18	0.9 (0.2)	[0.5, 1.2]	0.9 (0.2)	[0.5, 1.2]	0.0 (0.1)	[-0.1, 0.2]
Unscheduled	Pembrolizumab	40	1.0 (0.2)	[0.6, 1.2]	1.0 (0.3)	[0.6, 2.4]	0.1 (0.3)	[-0.3, 1.1]
	Placebo	22	0.9 (0.1)	[0.7, 1.2]	1.0 (0.2)	[0.8, 1.4]	0.1 (0.1)	[-0.1, 0.3]
End of Treatment	Pembrolizumab	1	0.5 (-)	[0.5, 0.5]	0.6 (-)	[0.6, 0.6]	0.1 (-)	[0.1, 0.1]
	Placebo	7	0.8 (0.2)	[0.4, 1.1]	0.8 (0.2)	[0.5, 1.1]	-0.0 (0.1)	[-0.2, 0.2]
Erythrocytes (/HPF) - Hematology								
Cycle 1	Pembrolizumab	1	5.1 (-)	[5.1, 5.1]	4.8 (-)	[4.8, 4.8]	-0.3 (-)	[-0.3, -0.3]
Cycle 2	Pembrolizumab	54	4.7 (0.4)	[3.7, 5.8]	4.7 (0.4)	[3.6, 5.9]	0.0 (0.2)	[-0.5, 0.9]
	Placebo	48	4.9 (0.4)	[4.0, 5.5]	4.9 (0.4)	[4.2, 5.7]	-0.0 (0.3)	[-0.9, 0.5]
Cycle 3	Pembrolizumab	475	4.8 (0.4)	[3.5, 6.8]	4.8 (0.4)	[3.0, 6.3]	0.0 (0.2)	[-0.9, 0.7]
	Placebo	481	4.8 (0.4)	[3.6, 6.2]	4.8 (0.5)	[3.7, 7.4]	0.0 (0.3)	[-1.4, 2.5]
Cycle 4	Pembrolizumab	42	4.7 (0.4)	[3.7, 5.3]	4.8 (0.4)	[3.7, 5.5]	0.1 (0.2)	[-0.3, 0.7]
	Placebo	39	4.8 (0.5)	[4.0, 5.9]	4.7 (0.6)	[3.6, 6.3]	-0.1 (0.3)	[-1.0, 0.4]
Cycle 5	Pembrolizumab	441	4.8 (0.4)	[3.7, 6.8]	4.9 (0.5)	[3.7, 7.9]	0.1 (0.3)	[-1.2, 2.8]
	Placebo	417	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.3, 6.1]	0.0 (0.3)	[-1.2, 1.5]
Cycle 6	Pembrolizumab	49	4.7 (0.4)	[3.7, 5.9]	4.7 (0.4)	[4.0, 5.5]	-0.0 (0.2)	[-0.6, 0.5]
	Placebo	30	4.8 (0.5)	[4.0, 5.6]	4.7 (0.5)	[3.8, 5.6]	-0.1 (0.4)	[-1.6, 0.4]
Cycle 7	Pembrolizumab	408	4.8 (0.4)	[3.7, 6.8]	4.8 (0.4)	[3.7, 6.5]	0.0 (0.3)	[-0.8, 0.8]
	Placebo	391	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.7, 6.1]	0.0 (0.2)	[-0.7, 1.0]
Cycle 8	Pembrolizumab	37	4.8 (0.5)	[3.7, 5.9]	4.8 (0.4)	[4.0, 6.0]	0.0 (0.3)	[-0.5, 0.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	37	4.9 (0.5)	[4.0, 5.6]	4.9 (0.4)	[4.0, 5.7]	-0.0 (0.3)	[-0.9, 0.5]
Cycle 9	Pembrolizumab	379	4.8 (0.4)	[3.7, 6.8]	4.8 (0.5)	[3.4, 7.0]	0.0 (0.3)	[-0.7, 0.9]
	Placebo	359	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.8, 6.3]	0.0 (0.2)	[-0.6, 1.0]
Cycle 10	Pembrolizumab	35	4.7 (0.4)	[3.7, 5.3]	4.7 (0.5)	[3.5, 5.3]	-0.0 (0.3)	[-0.7, 0.3]
	Placebo	32	4.9 (0.5)	[4.0, 5.7]	4.9 (0.4)	[3.9, 5.6]	-0.0 (0.3)	[-0.5, 0.5]
Cycle 11	Pembrolizumab	358	4.8 (0.4)	[3.7, 6.8]	4.8 (0.4)	[3.6, 6.4]	-0.0 (0.3)	[-0.7, 0.7]
	Placebo	337	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.8, 6.5]	0.0 (0.2)	[-0.7, 1.0]
Cycle 12	Pembrolizumab	30	4.8 (0.4)	[3.7, 5.5]	4.8 (0.5)	[3.8, 5.7]	0.0 (0.3)	[-0.9, 0.8]
	Placebo	29	4.8 (0.5)	[4.1, 5.6]	4.9 (0.4)	[4.2, 5.8]	0.1 (0.3)	[-0.4, 0.6]
Cycle 13	Pembrolizumab	336	4.8 (0.4)	[3.7, 6.8]	4.8 (0.5)	[3.8, 7.0]	0.0 (0.3)	[-1.3, 0.9]
	Placebo	315	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.6, 6.1]	0.0 (0.2)	[-0.6, 0.8]
Cycle 14	Pembrolizumab	37	4.7 (0.4)	[3.7, 5.5]	4.7 (0.5)	[3.9, 5.7]	-0.0 (0.3)	[-1.0, 0.7]
	Placebo	24	4.9 (0.4)	[4.1, 5.6]	4.8 (0.4)	[4.2, 5.5]	-0.1 (0.2)	[-0.5, 0.3]
Cycle 15	Pembrolizumab	326	4.8 (0.4)	[3.7, 6.8]	4.8 (0.5)	[2.3, 6.5]	-0.0 (0.3)	[-1.8, 1.1]
	Placebo	314	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.2, 6.4]	-0.0 (0.3)	[-2.2, 1.1]
Cycle 16	Pembrolizumab	41	4.8 (0.4)	[3.7, 5.9]	4.7 (0.4)	[4.0, 5.8]	-0.1 (0.4)	[-1.2, 0.6]
	Placebo	20	4.9 (0.4)	[4.2, 5.9]	4.8 (0.4)	[4.0, 5.5]	-0.1 (0.2)	[-0.5, 0.2]
Cycle 17	Pembrolizumab	303	4.8 (0.4)	[3.7, 6.8]	4.8 (0.5)	[3.5, 6.7]	-0.0 (0.3)	[-0.8, 1.6]
	Placebo	303	4.8 (0.4)	[3.6, 6.2]	4.8 (0.4)	[3.7, 6.3]	-0.0 (0.3)	[-0.7, 1.4]
Cycle 18	Pembrolizumab	41	4.8 (0.5)	[3.7, 5.8]	4.8 (0.6)	[3.7, 6.0]	-0.0 (0.3)	[-0.8, 0.7]
	Placebo	36	4.8 (0.4)	[3.9, 5.9]	4.8 (0.3)	[4.3, 5.7]	-0.0 (0.2)	[-0.6, 0.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 19	Pembrolizumab	43	4.8 (0.4)	[3.7, 5.5]	4.8 (0.5)	[3.6, 5.7]	-0.0 (0.3)	[-0.8, 0.5]
	Placebo	37	4.7 (0.5)	[3.9, 5.8]	4.7 (0.5)	[3.8, 5.7]	0.0 (0.3)	[-0.6, 0.6]
Cycle 20	Pembrolizumab	8	4.7 (0.4)	[4.3, 5.2]	4.5 (0.6)	[3.6, 5.6]	-0.2 (0.6)	[-1.1, 0.6]
	Placebo	2	4.7 (0.2)	[4.5, 4.8]	4.7 (0.1)	[4.7, 4.8]	0.0 (0.1)	[-0.1, 0.1]
Cycle 21	Pembrolizumab	4	5.0 (0.3)	[4.5, 5.2]	5.4 (0.4)	[5.1, 5.9]	0.4 (0.3)	[0.1, 0.7]
	Placebo	2	4.8 (0.1)	[4.7, 4.9]	4.9 (0.1)	[4.8, 5.0]	0.1 (0.2)	[-0.1, 0.2]
Cycle 22	Pembrolizumab	2	4.7 (0.7)	[4.1, 5.2]	4.4 (0.3)	[4.3, 4.6]	-0.2 (0.5)	[-0.5, 0.1]
Cycle 23	Pembrolizumab	1	4.1 (-)	[4.1, 4.1]	4.3 (-)	[4.3, 4.3]	0.1 (-)	[0.1, 0.1]
Missing	Pembrolizumab	23	4.9 (0.4)	[3.9, 5.6]	4.9 (0.5)	[4.0, 5.8]	0.1 (0.2)	[-0.4, 0.6]
	Placebo	16	4.9 (0.4)	[4.4, 5.6]	5.0 (0.2)	[4.6, 5.4]	0.1 (0.3)	[-0.3, 0.7]
Unscheduled	Pembrolizumab	22	4.7 (0.3)	[3.9, 5.2]	4.6 (0.3)	[4.2, 5.1]	-0.1 (0.3)	[-0.6, 0.3]
	Placebo	19	4.7 (0.6)	[4.0, 5.6]	4.7 (0.5)	[4.1, 5.9]	0.1 (0.3)	[-0.4, 0.4]
End of Treatment	Pembrolizumab	1	4.4 (-)	[4.4, 4.4]	4.4 (-)	[4.4, 4.4]	-0.0 (-)	[-0.0, -0.0]
	Placebo	5	4.8 (0.3)	[4.3, 5.1]	4.8 (0.3)	[4.2, 5.1]	0.1 (0.2)	[-0.1, 0.3]
Erythrocytes (/HPF) - Urinalysis								
Cycle 2	Pembrolizumab	1	58.0 (-)	[58.0, 58.0]	21.0 (-)	[21.0, 21.0]	-37.0 (-)	[-37.0, -37.0]
	Placebo	2	93.5 (92.6)	[28.0, 159.0]	27.0 (2.8)	[25.0, 29.0]	-66.5 (89.8)	[-130.0, -3.0]
Cycle 5	Pembrolizumab	18	14.4 (26.4)	[0.0, 100.0]	11.8 (25.8)	[0.0, 100.0]	-2.6 (7.7)	[-26.0, 7.0]
	Placebo	24	13.3 (32.0)	[0.0, 159.0]	9.9 (17.2)	[0.0, 84.0]	-3.4 (16.8)	[-75.0, 9.0]
Cycle 6	Placebo	1	19.0 (-)	[19.0, 19.0]	23.0 (-)	[23.0, 23.0]	4.0 (-)	[4.0, 4.0]
Cycle 8	Pembrolizumab	1	58.0 (-)	[58.0, 58.0]	14.0 (-)	[14.0, 14.0]	-44.0 (-)	[-44.0, -44.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 9	Pembrolizumab	16	19.4 (29.2)	[0.0, 100.0]	25.0 (38.2)	[0.0, 109.0]	5.6 (15.6)	[-23.0, 46.0]
	Placebo	12	8.7 (9.7)	[1.0, 34.0]	9.2 (11.4)	[0.0, 35.0]	0.5 (11.5)	[-25.0, 19.0]
Cycle 10	Pembrolizumab	1	18.0 (-)	[18.0, 18.0]	11.0 (-)	[11.0, 11.0]	-7.0 (-)	[-7.0, -7.0]
Cycle 11	Pembrolizumab	1	2.0 (-)	[2.0, 2.0]	2.0 (-)	[2.0, 2.0]	0.0 (-)	[0.0, 0.0]
Cycle 13	Pembrolizumab	9	3.6 (4.6)	[0.0, 15.0]	5.4 (5.7)	[0.0, 16.0]	1.9 (4.1)	[-5.0, 10.0]
	Placebo	16	11.9 (14.4)	[1.0, 48.0]	21.1 (26.3)	[1.0, 77.0]	9.2 (19.9)	[-22.0, 62.0]
Cycle 14	Placebo	1	3.0 (-)	[3.0, 3.0]	9.0 (-)	[9.0, 9.0]	6.0 (-)	[6.0, 6.0]
Cycle 17	Pembrolizumab	8	2.4 (1.5)	[1.0, 5.0]	1.9 (2.0)	[0.0, 5.0]	-0.5 (1.7)	[-4.0, 2.0]
	Placebo	9	9.0 (11.1)	[1.0, 34.0]	13.6 (28.8)	[0.0, 89.0]	4.6 (25.2)	[-16.0, 70.0]
Cycle 18	Pembrolizumab	2	9.0 (12.7)	[0.0, 18.0]	6.0 (8.5)	[0.0, 12.0]	-3.0 (4.2)	[-6.0, 0.0]
	Placebo	2	5.5 (3.5)	[3.0, 8.0]	10.0 (8.5)	[4.0, 16.0]	4.5 (12.0)	[-4.0, 13.0]
Unscheduled	Pembrolizumab	1	5.0 (-)	[5.0, 5.0]	10.0 (-)	[10.0, 10.0]	5.0 (-)	[5.0, 5.0]
End of Treatment	Placebo	1	28.0 (-)	[28.0, 28.0]	38.0 (-)	[38.0, 38.0]	10.0 (-)	[10.0, 10.0]
Hematocrit (%)								
Cycle 1	Pembrolizumab	1	45.9 (-)	[45.9, 45.9]	44.1 (-)	[44.1, 44.1]	-1.8 (-)	[-1.8, -1.8]
Cycle 2	Pembrolizumab	54	41.3 (3.8)	[32.6, 48.4]	41.2 (4.0)	[31.1, 48.4]	-0.1 (2.0)	[-5.2, 7.0]
	Placebo	49	42.2 (3.8)	[30.0, 50.3]	42.6 (3.2)	[35.0, 49.6]	0.4 (2.9)	[-7.0, 11.0]
Cycle 3	Pembrolizumab	474	42.4 (3.6)	[29.8, 54.2]	42.2 (3.7)	[28.2, 53.0]	-0.2 (2.2)	[-7.5, 13.0]
	Placebo	478	42.3 (3.6)	[30.0, 53.0]	42.5 (3.6)	[29.6, 52.5]	0.2 (2.2)	[-13.0, 13.0]
Cycle 4	Pembrolizumab	42	41.7 (3.2)	[34.0, 47.1]	41.9 (3.4)	[34.0, 49.0]	0.2 (2.2)	[-4.0, 6.0]
	Placebo	39	41.9 (3.7)	[34.4, 50.3]	41.1 (4.1)	[30.5, 49.0]	-0.8 (2.9)	[-9.2, 5.2]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 5	Pembrolizumab	441	42.4 (3.5)	[31.5, 54.0]	42.6 (3.6)	[30.0, 53.0]	0.2 (2.5)	[-9.0, 7.0]
	Placebo	415	42.3 (3.6)	[30.0, 53.0]	42.4 (3.6)	[30.0, 52.0]	0.1 (2.4)	[-12.0, 13.0]
Cycle 6	Pembrolizumab	50	41.9 (3.7)	[34.0, 54.2]	41.5 (3.8)	[33.7, 51.1]	-0.4 (2.0)	[-6.2, 4.0]
	Placebo	30	42.3 (4.3)	[36.0, 53.0]	40.9 (4.7)	[29.8, 50.0]	-1.4 (2.9)	[-9.9, 4.0]
Cycle 7	Pembrolizumab	408	42.4 (3.6)	[31.5, 54.0]	42.4 (3.7)	[30.2, 53.0]	-0.1 (2.4)	[-8.2, 6.8]
	Placebo	387	42.2 (3.6)	[30.0, 53.0]	42.3 (3.6)	[30.5, 51.0]	0.1 (2.4)	[-11.0, 13.0]
Cycle 8	Pembrolizumab	37	42.3 (4.0)	[34.0, 54.2]	42.0 (3.9)	[34.0, 51.3]	-0.3 (2.4)	[-7.0, 4.0]
	Placebo	38	42.6 (4.2)	[34.0, 53.0]	42.4 (4.0)	[34.0, 50.0]	-0.2 (2.4)	[-5.7, 4.8]
Cycle 9	Pembrolizumab	381	42.4 (3.5)	[31.5, 54.0]	42.5 (3.9)	[30.6, 53.0]	0.1 (2.4)	[-5.5, 7.0]
	Placebo	358	42.2 (3.6)	[30.0, 53.0]	42.4 (3.6)	[31.2, 54.0]	0.2 (2.4)	[-12.0, 14.0]
Cycle 10	Pembrolizumab	35	42.0 (3.4)	[34.0, 47.0]	41.5 (4.3)	[30.0, 48.0]	-0.5 (2.7)	[-7.9, 4.0]
	Placebo	32	42.7 (4.3)	[34.6, 53.0]	42.3 (3.6)	[34.2, 49.0]	-0.4 (2.7)	[-6.0, 5.0]
Cycle 11	Pembrolizumab	361	42.5 (3.6)	[31.5, 54.0]	42.5 (3.8)	[31.3, 55.0]	0.0 (2.5)	[-10.0, 8.0]
	Placebo	339	42.3 (3.6)	[30.0, 53.0]	42.5 (3.6)	[33.4, 52.2]	0.2 (2.4)	[-9.0, 12.0]
Cycle 12	Pembrolizumab	29	42.2 (3.6)	[34.0, 47.0]	42.0 (3.6)	[33.8, 49.0]	-0.2 (3.0)	[-9.1, 7.0]
	Placebo	29	42.1 (3.5)	[34.0, 49.5]	42.7 (3.9)	[36.0, 49.9]	0.7 (2.5)	[-4.0, 6.0]
Cycle 13	Pembrolizumab	338	42.5 (3.5)	[31.5, 54.0]	42.6 (3.7)	[32.0, 53.0]	0.0 (2.6)	[-11.5, 7.2]
	Placebo	315	42.2 (3.6)	[30.0, 53.0]	42.3 (3.5)	[32.0, 51.0]	0.2 (2.4)	[-11.0, 16.0]
Cycle 14	Pembrolizumab	35	42.4 (3.5)	[34.0, 48.0]	42.0 (3.7)	[34.7, 49.0]	-0.4 (3.1)	[-9.2, 7.0]
	Placebo	24	43.1 (3.7)	[37.0, 50.3]	42.7 (3.0)	[38.0, 48.4]	-0.4 (1.8)	[-4.0, 4.0]
Cycle 15	Pembrolizumab	328	42.6 (3.6)	[31.5, 54.0]	42.6 (3.8)	[29.8, 52.0]	-0.0 (2.6)	[-9.0, 8.8]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	312	42.2 (3.6)	[30.0, 53.0]	42.2 (3.5)	[32.7, 53.0]	0.0 (2.5)	[-10.2, 14.0]
Cycle 16	Pembrolizumab	40	42.2 (4.0)	[34.0, 54.2]	41.4 (3.7)	[34.0, 49.0]	-0.8 (3.2)	[-10.4, 7.0]
	Placebo	19	43.7 (3.8)	[36.9, 50.3]	42.4 (3.4)	[36.1, 47.8]	-1.3 (1.6)	[-4.9, 1.1]
Cycle 17	Pembrolizumab	304	42.5 (3.5)	[31.5, 52.5]	42.4 (3.8)	[30.0, 53.0]	-0.1 (2.5)	[-8.0, 6.4]
	Placebo	300	42.2 (3.6)	[30.0, 53.0]	42.3 (3.5)	[30.0, 51.5]	0.1 (2.4)	[-11.0, 12.0]
Cycle 18	Pembrolizumab	41	42.1 (4.2)	[31.5, 52.5]	41.4 (4.7)	[28.8, 50.4]	-0.6 (2.8)	[-8.3, 5.0]
	Placebo	36	43.0 (3.6)	[37.0, 49.5]	42.6 (3.3)	[37.1, 48.0]	-0.4 (2.0)	[-5.1, 4.0]
Cycle 19	Pembrolizumab	43	42.3 (3.3)	[35.0, 48.0]	42.3 (4.1)	[31.0, 49.0]	0.0 (3.5)	[-8.0, 10.0]
	Placebo	36	41.4 (4.3)	[34.0, 50.3]	41.8 (4.2)	[32.0, 50.3]	0.4 (2.1)	[-4.0, 5.0]
Cycle 20	Pembrolizumab	8	41.2 (3.4)	[36.5, 46.5]	41.3 (5.3)	[32.9, 49.0]	0.1 (6.2)	[-6.4, 10.0]
	Placebo	2	41.0 (1.4)	[40.0, 42.0]	41.5 (2.1)	[40.0, 43.0]	0.5 (0.7)	[0.0, 1.0]
Cycle 21	Pembrolizumab	4	42.3 (2.4)	[39.0, 44.0]	46.5 (2.1)	[44.0, 49.0]	4.2 (4.4)	[0.0, 10.0]
	Placebo	2	44.2 (0.3)	[44.0, 44.4]	45.4 (2.0)	[44.0, 46.8]	1.2 (1.7)	[0.0, 2.4]
Cycle 22	Pembrolizumab	1	46.5 (-)	[46.5, 46.5]	42.9 (-)	[42.9, 42.9]	-3.6 (-)	[-3.6, -3.6]
Missing	Pembrolizumab	24	42.6 (4.7)	[34.0, 54.0]	42.3 (4.7)	[29.0, 50.0]	-0.2 (3.6)	[-7.0, 9.0]
	Placebo	16	42.3 (2.8)	[38.0, 46.0]	43.4 (2.8)	[39.0, 49.0]	1.1 (2.5)	[-3.0, 5.0]
Unscheduled	Pembrolizumab	21	41.2 (2.7)	[35.0, 45.6]	40.1 (2.4)	[35.5, 45.0]	-1.1 (2.8)	[-5.2, 2.4]
	Placebo	20	40.9 (5.4)	[32.0, 50.3]	41.2 (4.4)	[34.0, 51.4]	0.3 (2.2)	[-3.6, 3.0]
End of Treatment	Pembrolizumab	1	38.5 (-)	[38.5, 38.5]	38.5 (-)	[38.5, 38.5]	0.0 (-)	[0.0, 0.0]
	Placebo	6	41.7 (3.3)	[37.0, 45.2]	41.9 (3.1)	[36.3, 45.0]	0.2 (1.4)	[-1.0, 2.7]
Hemoglobin (g/dL)								

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 1	Pembrolizumab	1	15.4 (-)	[15.4, 15.4]	14.1 (-)	[14.1, 14.1]	-1.3 (-)	[-1.3, -1.3]
Cycle 2	Pembrolizumab	54	13.8 (1.6)	[10.5, 16.6]	13.8 (1.6)	[10.0, 16.9]	0.0 (0.6)	[-1.3, 2.1]
	Placebo	49	14.4 (1.3)	[10.0, 17.5]	14.4 (1.1)	[11.6, 16.5]	0.1 (0.8)	[-2.6, 1.6]
Cycle 3	Pembrolizumab	479	14.2 (1.3)	[9.5, 17.9]	14.2 (1.4)	[9.3, 17.8]	-0.0 (0.7)	[-1.8, 4.5]
	Placebo	485	14.2 (1.3)	[10.0, 17.6]	14.3 (1.3)	[9.6, 18.0]	0.1 (0.7)	[-2.0, 2.2]
Cycle 4	Pembrolizumab	42	13.9 (1.3)	[10.5, 16.0]	13.9 (1.3)	[10.1, 16.4]	0.1 (0.7)	[-1.2, 1.2]
	Placebo	39	14.2 (1.4)	[11.3, 17.5]	13.9 (1.6)	[9.4, 16.7]	-0.3 (0.9)	[-3.0, 1.6]
Cycle 5	Pembrolizumab	445	14.2 (1.3)	[9.6, 17.7]	14.2 (1.3)	[9.5, 18.5]	0.0 (0.8)	[-2.8, 2.3]
	Placebo	422	14.2 (1.3)	[10.0, 17.6]	14.3 (1.3)	[9.4, 17.7]	0.1 (0.8)	[-3.7, 2.9]
Cycle 6	Pembrolizumab	51	14.1 (1.5)	[10.5, 17.9]	13.9 (1.6)	[9.8, 17.2]	-0.2 (0.7)	[-1.9, 1.2]
	Placebo	30	14.2 (1.5)	[12.1, 17.5]	13.7 (1.7)	[9.1, 16.6]	-0.5 (0.9)	[-3.3, 1.2]
Cycle 7	Pembrolizumab	412	14.2 (1.3)	[9.6, 17.7]	14.2 (1.4)	[9.5, 18.0]	-0.0 (0.8)	[-2.7, 2.2]
	Placebo	394	14.2 (1.3)	[10.0, 17.6]	14.2 (1.3)	[9.4, 17.2]	0.0 (0.7)	[-3.0, 3.2]
Cycle 8	Pembrolizumab	39	14.2 (1.4)	[10.5, 17.9]	14.1 (1.4)	[9.9, 17.2]	-0.1 (0.8)	[-2.2, 1.9]
	Placebo	38	14.4 (1.5)	[11.3, 17.5]	14.3 (1.4)	[10.7, 16.9]	-0.1 (0.8)	[-2.1, 1.9]
Cycle 9	Pembrolizumab	383	14.2 (1.3)	[9.6, 17.7]	14.3 (1.4)	[9.3, 18.4]	0.0 (0.8)	[-2.4, 3.4]
	Placebo	363	14.2 (1.3)	[10.0, 17.6]	14.2 (1.3)	[10.4, 17.9]	0.1 (0.7)	[-2.0, 3.4]
Cycle 10	Pembrolizumab	37	13.9 (1.4)	[10.5, 16.3]	13.8 (1.6)	[8.7, 16.6]	-0.1 (0.9)	[-2.2, 1.7]
	Placebo	32	14.5 (1.6)	[11.1, 17.5]	14.3 (1.3)	[11.2, 16.8]	-0.1 (0.9)	[-1.9, 2.1]
Cycle 11	Pembrolizumab	362	14.3 (1.3)	[9.6, 17.7]	14.2 (1.4)	[9.3, 18.5]	-0.0 (0.8)	[-2.9, 2.4]
	Placebo	343	14.2 (1.3)	[10.0, 17.6]	14.3 (1.3)	[10.4, 17.7]	0.1 (0.8)	[-2.2, 4.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 12	Pembrolizumab	30	14.1 (1.4)	[10.5, 16.2]	14.0 (1.4)	[11.0, 17.0]	-0.1 (1.0)	[-2.7, 2.1]
	Placebo	30	14.1 (1.3)	[11.9, 17.5]	14.4 (1.4)	[12.5, 17.5]	0.2 (0.9)	[-1.3, 2.4]
Cycle 13	Pembrolizumab	341	14.3 (1.3)	[9.6, 17.7]	14.3 (1.3)	[9.5, 17.8]	0.0 (0.9)	[-3.7, 2.7]
	Placebo	318	14.2 (1.3)	[10.0, 17.5]	14.2 (1.3)	[10.4, 17.0]	0.0 (0.8)	[-2.4, 3.5]
Cycle 14	Pembrolizumab	37	14.2 (1.3)	[10.5, 16.2]	14.2 (1.3)	[11.8, 16.8]	-0.1 (1.0)	[-3.2, 2.3]
	Placebo	25	14.4 (1.4)	[12.1, 17.5]	14.3 (1.2)	[12.6, 16.7]	-0.1 (0.7)	[-1.9, 0.9]
Cycle 15	Pembrolizumab	329	14.3 (1.3)	[9.6, 17.7]	14.3 (1.4)	[9.0, 17.6]	-0.0 (0.9)	[-3.2, 3.2]
	Placebo	317	14.2 (1.3)	[10.0, 17.5]	14.2 (1.3)	[10.5, 17.6]	0.0 (0.8)	[-2.9, 4.2]
Cycle 16	Pembrolizumab	41	14.2 (1.4)	[10.5, 17.9]	14.0 (1.4)	[11.1, 16.8]	-0.2 (1.1)	[-3.2, 2.5]
	Placebo	21	14.7 (1.4)	[12.4, 17.5]	14.3 (1.3)	[11.8, 16.8]	-0.4 (0.8)	[-1.4, 1.7]
Cycle 17	Pembrolizumab	309	14.3 (1.3)	[9.6, 17.7]	14.2 (1.3)	[8.9, 17.9]	-0.0 (0.9)	[-3.0, 2.6]
	Placebo	305	14.2 (1.3)	[10.0, 17.5]	14.2 (1.3)	[9.4, 17.7]	0.0 (0.8)	[-2.5, 4.3]
Cycle 18	Pembrolizumab	41	14.1 (1.7)	[9.6, 17.5]	14.0 (1.8)	[8.4, 17.8]	-0.2 (1.0)	[-3.1, 2.0]
	Placebo	36	14.4 (1.3)	[12.4, 17.5]	14.2 (1.1)	[12.2, 16.1]	-0.2 (0.7)	[-1.4, 1.1]
Cycle 19	Pembrolizumab	44	14.1 (1.4)	[11.1, 17.0]	14.1 (1.5)	[9.2, 16.6]	-0.0 (1.2)	[-2.6, 3.4]
	Placebo	38	14.1 (1.6)	[11.9, 17.5]	14.1 (1.5)	[11.3, 17.3]	0.0 (0.8)	[-1.5, 1.7]
Cycle 20	Pembrolizumab	8	13.5 (1.5)	[11.1, 15.0]	13.6 (1.6)	[11.0, 15.5]	0.1 (2.2)	[-2.7, 3.4]
	Placebo	2	13.7 (0.9)	[13.0, 14.3]	13.7 (0.9)	[13.0, 14.3]	0.0 (0.0)	[0.0, 0.0]
Cycle 21	Pembrolizumab	4	14.1 (1.7)	[11.8, 15.6]	15.6 (0.6)	[14.8, 16.0]	1.5 (2.0)	[-0.2, 4.2]
	Placebo	2	15.1 (0.6)	[14.6, 15.5]	15.0 (0.7)	[14.5, 15.5]	-0.0 (1.3)	[-1.0, 0.9]
Cycle 22	Pembrolizumab	2	14.0 (1.3)	[13.0, 14.9]	14.1 (0.6)	[13.7, 14.5]	0.1 (0.7)	[-0.4, 0.6]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 23	Pembrolizumab	1	13.0 (-)	[13.0, 13.0]	13.9 (-)	[13.9, 13.9]	0.8 (-)	[0.8, 0.8]
Missing	Pembrolizumab	24	14.0 (1.6)	[10.5, 17.3]	14.1 (1.8)	[9.3, 16.4]	0.1 (1.3)	[-2.3, 4.1]
	Placebo	16	14.1 (1.0)	[12.1, 15.6]	14.6 (1.0)	[13.3, 16.8]	0.5 (1.1)	[-1.4, 2.1]
Unscheduled	Pembrolizumab	22	14.1 (0.9)	[11.8, 15.5]	13.6 (0.9)	[12.0, 14.9]	-0.5 (0.8)	[-2.0, 0.6]
	Placebo	22	13.7 (2.1)	[10.0, 17.5]	13.9 (1.7)	[11.0, 18.3]	0.2 (0.8)	[-1.7, 1.0]
End of Treatment	Pembrolizumab	1	12.8 (-)	[12.8, 12.8]	12.9 (-)	[12.9, 12.9]	0.1 (-)	[0.1, 0.1]
	Placebo	6	14.0 (1.3)	[12.1, 15.5]	14.0 (1.1)	[12.4, 14.8]	-0.1 (0.4)	[-0.7, 0.4]
Leukocytes (/HPF)								
Cycle 2	Pembrolizumab	1	135.0 (-)	[135.0, 135.0]	3.0 (-)	[3.0, 3.0]	-132.0 (-)	[-132.0, -132.0]
	Placebo	2	399.5 (557.9)	[5.0, 794.0]	58.5 (70.0)	[9.0, 108.0]	-341.0 (487.9)	[-686.0, 4.0]
Cycle 5	Pembrolizumab	20	32.8 (67.2)	[0.0, 250.0]	28.7 (50.3)	[1.0, 210.0]	-4.1 (31.8)	[-97.0, 75.0]
	Placebo	21	41.2 (172.5)	[0.0, 794.0]	17.6 (46.5)	[0.0, 216.0]	-23.6 (127.4)	[-578.0, 31.0]
Cycle 6	Placebo	1	9.0 (-)	[9.0, 9.0]	51.0 (-)	[51.0, 51.0]	42.0 (-)	[42.0, 42.0]
Cycle 8	Pembrolizumab	1	135.0 (-)	[135.0, 135.0]	40.0 (-)	[40.0, 40.0]	-95.0 (-)	[-95.0, -95.0]
Cycle 9	Pembrolizumab	15	21.5 (35.9)	[1.0, 135.0]	9.5 (8.6)	[0.0, 27.0]	-12.0 (31.6)	[-108.0, 21.0]
	Placebo	12	6.8 (10.1)	[0.0, 37.0]	7.6 (9.6)	[1.0, 30.0]	0.8 (13.3)	[-34.0, 23.0]
Cycle 10	Pembrolizumab	1	194.0 (-)	[194.0, 194.0]	36.0 (-)	[36.0, 36.0]	-158.0 (-)	[-158.0, -158.0]
Cycle 11	Pembrolizumab	1	5.0 (-)	[5.0, 5.0]	2.0 (-)	[2.0, 2.0]	-3.0 (-)	[-3.0, -3.0]
Cycle 13	Pembrolizumab	9	5.8 (5.1)	[0.0, 16.0]	5.6 (7.8)	[1.0, 25.0]	-0.2 (6.5)	[-6.0, 15.0]
	Placebo	13	3.7 (3.6)	[0.0, 11.0]	4.4 (4.1)	[0.0, 12.0]	0.7 (3.1)	[-3.0, 9.0]
Cycle 14	Placebo	1	0.0 (-)	[0.0, 0.0]	5.0 (-)	[5.0, 5.0]	5.0 (-)	[5.0, 5.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 17	Pembrolizumab	9	11.1 (17.4)	[0.0, 50.0]	7.0 (7.1)	[1.0, 20.0]	-4.1 (16.9)	[-40.0, 20.0]
	Placebo	8	5.6 (6.5)	[1.0, 20.0]	13.8 (32.6)	[0.0, 94.0]	8.1 (32.9)	[-19.0, 88.0]
Cycle 18	Pembrolizumab	2	222.0 (39.6)	[194.0, 250.0]	188.0 (246.1)	[14.0, 362.0]	-34.0 (285.7)	[-236.0, 168.0]
	Placebo	2	3.0 (4.2)	[0.0, 6.0]	1.5 (0.7)	[1.0, 2.0]	-1.5 (3.5)	[-4.0, 1.0]
End of Treatment	Placebo	1	5.0 (-)	[5.0, 5.0]	3.0 (-)	[3.0, 3.0]	-2.0 (-)	[-2.0, -2.0]
Leukocytes (10^9/L)								
Cycle 1	Pembrolizumab	1	6.1 (-)	[6.1, 6.1]	12.1 (-)	[12.1, 12.1]	6.0 (-)	[6.0, 6.0]
Cycle 2	Pembrolizumab	54	6.4 (2.7)	[3.3, 21.9]	6.2 (2.0)	[2.8, 13.3]	-0.2 (2.3)	[-13.1, 4.6]
	Placebo	49	6.4 (1.7)	[3.8, 11.8]	6.4 (2.0)	[3.6, 11.6]	-0.0 (1.5)	[-3.1, 4.8]
Cycle 3	Pembrolizumab	479	6.5 (2.0)	[3.0, 21.9]	6.4 (1.8)	[3.0, 13.5]	-0.1 (1.6)	[-11.4, 4.9]
	Placebo	485	6.4 (1.8)	[2.8, 13.8]	6.2 (1.8)	[2.8, 15.2]	-0.2 (1.4)	[-5.9, 6.6]
Cycle 4	Pembrolizumab	42	6.0 (1.3)	[3.6, 9.5]	6.4 (1.8)	[3.4, 11.0]	0.4 (1.4)	[-2.2, 4.5]
	Placebo	39	6.6 (1.9)	[3.1, 13.8]	6.5 (1.9)	[3.2, 12.8]	-0.0 (2.0)	[-7.9, 5.2]
Cycle 5	Pembrolizumab	445	6.5 (2.0)	[3.0, 21.9]	6.5 (1.9)	[2.7, 14.0]	0.0 (1.7)	[-11.7, 5.1]
	Placebo	422	6.4 (1.7)	[2.8, 13.8]	6.3 (1.9)	[2.9, 16.1]	-0.0 (1.6)	[-7.5, 8.1]
Cycle 6	Pembrolizumab	51	6.4 (1.6)	[3.9, 10.9]	6.6 (1.8)	[3.6, 14.2]	0.2 (1.7)	[-3.2, 7.0]
	Placebo	30	6.5 (2.3)	[3.1, 13.5]	6.3 (2.3)	[2.7, 14.0]	-0.2 (1.3)	[-3.4, 2.3]
Cycle 7	Pembrolizumab	412	6.5 (2.0)	[3.0, 21.9]	6.7 (2.1)	[3.0, 17.0]	0.2 (1.9)	[-10.6, 9.3]
	Placebo	394	6.4 (1.7)	[2.8, 13.8]	6.3 (2.0)	[3.0, 27.4]	-0.1 (1.8)	[-8.5, 18.7]
Cycle 8	Pembrolizumab	39	6.4 (1.6)	[4.0, 10.9]	7.0 (2.1)	[4.0, 16.4]	0.6 (1.8)	[-2.4, 6.7]
	Placebo	38	6.5 (2.0)	[4.1, 13.5]	6.5 (2.4)	[3.0, 12.3]	0.0 (1.6)	[-2.4, 6.1]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 9	Pembrolizumab	383	6.4 (1.8)	[3.0, 14.8]	6.5 (1.8)	[2.4, 14.0]	0.1 (1.6)	[-5.1, 6.6]
	Placebo	363	6.3 (1.7)	[2.8, 13.8]	6.4 (1.9)	[2.8, 14.9]	0.0 (1.7)	[-6.9, 9.8]
Cycle 10	Pembrolizumab	37	6.5 (1.5)	[4.2, 10.9]	6.5 (1.8)	[4.1, 12.9]	0.1 (1.5)	[-2.6, 4.4]
	Placebo	32	6.6 (2.2)	[3.9, 13.8]	6.5 (1.8)	[3.4, 10.9]	-0.1 (1.6)	[-6.5, 2.6]
Cycle 11	Pembrolizumab	362	6.4 (1.8)	[3.0, 13.8]	6.3 (1.9)	[2.9, 20.4]	-0.0 (1.5)	[-4.6, 8.1]
	Placebo	343	6.4 (1.7)	[2.8, 13.8]	6.3 (1.8)	[2.7, 15.0]	-0.1 (1.5)	[-7.0, 8.0]
Cycle 12	Pembrolizumab	30	6.1 (1.3)	[4.0, 9.7]	6.0 (1.5)	[2.8, 9.6]	-0.1 (1.4)	[-2.5, 3.5]
	Placebo	30	6.2 (2.3)	[3.0, 13.8]	6.3 (2.4)	[3.5, 16.4]	0.1 (1.9)	[-5.9, 5.4]
Cycle 13	Pembrolizumab	341	6.4 (1.8)	[3.2, 13.8]	6.7 (2.0)	[3.2, 16.9]	0.2 (1.7)	[-5.2, 8.6]
	Placebo	318	6.4 (1.8)	[2.8, 13.8]	6.5 (2.2)	[3.0, 21.9]	0.1 (1.9)	[-8.6, 15.7]
Cycle 14	Pembrolizumab	37	6.4 (1.3)	[3.9, 9.7]	6.6 (1.4)	[3.4, 10.2]	0.2 (1.3)	[-2.1, 4.1]
	Placebo	25	6.1 (2.1)	[3.0, 13.8]	5.8 (1.5)	[3.3, 9.5]	-0.3 (2.1)	[-6.7, 3.8]
Cycle 15	Pembrolizumab	329	6.4 (1.8)	[3.2, 13.3]	6.6 (1.8)	[3.3, 16.8]	0.2 (1.6)	[-5.5, 7.9]
	Placebo	317	6.4 (1.8)	[2.8, 13.8]	6.4 (2.0)	[3.2, 16.3]	0.0 (1.7)	[-6.0, 8.6]
Cycle 16	Pembrolizumab	41	6.3 (1.2)	[3.7, 8.4]	6.9 (2.3)	[3.4, 15.4]	0.6 (1.8)	[-2.9, 7.1]
	Placebo	21	6.4 (2.4)	[3.0, 12.2]	5.9 (1.7)	[3.4, 10.1]	-0.5 (2.0)	[-5.4, 2.0]
Cycle 17	Pembrolizumab	308	6.4 (1.7)	[3.2, 13.3]	6.5 (1.8)	[3.3, 12.8]	0.1 (1.6)	[-5.3, 5.0]
	Placebo	305	6.4 (1.8)	[2.8, 13.8]	6.4 (2.0)	[2.3, 15.2]	-0.0 (1.8)	[-7.8, 10.2]
Cycle 18	Pembrolizumab	41	6.0 (1.4)	[3.3, 9.4]	6.0 (1.3)	[3.7, 9.7]	-0.1 (1.4)	[-3.9, 2.8]
	Placebo	36	6.2 (2.0)	[3.4, 13.8]	5.8 (1.4)	[3.7, 8.4]	-0.4 (1.8)	[-8.0, 2.5]
Cycle 19	Pembrolizumab	44	6.1 (1.6)	[3.3, 9.8]	6.6 (1.7)	[3.2, 11.0]	0.5 (1.4)	[-2.6, 2.9]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	38	5.9 (1.9)	[3.0, 12.2]	6.1 (1.9)	[3.2, 10.0]	0.2 (1.3)	[-2.5, 4.4]
Cycle 20	Pembrolizumab	8	6.5 (1.8)	[4.5, 9.8]	6.1 (1.6)	[4.3, 8.7]	-0.3 (0.9)	[-1.5, 1.5]
	Placebo	2	5.6 (0.2)	[5.4, 5.7]	5.5 (0.9)	[4.8, 6.1]	-0.1 (0.7)	[-0.6, 0.4]
Cycle 21	Pembrolizumab	4	6.4 (2.5)	[4.5, 9.8]	8.3 (1.6)	[5.9, 9.6]	1.9 (1.8)	[-0.2, 4.2]
	Placebo	2	9.3 (4.1)	[6.4, 12.2]	7.1 (2.2)	[5.5, 8.6]	-2.3 (1.9)	[-3.6, -0.9]
Cycle 22	Pembrolizumab	2	5.6 (0.9)	[5.0, 6.2]	7.3 (0.4)	[7.0, 7.6]	1.7 (1.3)	[0.8, 2.6]
Cycle 23	Pembrolizumab	1	5.0 (-)	[5.0, 5.0]	6.3 (-)	[6.3, 6.3]	1.3 (-)	[1.3, 1.3]
Missing	Pembrolizumab	24	7.6 (2.1)	[3.8, 11.4]	7.5 (2.5)	[4.0, 12.2]	-0.1 (1.3)	[-3.0, 2.5]
	Placebo	16	5.8 (1.1)	[4.3, 8.8]	7.4 (3.0)	[3.6, 15.4]	1.6 (2.6)	[-0.7, 8.7]
Unscheduled	Pembrolizumab	22	6.8 (1.9)	[3.7, 9.7]	7.4 (2.1)	[3.6, 12.8]	0.6 (2.3)	[-5.5, 4.7]
	Placebo	21	5.5 (1.1)	[4.0, 8.2]	6.9 (3.3)	[3.7, 14.3]	1.4 (2.7)	[-1.2, 8.8]
End of Treatment	Pembrolizumab	1	5.0 (-)	[5.0, 5.0]	5.4 (-)	[5.4, 5.4]	0.4 (-)	[0.4, 0.4]
	Placebo	6	7.6 (2.1)	[5.5, 10.9]	6.8 (2.4)	[4.0, 9.9]	-0.8 (2.7)	[-3.7, 4.4]
Lymphocytes (10^9/L)								
Cycle 2	Pembrolizumab	42	1.8 (0.7)	[0.4, 4.1]	1.7 (0.6)	[0.7, 2.9]	-0.1 (0.4)	[-1.6, 0.9]
	Placebo	42	1.7 (0.6)	[0.5, 3.3]	1.8 (0.7)	[0.4, 3.3]	0.1 (0.3)	[-0.6, 0.9]
Cycle 3	Pembrolizumab	425	1.8 (0.6)	[0.3, 4.1]	1.7 (0.6)	[0.5, 3.7]	-0.1 (0.4)	[-2.5, 1.2]
	Placebo	437	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.5, 4.6]	0.1 (0.4)	[-1.7, 1.5]
Cycle 4	Pembrolizumab	37	1.6 (0.6)	[0.4, 3.0]	1.7 (0.7)	[0.6, 4.8]	0.0 (0.5)	[-0.9, 1.8]
	Placebo	34	1.6 (0.5)	[0.5, 2.8]	1.7 (0.6)	[0.8, 2.6]	0.1 (0.4)	[-0.7, 1.1]
Cycle 5	Pembrolizumab	402	1.8 (0.6)	[0.3, 4.1]	1.7 (0.6)	[0.5, 6.0]	-0.1 (0.5)	[-2.2, 3.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	379	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.5, 4.0]	0.0 (0.4)	[-1.5, 1.4]
Cycle 6	Pembrolizumab	42	1.8 (0.6)	[0.8, 3.0]	1.8 (0.7)	[0.9, 4.8]	-0.0 (0.5)	[-0.7, 1.8]
	Placebo	26	1.8 (0.7)	[0.5, 3.5]	1.8 (0.7)	[0.8, 4.6]	-0.0 (0.6)	[-1.1, 1.9]
Cycle 7	Pembrolizumab	367	1.8 (0.6)	[0.5, 4.1]	1.7 (0.6)	[0.5, 7.0]	-0.1 (0.5)	[-2.0, 4.0]
	Placebo	356	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.6, 3.9]	0.1 (0.4)	[-1.6, 1.1]
Cycle 8	Pembrolizumab	32	1.9 (0.6)	[1.0, 3.3]	1.8 (1.0)	[0.6, 6.7]	-0.1 (0.8)	[-1.4, 3.7]
	Placebo	32	1.8 (0.7)	[0.5, 3.5]	1.7 (0.6)	[0.6, 2.8]	-0.1 (0.4)	[-1.2, 0.5]
Cycle 9	Pembrolizumab	342	1.8 (0.6)	[0.5, 3.8]	1.7 (0.6)	[0.6, 5.6]	-0.1 (0.5)	[-2.3, 2.6]
	Placebo	329	1.7 (0.6)	[0.4, 4.1]	1.8 (0.6)	[0.6, 4.2]	0.0 (0.4)	[-1.5, 1.8]
Cycle 10	Pembrolizumab	31	1.8 (0.6)	[1.0, 3.0]	1.7 (0.8)	[0.8, 5.4]	-0.1 (0.6)	[-1.3, 2.4]
	Placebo	26	1.8 (0.6)	[0.5, 3.3]	1.8 (0.6)	[0.9, 3.0]	0.1 (0.3)	[-0.3, 0.7]
Cycle 11	Pembrolizumab	322	1.8 (0.6)	[0.5, 3.8]	1.7 (0.6)	[0.5, 4.1]	-0.1 (0.5)	[-2.7, 1.7]
	Placebo	313	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.3, 4.2]	0.1 (0.5)	[-1.8, 2.7]
Cycle 12	Pembrolizumab	24	1.9 (0.5)	[1.0, 3.0]	1.8 (0.5)	[1.0, 3.2]	-0.0 (0.4)	[-0.8, 0.6]
	Placebo	28	1.6 (0.6)	[0.4, 3.1]	1.7 (0.6)	[0.6, 3.0]	0.0 (0.4)	[-1.0, 0.9]
Cycle 13	Pembrolizumab	304	1.8 (0.6)	[0.5, 3.8]	1.8 (0.6)	[0.6, 4.4]	-0.0 (0.5)	[-2.1, 1.8]
	Placebo	285	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.5, 4.0]	0.0 (0.5)	[-1.6, 2.2]
Cycle 14	Pembrolizumab	32	1.9 (0.4)	[1.2, 3.0]	1.8 (0.5)	[1.0, 3.2]	-0.1 (0.5)	[-1.2, 0.8]
	Placebo	23	1.4 (0.6)	[0.4, 2.5]	1.6 (0.6)	[0.5, 2.9]	0.2 (0.4)	[-0.4, 0.8]
Cycle 15	Pembrolizumab	293	1.8 (0.6)	[0.5, 3.8]	1.7 (0.5)	[0.6, 4.0]	-0.1 (0.4)	[-1.3, 1.8]
	Placebo	289	1.7 (0.6)	[0.3, 4.1]	1.8 (0.6)	[0.5, 3.6]	0.1 (0.4)	[-1.4, 1.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 16	Pembrolizumab	31	1.9 (0.6)	[1.1, 3.4]	1.8 (0.4)	[0.9, 2.6]	-0.1 (0.5)	[-2.2, 0.5]
	Placebo	18	1.7 (0.8)	[0.5, 3.4]	1.9 (0.8)	[0.7, 4.1]	0.1 (0.4)	[-0.7, 0.8]
Cycle 17	Pembrolizumab	276	1.8 (0.6)	[0.5, 3.8]	1.7 (0.5)	[0.6, 3.5]	-0.1 (0.4)	[-2.2, 1.4]
	Placebo	275	1.7 (0.6)	[0.3, 4.1]	1.8 (0.5)	[0.6, 4.3]	0.0 (0.5)	[-1.6, 2.0]
Cycle 18	Pembrolizumab	32	1.8 (0.7)	[0.6, 3.4]	1.7 (0.5)	[0.7, 2.6]	-0.1 (0.5)	[-2.1, 0.6]
	Placebo	35	1.6 (0.5)	[0.5, 2.7]	1.6 (0.5)	[0.8, 2.8]	0.1 (0.3)	[-0.5, 0.5]
Cycle 19	Pembrolizumab	39	1.7 (0.6)	[0.5, 3.5]	1.8 (0.5)	[1.0, 2.9]	0.0 (0.4)	[-0.9, 1.5]
	Placebo	35	1.7 (0.6)	[0.5, 3.3]	1.8 (0.6)	[0.7, 2.9]	0.1 (0.4)	[-0.5, 1.2]
Cycle 20	Pembrolizumab	7	2.1 (0.7)	[1.4, 3.5]	1.8 (0.5)	[1.2, 2.6]	-0.3 (0.6)	[-1.2, 0.4]
	Placebo	2	1.3 (0.3)	[1.0, 1.5]	1.2 (0.2)	[1.1, 1.3]	-0.1 (0.2)	[-0.2, 0.0]
Cycle 21	Pembrolizumab	4	1.8 (1.3)	[0.5, 3.5]	1.8 (0.7)	[0.9, 2.6]	0.0 (0.6)	[-0.9, 0.5]
	Placebo	2	1.7 (1.7)	[0.5, 2.9]	1.5 (0.9)	[0.8, 2.2]	-0.2 (0.8)	[-0.8, 0.3]
Cycle 22	Pembrolizumab	2	1.9 (0.3)	[1.7, 2.2]	1.6 (0.2)	[1.5, 1.7]	-0.3 (0.5)	[-0.7, 0.0]
Cycle 23	Pembrolizumab	1	2.2 (-)	[2.2, 2.2]	1.8 (-)	[1.8, 1.8]	-0.3 (-)	[-0.3, -0.3]
Missing	Pembrolizumab	22	2.1 (0.7)	[1.0, 3.8]	2.0 (0.6)	[1.0, 2.9]	-0.2 (0.5)	[-1.3, 0.7]
	Placebo	15	1.8 (0.7)	[0.7, 3.2]	1.9 (0.8)	[0.5, 3.4]	0.0 (0.5)	[-0.6, 0.7]
Unscheduled	Pembrolizumab	22	2.0 (0.6)	[1.0, 3.3]	1.6 (0.6)	[0.7, 3.0]	-0.4 (0.7)	[-1.9, 1.2]
	Placebo	17	1.6 (0.4)	[0.5, 2.1]	1.7 (0.7)	[0.3, 2.8]	0.1 (0.5)	[-1.0, 0.9]
End of Treatment	Pembrolizumab	1	1.8 (-)	[1.8, 1.8]	1.7 (-)	[1.7, 1.7]	-0.1 (-)	[-0.1, -0.1]
	Placebo	6	1.8 (0.8)	[0.4, 2.6]	1.6 (0.6)	[0.5, 2.2]	-0.2 (0.3)	[-0.6, 0.1]
Lymphocytes/Leukocytes (10^9/L)								

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 2	Pembrolizumab	12	2.0 (0.6)	[1.0, 3.1]	1.9 (0.4)	[1.4, 2.6]	-0.1 (0.3)	[-0.6, 0.4]
	Placebo	6	1.8 (0.8)	[1.0, 3.3]	1.9 (0.7)	[1.0, 3.2]	0.0 (0.2)	[-0.1, 0.4]
Cycle 3	Pembrolizumab	41	1.7 (0.5)	[0.6, 3.1]	1.6 (0.4)	[0.7, 2.3]	-0.1 (0.4)	[-0.9, 0.8]
	Placebo	39	1.7 (0.6)	[0.3, 3.4]	1.9 (0.6)	[0.7, 3.7]	0.1 (0.4)	[-0.8, 1.1]
Cycle 4	Pembrolizumab	4	1.7 (0.5)	[1.0, 2.2]	1.6 (0.3)	[1.2, 1.9]	-0.2 (0.3)	[-0.5, 0.3]
	Placebo	4	1.5 (0.8)	[0.5, 2.6]	1.7 (0.7)	[1.0, 2.6]	0.2 (0.3)	[-0.0, 0.5]
Cycle 5	Pembrolizumab	35	1.7 (0.5)	[0.9, 3.1]	1.6 (0.4)	[0.8, 2.5]	-0.1 (0.3)	[-0.7, 0.5]
	Placebo	30	1.8 (0.7)	[0.5, 3.4]	1.9 (0.7)	[0.8, 4.0]	0.1 (0.5)	[-0.9, 1.3]
Cycle 6	Pembrolizumab	7	1.7 (0.2)	[1.4, 1.9]	1.6 (0.4)	[1.0, 2.1]	-0.1 (0.4)	[-0.7, 0.5]
	Placebo	4	1.3 (0.9)	[0.5, 2.6]	1.8 (1.0)	[1.0, 3.0]	0.5 (0.2)	[0.2, 0.7]
Cycle 7	Pembrolizumab	32	1.8 (0.5)	[0.9, 3.1]	1.6 (0.5)	[0.6, 3.1]	-0.2 (0.4)	[-1.0, 1.0]
	Placebo	30	1.6 (0.6)	[0.3, 3.3]	1.7 (0.6)	[0.6, 3.2]	0.1 (0.5)	[-1.0, 1.4]
Cycle 8	Pembrolizumab	4	1.7 (0.2)	[1.4, 1.9]	1.7 (0.0)	[1.7, 1.7]	-0.1 (0.2)	[-0.2, 0.2]
	Placebo	5	1.4 (0.3)	[0.8, 1.7]	1.6 (0.4)	[1.2, 2.2]	0.2 (0.4)	[-0.1, 0.8]
Cycle 9	Pembrolizumab	32	1.8 (0.5)	[0.9, 3.1]	1.6 (0.4)	[0.8, 2.8]	-0.1 (0.4)	[-0.9, 0.7]
	Placebo	28	1.6 (0.6)	[0.3, 3.3]	1.7 (0.6)	[0.8, 3.3]	0.1 (0.4)	[-1.0, 1.3]
Cycle 10	Pembrolizumab	4	1.7 (0.2)	[1.4, 1.9]	1.3 (0.5)	[0.8, 1.8]	-0.5 (0.6)	[-0.9, 0.4]
	Placebo	5	1.6 (0.6)	[0.8, 2.6]	2.1 (0.8)	[1.4, 3.4]	0.6 (0.5)	[-0.1, 1.2]
Cycle 11	Pembrolizumab	27	1.7 (0.5)	[0.9, 3.1]	1.5 (0.4)	[0.9, 2.8]	-0.2 (0.4)	[-0.8, 0.6]
	Placebo	23	1.7 (0.6)	[0.8, 3.3]	1.8 (0.5)	[0.7, 2.5]	0.1 (0.5)	[-0.9, 1.3]
Cycle 12	Pembrolizumab	5	1.5 (0.4)	[0.9, 1.9]	1.6 (0.5)	[0.8, 2.1]	0.1 (0.3)	[-0.2, 0.6]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	2	2.0 (0.9)	[1.4, 2.6]	2.8 (0.2)	[2.6, 2.9]	0.8 (0.6)	[0.3, 1.2]
Cycle 13	Pembrolizumab	27	1.7 (0.5)	[0.9, 2.9]	1.8 (0.5)	[0.8, 3.2]	0.0 (0.5)	[-0.9, 1.3]
	Placebo	22	1.6 (0.7)	[0.3, 3.3]	1.9 (0.6)	[0.9, 3.1]	0.3 (0.4)	[-0.5, 1.1]
Cycle 14	Pembrolizumab	3	1.6 (0.3)	[1.4, 1.9]	2.1 (0.6)	[1.5, 2.7]	0.5 (0.6)	[0.1, 1.2]
	Placebo	2	2.1 (0.7)	[1.6, 2.6]	2.0 (0.2)	[1.9, 2.2]	-0.1 (0.5)	[-0.4, 0.3]
Cycle 15	Pembrolizumab	26	1.6 (0.4)	[0.9, 2.5]	1.7 (0.6)	[0.9, 3.2]	0.1 (0.5)	[-0.7, 1.7]
	Placebo	20	1.6 (0.7)	[0.3, 3.3]	1.9 (0.6)	[0.6, 2.9]	0.3 (0.5)	[-0.7, 1.1]
Cycle 16	Pembrolizumab	7	1.6 (0.4)	[0.9, 1.9]	1.6 (0.6)	[0.9, 2.8]	0.0 (0.6)	[-0.6, 1.3]
	Placebo	1	1.8 (-)	[1.8, 1.8]	1.4 (-)	[1.4, 1.4]	-0.5 (-)	[-0.5, -0.5]
Cycle 17	Pembrolizumab	24	1.6 (0.5)	[0.9, 2.9]	1.7 (0.5)	[0.9, 2.9]	0.1 (0.5)	[-0.8, 1.3]
	Placebo	21	1.6 (0.6)	[0.3, 3.3]	1.9 (0.7)	[0.6, 3.1]	0.3 (0.5)	[-0.5, 1.5]
Cycle 18	Pembrolizumab	7	1.6 (0.3)	[1.1, 2.1]	1.5 (0.7)	[0.6, 2.6]	-0.0 (0.6)	[-0.9, 1.1]
Cycle 19	Pembrolizumab	4	1.8 (0.4)	[1.5, 2.3]	1.6 (0.5)	[1.1, 2.3]	-0.2 (0.7)	[-0.9, 0.8]
	Placebo	1	1.8 (-)	[1.8, 1.8]	1.2 (-)	[1.2, 1.2]	-0.6 (-)	[-0.6, -0.6]
Cycle 20	Pembrolizumab	1	1.9 (-)	[1.9, 1.9]	1.6 (-)	[1.6, 1.6]	-0.3 (-)	[-0.3, -0.3]
Missing	Pembrolizumab	2	1.5 (0.9)	[0.9, 2.1]	1.7 (1.1)	[0.9, 2.4]	0.2 (0.2)	[0.0, 0.3]
	Placebo	1	1.6 (-)	[1.6, 1.6]	1.4 (-)	[1.4, 1.4]	-0.2 (-)	[-0.2, -0.2]
Unscheduled	Placebo	2	1.2 (0.5)	[0.8, 1.6]	1.5 (0.8)	[0.9, 2.1]	0.3 (0.3)	[0.1, 0.5]
Monocytes (10^9/L)								
Cycle 2	Pembrolizumab	43	0.5 (0.3)	[0.3, 1.9]	0.5 (0.2)	[0.3, 1.0]	-0.0 (0.2)	[-1.0, 0.3]
	Placebo	41	0.5 (0.2)	[0.3, 1.2]	0.5 (0.2)	[0.1, 0.9]	-0.0 (0.2)	[-0.3, 0.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 3	Pembrolizumab	426	0.5 (0.2)	[0.0, 1.9]	0.5 (0.2)	[0.1, 1.4]	0.0 (0.2)	[-1.1, 0.8]
	Placebo	438	0.5 (0.2)	[0.2, 1.4]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.1)	[-0.8, 0.5]
Cycle 4	Pembrolizumab	37	0.5 (0.1)	[0.2, 0.8]	0.5 (0.1)	[0.3, 0.8]	0.0 (0.1)	[-0.2, 0.3]
	Placebo	34	0.5 (0.1)	[0.2, 0.8]	0.5 (0.2)	[0.3, 1.0]	0.0 (0.1)	[-0.3, 0.4]
Cycle 5	Pembrolizumab	404	0.5 (0.2)	[0.0, 1.9]	0.5 (0.2)	[0.1, 1.5]	0.0 (0.2)	[-1.2, 0.8]
	Placebo	378	0.5 (0.2)	[0.2, 1.4]	0.5 (0.2)	[0.1, 1.4]	0.0 (0.2)	[-0.6, 0.8]
Cycle 6	Pembrolizumab	39	0.5 (0.1)	[0.2, 0.9]	0.6 (0.2)	[0.3, 1.0]	0.1 (0.2)	[-0.4, 0.5]
	Placebo	26	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.2, 0.9]	-0.0 (0.1)	[-0.3, 0.2]
Cycle 7	Pembrolizumab	366	0.5 (0.2)	[0.1, 1.9]	0.5 (0.2)	[0.1, 1.7]	0.0 (0.2)	[-1.1, 1.1]
	Placebo	355	0.5 (0.2)	[0.2, 1.4]	0.5 (0.2)	[0.1, 1.1]	0.0 (0.1)	[-1.2, 0.4]
Cycle 8	Pembrolizumab	32	0.5 (0.2)	[0.2, 0.8]	0.5 (0.1)	[0.4, 1.0]	0.1 (0.2)	[-0.2, 0.5]
	Placebo	32	0.5 (0.2)	[0.3, 1.0]	0.5 (0.2)	[0.3, 1.0]	-0.0 (0.1)	[-0.4, 0.3]
Cycle 9	Pembrolizumab	344	0.5 (0.2)	[0.1, 1.2]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.2)	[-0.5, 0.7]
	Placebo	328	0.5 (0.2)	[0.2, 1.4]	0.5 (0.2)	[0.0, 1.4]	0.0 (0.2)	[-0.5, 0.6]
Cycle 10	Pembrolizumab	31	0.5 (0.1)	[0.3, 0.8]	0.5 (0.2)	[0.3, 0.9]	0.1 (0.1)	[-0.1, 0.4]
	Placebo	26	0.5 (0.1)	[0.3, 0.9]	0.5 (0.2)	[0.2, 1.1]	0.0 (0.1)	[-0.4, 0.3]
Cycle 11	Pembrolizumab	323	0.5 (0.2)	[0.1, 1.2]	0.5 (0.2)	[0.1, 1.2]	0.0 (0.1)	[-0.5, 0.6]
	Placebo	310	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.1, 1.1]	0.0 (0.1)	[-0.5, 0.5]
Cycle 12	Pembrolizumab	24	0.4 (0.1)	[0.3, 0.7]	0.5 (0.1)	[0.2, 0.9]	0.0 (0.1)	[-0.1, 0.4]
	Placebo	28	0.5 (0.1)	[0.2, 0.8]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.2)	[-0.2, 0.7]
Cycle 13	Pembrolizumab	304	0.5 (0.2)	[0.1, 1.2]	0.5 (0.2)	[0.2, 1.7]	0.0 (0.2)	[-0.5, 1.2]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	285	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.0, 1.5]	0.0 (0.2)	[-0.4, 1.1]
Cycle 14	Pembrolizumab	33	0.5 (0.1)	[0.3, 0.7]	0.6 (0.2)	[0.2, 1.0]	0.1 (0.2)	[-0.2, 0.7]
	Placebo	23	0.5 (0.1)	[0.3, 0.8]	0.5 (0.2)	[0.2, 0.8]	0.0 (0.1)	[-0.3, 0.2]
Cycle 15	Pembrolizumab	295	0.5 (0.1)	[0.1, 1.0]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.1)	[-0.4, 0.6]
	Placebo	289	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.2, 1.2]	0.0 (0.1)	[-0.4, 0.7]
Cycle 16	Pembrolizumab	31	0.5 (0.1)	[0.3, 0.7]	0.5 (0.2)	[0.3, 1.0]	0.0 (0.1)	[-0.3, 0.4]
	Placebo	18	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.2, 0.9]	0.1 (0.1)	[-0.2, 0.3]
Cycle 17	Pembrolizumab	275	0.5 (0.2)	[0.1, 1.0]	0.5 (0.2)	[0.1, 1.2]	0.0 (0.2)	[-0.5, 0.6]
	Placebo	275	0.5 (0.2)	[0.2, 1.0]	0.5 (0.2)	[0.2, 1.5]	0.0 (0.2)	[-0.5, 1.0]
Cycle 18	Pembrolizumab	33	0.5 (0.1)	[0.1, 0.9]	0.5 (0.2)	[0.2, 1.2]	-0.0 (0.2)	[-0.2, 0.6]
	Placebo	35	0.5 (0.1)	[0.3, 0.8]	0.5 (0.2)	[0.3, 1.0]	0.0 (0.2)	[-0.4, 0.4]
Cycle 19	Pembrolizumab	39	0.5 (0.2)	[0.2, 0.8]	0.5 (0.2)	[0.2, 1.4]	0.1 (0.2)	[-0.4, 0.8]
	Placebo	35	0.5 (0.2)	[0.3, 1.0]	0.5 (0.2)	[0.2, 1.0]	0.0 (0.2)	[-0.4, 0.4]
Cycle 20	Pembrolizumab	7	0.5 (0.2)	[0.3, 0.8]	0.5 (0.2)	[0.3, 0.9]	0.1 (0.2)	[-0.2, 0.5]
	Placebo	2	0.3 (0.0)	[0.3, 0.4]	0.3 (0.1)	[0.2, 0.4]	-0.0 (0.1)	[-0.1, 0.0]
Cycle 21	Pembrolizumab	4	0.5 (0.3)	[0.2, 0.8]	0.7 (0.1)	[0.6, 0.7]	0.1 (0.3)	[-0.2, 0.4]
	Placebo	2	0.8 (0.3)	[0.5, 1.0]	0.6 (0.0)	[0.6, 0.6]	-0.1 (0.3)	[-0.4, 0.1]
Cycle 22	Pembrolizumab	2	0.3 (0.2)	[0.2, 0.5]	0.7 (0.3)	[0.5, 1.0]	0.4 (0.2)	[0.3, 0.5]
Cycle 23	Pembrolizumab	1	0.2 (-)	[0.2, 0.2]	0.4 (-)	[0.4, 0.4]	0.2 (-)	[0.2, 0.2]
Missing	Pembrolizumab	22	0.5 (0.2)	[0.2, 0.8]	0.5 (0.1)	[0.2, 0.8]	-0.0 (0.1)	[-0.2, 0.3]
	Placebo	15	0.4 (0.1)	[0.2, 0.6]	0.5 (0.3)	[0.3, 1.3]	0.1 (0.2)	[-0.1, 0.9]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Unscheduled	Pembrolizumab	21	0.5 (0.1)	[0.3, 0.8]	0.6 (0.2)	[0.3, 0.9]	0.0 (0.2)	[-0.4, 0.6]
	Placebo	17	0.5 (0.1)	[0.2, 0.7]	0.6 (0.2)	[0.3, 1.1]	0.1 (0.1)	[-0.1, 0.4]
End of Treatment	Pembrolizumab	1	0.4 (-)	[0.4, 0.4]	0.5 (-)	[0.5, 0.5]	0.1 (-)	[0.1, 0.1]
	Placebo	6	0.5 (0.2)	[0.3, 0.8]	0.4 (0.2)	[0.2, 0.7]	-0.1 (0.3)	[-0.5, 0.3]
Monocytes/Leukocytes (10^9/L)								
Cycle 2	Pembrolizumab	11	0.4 (0.1)	[0.2, 0.5]	0.4 (0.2)	[0.0, 0.7]	-0.0 (0.2)	[-0.5, 0.2]
	Placebo	6	0.4 (0.2)	[0.3, 0.7]	0.5 (0.3)	[0.0, 0.9]	0.0 (0.2)	[-0.3, 0.5]
Cycle 3	Pembrolizumab	43	0.4 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 0.9]	0.0 (0.1)	[-0.1, 0.4]
	Placebo	39	0.4 (0.2)	[0.0, 0.9]	0.5 (0.2)	[0.1, 1.6]	0.1 (0.2)	[-0.3, 0.6]
Cycle 4	Pembrolizumab	4	0.4 (0.2)	[0.2, 0.6]	0.5 (0.2)	[0.2, 0.5]	0.0 (0.1)	[-0.0, 0.1]
	Placebo	4	0.5 (0.1)	[0.4, 0.5]	0.8 (0.3)	[0.5, 1.3]	0.3 (0.3)	[0.0, 0.7]
Cycle 5	Pembrolizumab	34	0.5 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 1.4]	0.0 (0.2)	[-0.2, 0.5]
	Placebo	30	0.4 (0.2)	[0.0, 0.9]	0.5 (0.2)	[0.2, 1.1]	0.1 (0.2)	[-0.3, 0.7]
Cycle 6	Pembrolizumab	7	0.4 (0.1)	[0.3, 0.5]	0.4 (0.1)	[0.3, 0.6]	-0.0 (0.1)	[-0.2, 0.2]
	Placebo	4	0.5 (0.2)	[0.3, 0.6]	0.4 (0.3)	[0.1, 0.6]	-0.1 (0.3)	[-0.5, 0.2]
Cycle 7	Pembrolizumab	33	0.5 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 1.3]	0.0 (0.2)	[-0.2, 0.5]
	Placebo	30	0.4 (0.2)	[0.0, 0.9]	0.6 (0.3)	[0.2, 1.9]	0.1 (0.3)	[-0.3, 1.3]
Cycle 8	Pembrolizumab	3	0.5 (0.1)	[0.4, 0.5]	0.5 (0.1)	[0.4, 0.6]	0.0 (0.2)	[-0.1, 0.2]
	Placebo	5	0.5 (0.2)	[0.3, 0.7]	0.3 (0.1)	[0.2, 0.4]	-0.1 (0.1)	[-0.3, -0.1]
Cycle 9	Pembrolizumab	30	0.5 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 1.0]	0.0 (0.1)	[-0.2, 0.2]
	Placebo	28	0.4 (0.2)	[0.0, 0.9]	0.5 (0.2)	[0.1, 1.0]	0.0 (0.1)	[-0.3, 0.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 10	Pembrolizumab	4	0.5 (0.1)	[0.4, 0.6]	0.4 (0.1)	[0.3, 0.5]	-0.1 (0.1)	[-0.2, 0.0]
	Placebo	5	0.4 (0.1)	[0.3, 0.6]	0.5 (0.2)	[0.3, 0.7]	0.0 (0.2)	[-0.1, 0.2]
Cycle 11	Pembrolizumab	28	0.4 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 1.0]	0.0 (0.1)	[-0.1, 0.4]
	Placebo	23	0.4 (0.2)	[0.0, 0.9]	0.5 (0.2)	[0.1, 1.1]	0.1 (0.3)	[-0.5, 0.7]
Cycle 12	Pembrolizumab	6	0.4 (0.1)	[0.2, 0.5]	0.3 (0.1)	[0.2, 0.4]	-0.0 (0.1)	[-0.1, 0.1]
	Placebo	2	0.4 (0.1)	[0.3, 0.4]	0.4 (0.2)	[0.3, 0.5]	0.0 (0.1)	[-0.0, 0.1]
Cycle 13	Pembrolizumab	28	0.5 (0.2)	[0.2, 0.9]	0.5 (0.2)	[0.2, 1.2]	0.1 (0.2)	[-0.2, 0.5]
	Placebo	22	0.4 (0.2)	[0.0, 0.9]	0.5 (0.2)	[0.2, 1.1]	0.1 (0.2)	[-0.2, 0.6]
Cycle 14	Pembrolizumab	3	0.4 (0.1)	[0.3, 0.5]	0.5 (0.2)	[0.4, 0.8]	0.1 (0.3)	[-0.1, 0.5]
	Placebo	2	0.6 (0.2)	[0.4, 0.7]	0.5 (0.1)	[0.4, 0.5]	-0.1 (0.1)	[-0.2, -0.0]
Cycle 15	Pembrolizumab	27	0.4 (0.2)	[0.2, 0.9]	0.6 (0.3)	[0.2, 1.3]	0.1 (0.2)	[-0.2, 0.6]
	Placebo	20	0.5 (0.2)	[0.0, 0.9]	0.6 (0.3)	[0.2, 1.1]	0.1 (0.2)	[-0.3, 0.8]
Cycle 16	Pembrolizumab	8	0.4 (0.1)	[0.2, 0.6]	0.5 (0.2)	[0.2, 1.0]	0.1 (0.3)	[-0.2, 0.6]
	Placebo	1	0.0 (-)	[0.0, 0.0]	0.5 (-)	[0.5, 0.5]	0.5 (-)	[0.5, 0.5]
Cycle 17	Pembrolizumab	22	0.4 (0.2)	[0.2, 0.8]	0.5 (0.3)	[0.2, 1.5]	0.1 (0.2)	[-0.2, 0.7]
	Placebo	22	0.4 (0.2)	[0.0, 0.9]	0.5 (0.3)	[0.2, 1.2]	0.1 (0.2)	[-0.3, 0.6]
Cycle 18	Pembrolizumab	7	0.5 (0.2)	[0.3, 0.8]	0.5 (0.3)	[0.2, 1.1]	0.0 (0.1)	[-0.2, 0.3]
Cycle 19	Pembrolizumab	4	0.4 (0.1)	[0.3, 0.5]	0.5 (0.2)	[0.4, 0.8]	0.1 (0.2)	[-0.1, 0.4]
	Placebo	1	0.0 (-)	[0.0, 0.0]	0.5 (-)	[0.5, 0.5]	0.5 (-)	[0.5, 0.5]
Cycle 20	Pembrolizumab	1	0.5 (-)	[0.5, 0.5]	0.4 (-)	[0.4, 0.4]	-0.1 (-)	[-0.1, -0.1]
Missing	Pembrolizumab	2	0.6 (0.5)	[0.2, 0.9]	0.7 (0.6)	[0.3, 1.1]	0.1 (0.1)	[0.1, 0.2]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	1	0.4 (-)	[0.4, 0.4]	0.4 (-)	[0.4, 0.4]	-0.0 (-)	[-0.0, -0.0]
Unscheduled	Placebo	2	0.5 (0.2)	[0.4, 0.6]	0.4 (0.0)	[0.4, 0.4]	-0.2 (0.2)	[-0.3, -0.0]
Neutrophils (10^9/L)								
Cycle 2	Pembrolizumab	44	4.0 (2.2)	[1.6, 15.2]	3.7 (1.8)	[1.4, 11.1]	-0.3 (2.2)	[-11.1, 3.8]
	Placebo	42	3.9 (1.5)	[1.6, 7.5]	3.8 (1.8)	[1.5, 10.4]	-0.1 (1.3)	[-2.8, 5.0]
Cycle 3	Pembrolizumab	436	4.1 (1.7)	[1.5, 15.2]	3.9 (1.5)	[1.4, 10.6]	-0.1 (1.5)	[-8.7, 5.6]
	Placebo	443	3.9 (1.5)	[1.6, 11.6]	3.6 (1.4)	[0.9, 11.9]	-0.3 (1.2)	[-4.5, 5.4]
Cycle 4	Pembrolizumab	37	3.7 (1.3)	[1.8, 7.3]	3.9 (1.7)	[1.6, 9.3]	0.2 (1.3)	[-2.7, 3.5]
	Placebo	34	4.3 (1.9)	[2.0, 11.6]	3.8 (1.3)	[1.9, 7.8]	-0.5 (1.7)	[-7.7, 2.5]
Cycle 5	Pembrolizumab	409	4.0 (1.6)	[1.5, 15.2]	4.0 (1.5)	[1.1, 10.7]	-0.0 (1.6)	[-9.2, 5.8]
	Placebo	385	3.9 (1.4)	[1.6, 11.6]	3.8 (1.5)	[1.0, 11.6]	-0.1 (1.4)	[-7.4, 7.3]
Cycle 6	Pembrolizumab	42	3.8 (1.3)	[1.6, 7.0]	4.1 (1.7)	[2.0, 10.9]	0.3 (1.7)	[-3.4, 7.3]
	Placebo	26	4.1 (1.8)	[2.0, 8.6]	3.9 (1.9)	[1.6, 10.4]	-0.3 (1.1)	[-2.5, 1.8]
Cycle 7	Pembrolizumab	374	4.0 (1.7)	[1.5, 15.2]	4.1 (1.8)	[1.3, 14.6]	0.1 (1.8)	[-8.0, 10.4]
	Placebo	358	3.9 (1.4)	[1.6, 11.6]	3.7 (1.4)	[1.2, 10.3]	-0.2 (1.3)	[-8.6, 4.5]
Cycle 8	Pembrolizumab	32	3.9 (1.5)	[1.9, 7.8]	4.5 (2.2)	[2.0, 13.9]	0.6 (1.8)	[-1.9, 8.0]
	Placebo	32	4.1 (1.6)	[2.4, 8.6]	4.3 (2.2)	[2.1, 10.5]	0.2 (1.7)	[-2.2, 6.9]
Cycle 9	Pembrolizumab	347	3.9 (1.6)	[1.5, 11.9]	3.9 (1.6)	[1.5, 11.0]	0.0 (1.5)	[-7.9, 6.6]
	Placebo	330	3.9 (1.4)	[1.6, 11.6]	3.9 (1.6)	[0.9, 11.8]	-0.0 (1.5)	[-6.9, 8.8]
Cycle 10	Pembrolizumab	33	4.0 (1.3)	[1.9, 7.8]	4.2 (1.5)	[2.0, 9.0]	0.2 (1.3)	[-2.5, 4.2]
	Placebo	26	4.2 (2.0)	[2.0, 11.6]	3.9 (1.3)	[1.9, 6.7]	-0.4 (1.6)	[-5.9, 2.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 11	Pembrolizumab	328	3.9 (1.5)	[1.5, 11.4]	3.8 (1.6)	[1.3, 16.2]	-0.1 (1.3)	[-3.4, 8.6]
	Placebo	313	3.9 (1.4)	[1.6, 11.6]	3.7 (1.4)	[1.4, 10.7]	-0.2 (1.3)	[-7.3, 4.8]
Cycle 12	Pembrolizumab	25	3.6 (1.1)	[1.9, 5.9]	3.6 (1.1)	[1.9, 6.4]	-0.0 (1.2)	[-2.1, 2.9]
	Placebo	28	4.0 (2.1)	[1.8, 11.6]	3.9 (2.1)	[1.4, 12.8]	-0.1 (1.8)	[-6.2, 5.0]
Cycle 13	Pembrolizumab	311	3.9 (1.5)	[1.5, 11.4]	4.1 (1.8)	[1.7, 12.9]	0.1 (1.6)	[-4.6, 7.6]
	Placebo	287	3.9 (1.5)	[1.7, 11.6]	4.0 (1.9)	[1.2, 18.3]	0.0 (1.8)	[-8.3, 15.1]
Cycle 14	Pembrolizumab	33	3.6 (1.1)	[1.9, 6.2]	3.8 (1.2)	[2.0, 7.0]	0.2 (1.2)	[-2.3, 3.6]
	Placebo	23	3.9 (2.0)	[2.0, 11.6]	3.5 (1.2)	[1.5, 6.8]	-0.4 (1.9)	[-6.5, 3.2]
Cycle 15	Pembrolizumab	299	3.9 (1.5)	[1.5, 11.1]	4.0 (1.6)	[1.1, 13.1]	0.1 (1.5)	[-4.9, 8.0]
	Placebo	291	3.9 (1.5)	[1.7, 11.6]	3.8 (1.6)	[1.4, 14.7]	-0.1 (1.5)	[-6.5, 8.5]
Cycle 16	Pembrolizumab	34	3.7 (1.1)	[1.8, 5.9]	4.2 (2.2)	[1.2, 11.9]	0.5 (1.6)	[-2.3, 6.6]
	Placebo	19	3.7 (1.8)	[2.0, 8.1]	3.2 (1.5)	[1.6, 7.4]	-0.5 (1.5)	[-4.4, 1.7]
Cycle 17	Pembrolizumab	280	3.9 (1.5)	[1.5, 11.1]	3.9 (1.5)	[1.1, 10.9]	0.0 (1.4)	[-4.7, 5.6]
	Placebo	276	3.9 (1.5)	[1.7, 11.6]	3.8 (1.7)	[1.3, 12.6]	-0.1 (1.7)	[-7.8, 9.7]
Cycle 18	Pembrolizumab	36	3.5 (1.0)	[1.6, 5.3]	3.4 (0.9)	[1.9, 5.2]	-0.0 (1.1)	[-1.9, 2.3]
	Placebo	35	3.9 (1.9)	[1.8, 11.6]	3.4 (1.0)	[1.9, 6.0]	-0.5 (1.7)	[-8.0, 1.4]
Cycle 19	Pembrolizumab	40	3.6 (1.2)	[1.6, 6.3]	3.9 (1.5)	[1.6, 8.0]	0.3 (1.3)	[-2.6, 3.2]
	Placebo	35	3.6 (1.6)	[1.8, 8.1]	3.6 (1.5)	[1.2, 6.9]	0.0 (1.1)	[-1.9, 3.6]
Cycle 20	Pembrolizumab	7	3.8 (1.2)	[2.5, 5.6]	3.6 (1.0)	[2.3, 5.1]	-0.1 (1.1)	[-1.6, 1.4]
	Placebo	2	3.8 (0.2)	[3.6, 3.9]	3.8 (0.7)	[3.3, 4.3]	0.1 (0.9)	[-0.6, 0.7]
Cycle 21	Pembrolizumab	4	3.8 (1.0)	[2.7, 5.0]	5.3 (1.5)	[3.4, 7.0]	1.5 (1.4)	[0.7, 3.6]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	2	6.7 (2.0)	[5.3, 8.1]	4.7 (1.3)	[3.7, 5.6]	-2.0 (0.7)	[-2.5, -1.5]
Cycle 22	Pembrolizumab	2	3.0 (0.9)	[2.4, 3.7]	4.6 (1.0)	[3.9, 5.3]	1.6 (1.9)	[0.2, 2.9]
Cycle 23	Pembrolizumab	1	2.4 (-)	[2.4, 2.4]	3.9 (-)	[3.9, 3.9]	1.5 (-)	[1.5, 1.5]
Missing	Pembrolizumab	22	4.7 (1.8)	[1.7, 8.4]	4.8 (2.2)	[1.9, 8.6]	0.1 (1.3)	[-2.6, 3.8]
	Placebo	15	3.4 (1.0)	[2.4, 5.3]	5.0 (3.2)	[2.7, 13.6]	1.6 (2.5)	[-0.4, 8.3]
Unscheduled	Pembrolizumab	22	4.0 (1.5)	[1.8, 6.6]	4.9 (2.3)	[1.6, 10.7]	0.9 (2.2)	[-5.0, 4.8]
	Placebo	17	3.4 (1.1)	[1.8, 5.5]	5.2 (3.6)	[1.7, 13.5]	1.8 (3.2)	[-1.3, 9.9]
End of Treatment	Pembrolizumab	1	2.7 (-)	[2.7, 2.7]	2.9 (-)	[2.9, 2.9]	0.3 (-)	[0.3, 0.3]
	Placebo	6	5.1 (1.6)	[3.0, 7.9]	4.7 (1.9)	[3.0, 7.5]	-0.4 (2.5)	[-2.6, 4.5]
Neutrophils/Leukocytes (10^9/L)								
Cycle 2	Pembrolizumab	8	3.5 (1.1)	[2.1, 5.0]	3.8 (1.6)	[2.1, 7.3]	0.3 (1.2)	[-1.4, 2.3]
	Placebo	6	4.0 (1.1)	[2.6, 5.3]	4.1 (1.6)	[2.5, 7.0]	0.1 (1.4)	[-1.9, 2.2]
Cycle 3	Pembrolizumab	31	3.8 (1.4)	[2.1, 6.7]	3.8 (1.2)	[1.7, 6.5]	0.0 (1.1)	[-2.2, 2.4]
	Placebo	37	3.9 (1.8)	[2.0, 12.1]	3.6 (1.4)	[1.5, 8.8]	-0.3 (1.6)	[-8.0, 3.5]
Cycle 4	Pembrolizumab	3	3.4 (1.4)	[2.1, 4.9]	3.8 (1.4)	[2.3, 5.1]	0.4 (1.5)	[-0.9, 2.0]
	Placebo	3	4.6 (1.9)	[2.6, 6.5]	7.0 (2.9)	[5.2, 10.4]	2.4 (1.8)	[0.4, 3.9]
Cycle 5	Pembrolizumab	27	3.9 (1.3)	[2.1, 6.7]	4.3 (1.6)	[2.1, 8.4]	0.4 (1.5)	[-2.2, 3.7]
	Placebo	28	4.1 (2.0)	[2.0, 12.1]	3.7 (1.2)	[1.7, 6.4]	-0.4 (1.9)	[-8.8, 1.9]
Cycle 6	Pembrolizumab	6	3.9 (1.3)	[2.1, 5.8]	3.7 (1.5)	[2.4, 6.7]	-0.2 (1.9)	[-2.4, 3.0]
	Placebo	2	4.4 (2.9)	[2.3, 6.5]	3.4 (3.1)	[1.3, 5.6]	-1.0 (0.1)	[-1.0, -0.9]
Cycle 7	Pembrolizumab	27	4.1 (1.3)	[2.1, 6.7]	4.2 (1.6)	[2.0, 8.7]	0.2 (1.2)	[-2.1, 3.5]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	28	4.3 (2.0)	[2.0, 12.1]	4.6 (4.1)	[1.6, 24.1]	0.3 (3.8)	[-7.1, 17.6]
Cycle 8	Pembrolizumab	4	3.5 (1.2)	[2.1, 5.0]	3.6 (1.0)	[2.2, 4.6]	0.1 (0.5)	[-0.4, 0.8]
	Placebo	4	3.3 (1.4)	[2.2, 5.3]	2.2 (0.8)	[1.3, 3.1]	-1.2 (0.7)	[-2.2, -0.6]
Cycle 9	Pembrolizumab	24	3.9 (1.3)	[2.1, 6.7]	4.0 (1.4)	[1.9, 7.6]	0.1 (1.2)	[-2.1, 2.6]
	Placebo	25	4.4 (2.0)	[2.2, 12.1]	3.8 (1.3)	[1.3, 7.2]	-0.6 (1.6)	[-6.5, 1.2]
Cycle 10	Pembrolizumab	3	3.9 (1.0)	[3.1, 5.0]	4.2 (1.3)	[2.9, 5.5]	0.3 (1.4)	[-0.7, 1.9]
	Placebo	4	3.8 (1.9)	[2.2, 6.1]	3.3 (2.5)	[1.3, 6.5]	-0.5 (0.7)	[-1.0, 0.5]
Cycle 11	Pembrolizumab	22	3.9 (1.3)	[2.1, 6.7]	3.9 (1.4)	[1.8, 7.1]	0.0 (1.2)	[-3.2, 2.2]
	Placebo	21	4.4 (2.1)	[2.2, 12.1]	4.3 (2.2)	[1.6, 11.5]	-0.1 (2.6)	[-6.9, 6.7]
Cycle 12	Pembrolizumab	4	3.6 (1.1)	[2.4, 5.0]	2.6 (1.0)	[1.7, 3.9]	-1.0 (1.5)	[-2.3, 0.8]
	Placebo	1	2.3 (-)	[2.3, 2.3]	3.9 (-)	[3.9, 3.9]	1.6 (-)	[1.6, 1.6]
Cycle 13	Pembrolizumab	23	3.9 (1.2)	[2.1, 6.7]	3.8 (1.2)	[2.0, 6.8]	-0.1 (1.1)	[-2.0, 2.7]
	Placebo	21	4.6 (2.0)	[2.4, 12.1]	4.0 (1.4)	[2.1, 8.0]	-0.6 (2.2)	[-8.3, 2.7]
Cycle 14	Pembrolizumab	2	4.0 (1.3)	[3.1, 5.0]	3.2 (0.5)	[2.8, 3.6]	-0.8 (0.8)	[-1.4, -0.3]
Cycle 15	Pembrolizumab	20	3.9 (1.3)	[2.1, 6.7]	3.9 (1.2)	[2.1, 5.8]	0.1 (1.2)	[-2.1, 2.4]
	Placebo	19	4.5 (2.1)	[2.4, 12.1]	4.4 (1.6)	[2.6, 7.6]	-0.2 (2.4)	[-7.3, 3.2]
Cycle 16	Pembrolizumab	3	3.6 (0.5)	[3.1, 4.0]	3.5 (0.2)	[3.2, 3.7]	-0.2 (0.3)	[-0.5, 0.2]
	Placebo	2	4.6 (2.0)	[3.2, 6.1]	2.8 (0.6)	[2.4, 3.2]	-1.8 (2.7)	[-3.7, 0.1]
Cycle 17	Pembrolizumab	18	3.8 (1.0)	[2.3, 5.0]	3.6 (1.2)	[1.8, 7.6]	-0.2 (1.3)	[-2.1, 3.0]
	Placebo	21	4.6 (2.0)	[2.4, 12.1]	4.2 (1.6)	[1.7, 8.4]	-0.3 (2.3)	[-8.0, 3.6]
Cycle 18	Pembrolizumab	2	4.3 (0.5)	[3.9, 4.7]	5.5 (0.1)	[5.4, 5.6]	1.2 (0.4)	[1.0, 1.5]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 19	Pembrolizumab	3	3.5 (1.2)	[2.6, 4.8]	4.5 (1.9)	[3.4, 6.7]	1.0 (0.8)	[0.3, 1.9]
	Placebo	2	3.4 (0.4)	[3.2, 3.7]	3.6 (1.1)	[2.8, 4.3]	0.1 (0.7)	[-0.3, 0.6]
Cycle 20	Pembrolizumab	1	3.1 (-)	[3.1, 3.1]	3.1 (-)	[3.1, 3.1]	-0.0 (-)	[-0.0, -0.0]
Missing	Pembrolizumab	2	5.3 (1.9)	[4.0, 6.7]	4.8 (2.6)	[3.0, 6.6]	-0.6 (0.7)	[-1.0, -0.1]
	Placebo	1	2.2 (-)	[2.2, 2.2]	1.7 (-)	[1.7, 1.7]	-0.5 (-)	[-0.5, -0.5]
Unscheduled	Placebo	1	2.1 (-)	[2.1, 2.1]	1.9 (-)	[1.9, 1.9]	-0.2 (-)	[-0.2, -0.2]
Platelets (10^9/L)								
Cycle 1	Pembrolizumab	1	243.0 (-)	[243.0, 243.0]	364.0 (-)	[364.0, 364.0]	121.0 (-)	[121.0, 121.0]
Cycle 2	Pembrolizumab	54	244.2 (61.8)	[120.0, 414.0]	242.3 (59.0)	[115.0, 367.0]	-1.9 (41.1)	[-158.0, 123.0]
	Placebo	49	238.5 (47.8)	[150.0, 363.0]	235.7 (49.6)	[146.0, 357.0]	-2.8 (25.7)	[-70.0, 64.0]
Cycle 3	Pembrolizumab	478	246.4 (64.3)	[106.0, 658.0]	243.1 (59.0)	[82.0, 605.0]	-3.3 (43.1)	[-307.0, 167.0]
	Placebo	485	246.2 (62.5)	[100.0, 506.0]	239.5 (59.8)	[70.0, 750.0]	-6.7 (37.8)	[-289.0, 253.0]
Cycle 4	Pembrolizumab	42	246.6 (72.4)	[136.0, 482.0]	241.9 (68.6)	[137.0, 452.0]	-4.7 (51.2)	[-129.0, 149.0]
	Placebo	39	257.5 (72.1)	[150.0, 497.0]	262.2 (90.3)	[151.0, 692.0]	4.7 (52.0)	[-102.0, 195.0]
Cycle 5	Pembrolizumab	444	245.5 (63.5)	[106.0, 658.0]	242.0 (59.3)	[101.0, 577.0]	-3.5 (42.8)	[-274.0, 152.0]
	Placebo	422	247.1 (62.8)	[100.0, 506.0]	241.3 (57.9)	[94.0, 523.0]	-5.7 (39.3)	[-275.0, 132.0]
Cycle 6	Pembrolizumab	51	238.1 (67.4)	[106.0, 475.0]	233.0 (51.6)	[124.0, 362.0]	-5.1 (49.2)	[-231.0, 84.0]
	Placebo	30	260.4 (73.4)	[150.0, 497.0]	268.3 (101.4)	[150.0, 709.0]	7.8 (50.9)	[-60.0, 212.0]
Cycle 7	Pembrolizumab	412	245.3 (65.6)	[106.0, 658.0]	241.8 (59.4)	[106.0, 540.0]	-3.5 (46.2)	[-325.0, 274.0]
	Placebo	393	247.8 (64.4)	[100.0, 506.0]	241.1 (63.1)	[100.0, 617.0]	-6.7 (41.2)	[-278.0, 153.0]
Cycle 8	Pembrolizumab	39	252.6 (63.2)	[136.0, 482.0]	249.4 (46.7)	[147.0, 352.0]	-3.2 (47.7)	[-183.0, 99.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	39	239.1 (61.4)	[111.0, 393.0]	240.2 (67.3)	[66.0, 420.0]	1.2 (34.0)	[-69.0, 87.0]
Cycle 9	Pembrolizumab	383	243.9 (63.8)	[106.0, 658.0]	238.9 (56.9)	[103.0, 539.0]	-5.0 (43.5)	[-319.0, 135.0]
	Placebo	363	248.9 (61.8)	[111.0, 506.0]	245.6 (62.7)	[79.0, 539.0]	-3.3 (40.5)	[-277.0, 192.0]
Cycle 10	Pembrolizumab	37	248.3 (70.3)	[106.0, 482.0]	241.5 (65.5)	[102.0, 379.0]	-6.8 (61.3)	[-178.0, 183.0]
	Placebo	32	243.8 (63.3)	[148.0, 393.0]	232.8 (55.9)	[157.0, 368.0]	-11.1 (31.7)	[-128.0, 55.0]
Cycle 11	Pembrolizumab	362	242.3 (62.0)	[106.0, 658.0]	237.3 (56.0)	[108.0, 564.0]	-5.1 (38.2)	[-197.0, 104.0]
	Placebo	343	250.0 (63.5)	[111.0, 506.0]	242.2 (58.2)	[95.0, 551.0]	-7.8 (41.7)	[-261.0, 114.0]
Cycle 12	Pembrolizumab	30	230.8 (66.1)	[130.0, 482.0]	237.7 (48.5)	[131.0, 348.0]	6.9 (42.3)	[-160.0, 51.0]
	Placebo	30	256.1 (61.6)	[150.0, 382.0]	255.4 (63.3)	[141.0, 403.0]	-0.7 (29.8)	[-71.0, 74.0]
Cycle 13	Pembrolizumab	341	243.2 (62.1)	[106.0, 658.0]	241.7 (67.2)	[105.0, 860.0]	-1.5 (43.1)	[-193.0, 202.0]
	Placebo	317	251.4 (64.1)	[115.0, 506.0]	244.7 (61.7)	[84.0, 580.0]	-6.7 (42.6)	[-295.0, 156.0]
Cycle 14	Pembrolizumab	37	242.1 (61.6)	[130.0, 482.0]	243.9 (47.7)	[132.0, 341.0]	1.8 (34.0)	[-141.0, 60.0]
	Placebo	25	243.0 (53.9)	[150.0, 363.0]	222.8 (50.2)	[143.0, 351.0]	-20.2 (25.6)	[-90.0, 30.0]
Cycle 15	Pembrolizumab	327	242.4 (62.5)	[106.0, 658.0]	237.3 (55.7)	[103.0, 539.0]	-5.1 (41.4)	[-184.0, 147.0]
	Placebo	317	249.9 (64.9)	[111.0, 506.0]	243.6 (59.9)	[83.0, 524.0]	-6.3 (42.1)	[-304.0, 116.0]
Cycle 16	Pembrolizumab	41	246.4 (58.5)	[167.0, 482.0]	246.8 (66.3)	[135.0, 458.0]	0.4 (53.1)	[-187.0, 161.0]
	Placebo	21	273.0 (73.8)	[176.0, 496.0]	255.0 (41.2)	[195.0, 344.0]	-18.0 (59.5)	[-245.0, 36.0]
Cycle 17	Pembrolizumab	308	243.0 (59.0)	[106.0, 658.0]	237.3 (57.2)	[91.0, 568.0]	-5.6 (40.5)	[-213.0, 144.0]
	Placebo	305	250.1 (65.3)	[111.0, 506.0]	240.4 (58.7)	[95.0, 536.0]	-9.8 (42.6)	[-286.0, 125.0]
Cycle 18	Pembrolizumab	41	228.1 (56.2)	[130.0, 381.0]	223.9 (60.0)	[102.0, 359.0]	-4.1 (29.7)	[-80.0, 63.0]
	Placebo	36	255.2 (53.4)	[176.0, 363.0]	253.8 (49.8)	[171.0, 361.0]	-1.4 (31.0)	[-72.0, 88.0]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 19	Pembrolizumab	44	256.3 (74.1)	[136.0, 548.0]	250.4 (75.0)	[98.0, 490.0]	-5.9 (48.6)	[-101.0, 197.0]
	Placebo	38	241.3 (73.5)	[111.0, 496.0]	225.2 (53.3)	[89.0, 365.0]	-16.1 (49.8)	[-258.0, 48.0]
Cycle 20	Pembrolizumab	8	297.0 (119.9)	[195.0, 548.0]	279.3 (53.4)	[220.0, 359.0]	-17.8 (80.5)	[-189.0, 81.0]
	Placebo	2	250.5 (60.1)	[208.0, 293.0]	223.5 (27.6)	[204.0, 243.0]	-27.0 (32.5)	[-50.0, -4.0]
Cycle 21	Pembrolizumab	4	300.8 (167.9)	[173.0, 548.0]	293.8 (111.1)	[165.0, 436.0]	-7.0 (74.9)	[-112.0, 56.0]
	Placebo	2	334.0 (229.1)	[172.0, 496.0]	196.0 (5.7)	[192.0, 200.0]	-138.0 (234.8)	[-304.0, 28.0]
Cycle 22	Pembrolizumab	2	219.5 (34.6)	[195.0, 244.0]	277.0 (46.7)	[244.0, 310.0]	57.5 (12.0)	[49.0, 66.0]
Cycle 23	Pembrolizumab	1	244.0 (-)	[244.0, 244.0]	256.0 (-)	[256.0, 256.0]	12.0 (-)	[12.0, 12.0]
Missing	Pembrolizumab	24	272.4 (111.8)	[129.0, 548.0]	274.4 (119.9)	[137.0, 670.0]	2.0 (95.6)	[-120.0, 403.0]
	Placebo	16	215.0 (53.7)	[148.0, 363.0]	212.6 (52.8)	[147.0, 349.0]	-2.4 (19.8)	[-38.0, 37.0]
Unscheduled	Pembrolizumab	22	237.5 (62.5)	[178.0, 360.0]	249.0 (71.3)	[125.0, 358.0]	11.5 (41.7)	[-56.0, 117.0]
	Placebo	21	215.5 (71.5)	[116.0, 393.0]	204.0 (75.4)	[70.0, 334.0]	-11.6 (32.3)	[-92.0, 51.0]
End of Treatment	Pembrolizumab	1	255.0 (-)	[255.0, 255.0]	243.0 (-)	[243.0, 243.0]	-12.0 (-)	[-12.0, -12.0]
	Placebo	6	252.2 (50.0)	[199.0, 327.0]	250.2 (64.5)	[173.0, 352.0]	-2.0 (32.2)	[-48.0, 40.0]
Protein (g/dL)								
Cycle 2	Pembrolizumab	45	7.1 (0.5)	[5.9, 8.5]	7.1 (0.4)	[5.9, 7.8]	-0.0 (0.5)	[-1.8, 1.3]
	Placebo	44	7.2 (0.5)	[6.1, 8.7]	7.1 (0.6)	[5.6, 8.9]	-0.1 (0.5)	[-1.4, 0.8]
Cycle 3	Pembrolizumab	445	7.2 (0.5)	[5.1, 8.5]	7.1 (0.5)	[5.0, 8.5]	-0.1 (0.4)	[-1.2, 1.3]
	Placebo	454	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[5.8, 8.4]	-0.1 (0.4)	[-1.3, 1.3]
Cycle 4	Pembrolizumab	45	7.0 (0.4)	[5.9, 7.8]	7.0 (0.4)	[5.6, 8.0]	-0.0 (0.4)	[-1.1, 1.2]
	Placebo	33	7.3 (0.4)	[6.3, 8.3]	7.1 (0.5)	[6.2, 8.1]	-0.2 (0.5)	[-1.5, 0.6]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cycle 5	Pembrolizumab	415	7.1 (0.5)	[5.1, 8.5]	7.1 (0.5)	[5.1, 8.6]	-0.0 (0.4)	[-1.4, 1.3]
	Placebo	399	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[5.9, 9.0]	-0.1 (0.4)	[-1.4, 1.3]
Cycle 6	Pembrolizumab	51	7.1 (0.4)	[6.1, 7.9]	7.1 (0.5)	[6.0, 8.5]	0.0 (0.5)	[-0.9, 1.2]
	Placebo	28	7.2 (0.4)	[6.3, 8.3]	7.0 (0.4)	[6.3, 7.9]	-0.1 (0.4)	[-1.1, 0.6]
Cycle 7	Pembrolizumab	383	7.2 (0.4)	[5.7, 8.5]	7.1 (0.5)	[5.9, 8.4]	-0.0 (0.4)	[-1.3, 1.7]
	Placebo	358	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[5.8, 8.7]	-0.1 (0.4)	[-1.8, 1.0]
Cycle 8	Pembrolizumab	38	7.2 (0.4)	[6.2, 8.2]	7.0 (0.5)	[6.1, 8.4]	-0.2 (0.4)	[-1.0, 0.8]
	Placebo	35	7.1 (0.5)	[6.1, 8.3]	7.0 (0.5)	[6.3, 8.0]	-0.1 (0.4)	[-1.0, 0.8]
Cycle 9	Pembrolizumab	356	7.2 (0.5)	[5.7, 8.5]	7.1 (0.5)	[5.3, 8.4]	-0.0 (0.4)	[-1.7, 1.3]
	Placebo	335	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[6.0, 8.5]	-0.1 (0.4)	[-1.1, 1.3]
Cycle 10	Pembrolizumab	38	7.2 (0.5)	[6.2, 8.5]	7.0 (0.4)	[6.1, 8.2]	-0.2 (0.5)	[-1.4, 1.1]
	Placebo	30	7.2 (0.4)	[6.1, 8.1]	7.1 (0.5)	[6.0, 8.0]	-0.1 (0.4)	[-0.9, 0.6]
Cycle 11	Pembrolizumab	341	7.1 (0.4)	[5.9, 8.5]	7.1 (0.5)	[5.4, 9.4]	-0.1 (0.5)	[-1.6, 3.0]
	Placebo	316	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[6.0, 8.6]	-0.1 (0.4)	[-1.3, 1.2]
Cycle 12	Pembrolizumab	28	7.3 (0.5)	[6.5, 8.5]	7.2 (0.4)	[6.1, 7.9]	-0.1 (0.5)	[-1.0, 1.2]
	Placebo	24	7.3 (0.4)	[6.0, 8.0]	7.1 (0.4)	[6.4, 7.9]	-0.2 (0.4)	[-1.1, 0.5]
Cycle 13	Pembrolizumab	318	7.1 (0.4)	[5.9, 8.5]	7.1 (0.4)	[5.7, 8.5]	-0.1 (0.4)	[-1.4, 1.3]
	Placebo	302	7.2 (0.5)	[5.8, 8.7]	7.1 (0.4)	[5.8, 8.5]	-0.1 (0.4)	[-1.3, 1.1]
Cycle 14	Pembrolizumab	38	7.2 (0.5)	[6.5, 8.5]	7.2 (0.5)	[5.6, 8.1]	0.0 (0.5)	[-2.0, 0.9]
	Placebo	25	7.3 (0.4)	[6.4, 7.9]	7.1 (0.4)	[6.3, 7.7]	-0.2 (0.5)	[-1.0, 0.6]
Cycle 15	Pembrolizumab	312	7.1 (0.4)	[5.9, 8.3]	7.1 (0.4)	[5.6, 8.4]	-0.0 (0.4)	[-1.0, 1.5]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
	Placebo	294	7.2 (0.5)	[5.8, 8.7]	7.1 (0.4)	[5.7, 8.6]	-0.1 (0.4)	[-1.3, 1.0]
Cycle 16	Pembrolizumab	34	7.1 (0.4)	[6.2, 8.0]	7.0 (0.4)	[6.2, 8.0]	-0.1 (0.6)	[-1.3, 0.9]
	Placebo	19	7.2 (0.4)	[6.4, 7.8]	6.9 (0.3)	[6.4, 7.8]	-0.3 (0.4)	[-0.9, 0.3]
Cycle 17	Pembrolizumab	296	7.1 (0.4)	[5.9, 8.3]	7.1 (0.4)	[4.9, 8.6]	-0.1 (0.4)	[-1.4, 1.2]
	Placebo	282	7.2 (0.4)	[5.8, 8.7]	7.1 (0.4)	[5.8, 8.3]	-0.1 (0.4)	[-1.6, 1.1]
Cycle 18	Pembrolizumab	42	7.2 (0.5)	[6.2, 8.3]	7.2 (0.5)	[6.1, 8.2]	-0.0 (0.4)	[-0.8, 1.1]
	Placebo	34	7.1 (0.5)	[6.0, 8.3]	7.0 (0.4)	[6.3, 7.9]	-0.1 (0.4)	[-1.0, 0.7]
Cycle 19	Pembrolizumab	41	7.2 (0.5)	[6.3, 8.3]	7.1 (0.6)	[4.8, 8.2]	-0.1 (0.5)	[-1.8, 0.7]
	Placebo	34	7.3 (0.5)	[6.5, 8.7]	7.0 (0.4)	[6.0, 8.3]	-0.3 (0.4)	[-1.0, 0.5]
Cycle 20	Pembrolizumab	8	7.4 (0.5)	[6.6, 8.0]	7.2 (0.7)	[5.9, 8.2]	-0.2 (0.6)	[-0.9, 1.1]
	Placebo	2	7.1 (0.9)	[6.4, 7.7]	7.6 (0.8)	[7.0, 8.1]	0.5 (0.1)	[0.4, 0.6]
Cycle 21	Pembrolizumab	4	7.2 (0.9)	[6.3, 8.0]	7.0 (0.6)	[6.2, 7.5]	-0.2 (0.4)	[-0.6, 0.3]
	Placebo	2	7.4 (0.2)	[7.2, 7.5]	6.7 (0.1)	[6.6, 6.8]	-0.7 (0.1)	[-0.7, -0.6]
Cycle 22	Pembrolizumab	1	6.9 (-)	[6.9, 6.9]	8.0 (-)	[8.0, 8.0]	1.1 (-)	[1.1, 1.1]
Missing	Pembrolizumab	25	7.2 (0.5)	[6.4, 8.2]	7.0 (0.5)	[6.0, 8.1]	-0.2 (0.5)	[-1.3, 0.6]
	Placebo	15	6.9 (0.5)	[6.0, 8.3]	7.0 (0.6)	[6.0, 8.6]	0.1 (0.4)	[-1.0, 0.8]
Unscheduled	Pembrolizumab	24	7.2 (0.3)	[6.7, 8.0]	6.6 (0.8)	[5.4, 8.1]	-0.5 (0.7)	[-1.6, 0.4]

Mean Change (SD) in Laboratory Values from Baseline over Time
Treatment Phase (ASaT Population)

Visit	Treatment	N	Baseline		Value		Change from Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
End of Treatment	Placebo	11	7.1 (0.4)	[6.4, 7.4]	6.9 (0.5)	[6.3, 7.7]	-0.1 (0.4)	[-0.9, 0.3]
	Pembrolizumab	1	7.4 (-)	[7.4, 7.4]	7.8 (-)	[7.8, 7.8]	0.4 (-)	[0.4, 0.4]
	Placebo	5	7.2 (0.2)	[6.9, 7.4]	6.9 (0.3)	[6.5, 7.2]	-0.4 (0.3)	[-0.6, 0.0]

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
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adlb]

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)
(ASaT Population)

Laboratory Test	Pembrolizumab (N=509) n	(%)	Placebo (N=502) n	(%)	Total (N=1011) n	(%)
Alanine Aminotransferase Increased (Alanine aminotransferase increased)						
Subjects with Baseline and Post-baseline Measurements	507		498		1005	
Grade 1	135	(26.6)	96	(19.3)	231	(23.0)
Grade 2	11	(2.2)	8	(1.6)	19	(1.9)
Grade 3	13	(2.6)	2	(0.4)	15	(1.5)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	14	(2.8)	2	(0.4)	16	(1.6)
All Grades	160	(31.6)	106	(21.3)	266	(26.5)
Albumin Decreased (Hypoalbuminemia)						
Subjects with Baseline and Post-baseline Measurements	492		482		974	
Grade 1	63	(12.8)	25	(5.2)	88	(9.0)
Grade 2	9	(1.8)	5	(1.0)	14	(1.4)
Grade 3	0	(0.0)	2	(0.4)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	0	(0.0)	2	(0.4)	2	(0.2)
All Grades	72	(14.6)	32	(6.6)	104	(10.7)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)						
Subjects with Baseline and Post-baseline Measurements	504		491		995	
Grade 1	66	(13.1)	35	(7.1)	101	(10.2)
Grade 2	12	(2.4)	2	(0.4)	14	(1.4)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	1	(0.2)	1	(0.2)	2	(0.2)
All Grades	79	(15.7)	38	(7.7)	117	(11.8)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)						
Subjects with Baseline and Post-baseline Measurements	507		495		1002	
Grade 1	111	(21.9)	81	(16.4)	192	(19.2)
Grade 2	15	(3.0)	6	(1.2)	21	(2.1)

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) (ASaT Population)

Laboratory Test	Pembrolizumab (N=509) n	(%)	Placebo (N=502) n	(%)	Total (N=1011) n	(%)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)						
Grade 3	9	(1.8)	2	(0.4)	11	(1.1)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	10	(2.0)	2	(0.4)	12	(1.2)
All Grades	136	(26.8)	89	(18.0)	225	(22.5)
Bilirubin Increased (Blood bilirubin increased)						
Subjects with Baseline and Post-baseline Measurements	507		498		1005	
Grade 1	43	(8.5)	42	(8.4)	85	(8.5)
Grade 2	24	(4.7)	19	(3.8)	43	(4.3)
Grade 3	1	(0.2)	1	(0.2)	2	(0.2)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	1	(0.2)	1	(0.2)	2	(0.2)
All Grades	68	(13.4)	62	(12.4)	130	(12.9)
Calcium Decreased (Hypocalcemia)						
Subjects with Baseline and Post-baseline Measurements	503		491		994	
Grade 1	79	(15.7)	47	(9.6)	126	(12.7)
Grade 2	7	(1.4)	4	(0.8)	11	(1.1)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3-4	0	(0.0)	1	(0.2)	1	(0.1)
All Grades	86	(17.1)	52	(10.6)	138	(13.9)
Calcium Increased (Hypercalcemia)						
Subjects with Baseline and Post-baseline Measurements	503		491		994	
Grade 1	25	(5.0)	33	(6.7)	58	(5.8)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	3	(0.6)	1	(0.2)	4	(0.4)
Grade 3-4	3	(0.6)	1	(0.2)	4	(0.4)
All Grades	29	(5.8)	34	(6.9)	63	(6.3)

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)
(ASaT Population)

Laboratory Test	Pembrolizumab (N=509) n	(%)	Placebo (N=502) n	(%)	Total (N=1011) n	(%)
Creatinine Increased (Creatinine increased)						
Subjects with Baseline and Post-baseline Measurements	506		498		1004	
Grade 1	83	(16.4)	61	(12.2)	144	(14.3)
Grade 2	9	(1.8)	3	(0.6)	12	(1.2)
Grade 3	3	(0.6)	0	(0.0)	3	(0.3)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	3	(0.6)	0	(0.0)	3	(0.3)
All Grades	95	(18.8)	64	(12.9)	159	(15.8)
Leukocytes Decreased (White blood cell decreased)						
Subjects with Baseline and Post-baseline Measurements	507		498		1005	
Grade 1	62	(12.2)	82	(16.5)	144	(14.3)
Grade 2	11	(2.2)	13	(2.6)	24	(2.4)
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	73	(14.4)	95	(19.1)	168	(16.7)
Lymphocytes Decreased (Lymphocyte count decreased)						
Subjects with Baseline and Post-baseline Measurements	503		493		996	
Grade 1	87	(17.3)	57	(11.6)	144	(14.5)
Grade 2	52	(10.3)	33	(6.7)	85	(8.5)
Grade 3	9	(1.8)	8	(1.6)	17	(1.7)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	10	(2.0)	8	(1.6)	18	(1.8)
All Grades	149	(29.6)	98	(19.9)	247	(24.8)
Neutrophils Decreased (Neutrophil count decreased)						
Subjects with Baseline and Post-baseline Measurements	504		491		995	
Grade 1	38	(7.5)	43	(8.8)	81	(8.1)
Grade 2	25	(5.0)	20	(4.1)	45	(4.5)

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) (ASaT Population)

Laboratory Test	Pembrolizumab (N=509) n	(%)	Placebo (N=502) n	(%)	Total (N=1011) n	(%)
Neutrophils Decreased (Neutrophil count decreased)						
Grade 3	3	(0.6)	3	(0.6)	6	(0.6)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	3	(0.6)	3	(0.6)	6	(0.6)
All Grades	66	(13.1)	66	(13.4)	132	(13.3)
Platelets Decreased (Platelet count decreased)						
Subjects with Baseline and Post-baseline Measurements	507		498		1005	
Grade 1	43	(8.5)	25	(5.0)	68	(6.8)
Grade 2	0	(0.0)	2	(0.4)	2	(0.2)
Grade 3	0	(0.0)	0	(0.0)	0	(0.0)
Grade 4	1	(0.2)	0	(0.0)	1	(0.1)
Grade 3-4	1	(0.2)	0	(0.0)	1	(0.1)
All Grades	44	(8.7)	27	(5.4)	71	(7.1)
Potassium Decreased (Hypokalemia)						
Subjects with Baseline and Post-baseline Measurements	505		493		998	
Grade 1	52	(10.3)	35	(7.1)	87	(8.7)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	6	(1.2)	3	(0.6)	9	(0.9)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	6	(1.2)	3	(0.6)	9	(0.9)
All Grades	58	(11.5)	38	(7.7)	96	(9.6)
Potassium Increased (Hyperkalemia)						
Subjects with Baseline and Post-baseline Measurements	505		493		998	
Grade 1	79	(15.6)	66	(13.4)	145	(14.5)
Grade 2	16	(3.2)	19	(3.9)	35	(3.5)
Grade 3	3	(0.6)	1	(0.2)	4	(0.4)
Grade 4	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3-4	3	(0.6)	1	(0.2)	4	(0.4)
All Grades	98	(19.4)	86	(17.4)	184	(18.4)

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) (ASaT Population)

Laboratory Test	Pembrolizumab (N=509) n	(%)	Placebo (N=502) n	(%)	Total (N=1011) n	(%)
Sodium Decreased (Hyponatremia)						
Subjects with Baseline and Post-baseline Measurements	506		497		1003	
Grade 1	84	(16.6)	73	(14.7)	157	(15.7)
Grade 2	0	(0.0)	0	(0.0)	0	(0.0)
Grade 3	12	(2.4)	4	(0.8)	16	(1.6)
Grade 4	0	(0.0)	1	(0.2)	1	(0.1)
Grade 3-4	12	(2.4)	5	(1.0)	17	(1.7)
All Grades	96	(19.0)	78	(15.7)	174	(17.3)
Sodium Increased (Hypernatremia)						
Subjects with Baseline and Post-baseline Measurements	506		497		1003	
Grade 1	44	(8.7)	40	(8.0)	84	(8.4)
Grade 2	1	(0.2)	0	(0.0)	1	(0.1)
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	45	(8.9)	40	(8.0)	85	(8.5)

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.
Database Cutoff Date: 03APR2020

Source: [P054V02MK3475: adam-adsl; adlbgrd]

Table 14.4-3

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Alanine Aminotransferase Increased (Alanine aminotransferase increased)												
Grade 0	298 (58.8)	135 (26.6)	8 (1.6)	10 (2.0)	0 (0.0)	451 (89.0)	350 (70.3)	96 (19.3)	4 (0.8)	1 (0.2)	0 (0.0)	451 (90.6)
Grade 1	15 (3.0)	34 (6.7)	3 (0.6)	3 (0.6)	1 (0.2)	56 (11.0)	9 (1.8)	33 (6.6)	4 (0.8)	1 (0.2)	0 (0.0)	47 (9.4)
Total	313 (61.7)	169 (33.3)	11 (2.2)	13 (2.6)	1 (0.2)	507 (100.0)	359 (72.1)	129 (25.9)	8 (1.6)	2 (0.4)	0 (0.0)	498 (100.0)
Albumin Decreased (Hypoalbuminemia)												
Grade 0	412 (83.7)	63 (12.8)	7 (1.4)	0 (0.0)	0 (0.0)	482 (98.0)	444 (92.1)	25 (5.2)	4 (0.8)	2 (0.4)	0 (0.0)	475 (98.5)
Grade 1	3 (0.6)	3 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	8 (1.6)	2 (0.4)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	6 (1.2)
Grade 2	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Total	415 (84.3)	67 (13.6)	10 (2.0)	0 (0.0)	0 (0.0)	492 (100.0)	447 (92.7)	28 (5.8)	5 (1.0)	2 (0.4)	0 (0.0)	482 (100.0)
Alkaline Phosphatase Increased (Alkaline phosphatase increased)												
Grade 0	406 (80.6)	66 (13.1)	9 (1.8)	1 (0.2)	0 (0.0)	482 (95.6)	433 (88.2)	35 (7.1)	2 (0.4)	1 (0.2)	0 (0.0)	471 (95.9)
Grade 1	4 (0.8)	15 (3.0)	3 (0.6)	0 (0.0)	0 (0.0)	22 (4.4)	3 (0.6)	17 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	20 (4.1)
Total	410 (81.3)	81 (16.1)	12 (2.4)	1 (0.2)	0 (0.0)	504 (100.0)	436 (88.8)	52 (10.6)	2 (0.4)	1 (0.2)	0 (0.0)	491 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Aspartate Aminotransferase Increased (Aspartate aminotransferase increased)												
Grade 0	350 (69.0)	111 (21.9)	14 (2.8)	9 (1.8)	1 (0.2)	485 (95.7)	387 (78.2)	81 (16.4)	3 (0.6)	2 (0.4)	0 (0.0)	473 (95.6)
Grade 1	3 (0.6)	18 (3.6)	1 (0.2)	0 (0.0)	0 (0.0)	22 (4.3)	8 (1.6)	11 (2.2)	3 (0.6)	0 (0.0)	0 (0.0)	22 (4.4)
Total	353 (69.6)	129 (25.4)	15 (3.0)	9 (1.8)	1 (0.2)	507 (100.0)	395 (79.8)	92 (18.6)	6 (1.2)	2 (0.4)	0 (0.0)	495 (100.0)
Bilirubin Increased (Blood bilirubin increased)												
Grade 0	432 (85.2)	43 (8.5)	12 (2.4)	1 (0.2)	0 (0.0)	488 (96.3)	417 (83.7)	42 (8.4)	12 (2.4)	1 (0.2)	0 (0.0)	472 (94.8)
Grade 1	0 (0.0)	2 (0.4)	12 (2.4)	0 (0.0)	0 (0.0)	14 (2.8)	2 (0.4)	14 (2.8)	7 (1.4)	0 (0.0)	0 (0.0)	23 (4.6)
Grade 2	0 (0.0)	2 (0.4)	3 (0.6)	0 (0.0)	0 (0.0)	5 (1.0)	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	3 (0.6)
Total	432 (85.2)	47 (9.3)	27 (5.3)	1 (0.2)	0 (0.0)	507 (100.0)	419 (84.1)	56 (11.2)	22 (4.4)	1 (0.2)	0 (0.0)	498 (100.0)
Calcium Decreased (Hypocalcemia)												
Grade 0	407 (80.9)	79 (15.7)	5 (1.0)	0 (0.0)	0 (0.0)	491 (97.6)	431 (87.8)	47 (9.6)	4 (0.8)	0 (0.0)	1 (0.2)	483 (98.4)
Grade 1	4 (0.8)	6 (1.2)	2 (0.4)	0 (0.0)	0 (0.0)	12 (2.4)	2 (0.4)	6 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.6)
Total	411 (81.7)	85 (16.9)	7 (1.4)	0 (0.0)	0 (0.0)	503 (100.0)	433 (88.2)	53 (10.8)	4 (0.8)	0 (0.0)	1 (0.2)	491 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Calcium Increased (Hypercalcemia)												
Grade 0	471 (93.6)	25 (5.0)	1 (0.2)	0 (0.0)	3 (0.6)	500 (99.4)	452 (92.1)	33 (6.7)	0 (0.0)	0 (0.0)	1 (0.2)	486 (99.0)
Grade 1	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)	2 (0.4)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.0)
Total	473 (94.0)	26 (5.2)	1 (0.2)	0 (0.0)	3 (0.6)	503 (100.0)	454 (92.5)	36 (7.3)	0 (0.0)	0 (0.0)	1 (0.2)	491 (100.0)
Creatinine Increased (Creatinine increased)												
Grade 0	394 (77.9)	83 (16.4)	6 (1.2)	3 (0.6)	0 (0.0)	486 (96.0)	415 (83.3)	61 (12.2)	1 (0.2)	0 (0.0)	0 (0.0)	477 (95.8)
Grade 1	4 (0.8)	13 (2.6)	3 (0.6)	0 (0.0)	0 (0.0)	20 (4.0)	2 (0.4)	17 (3.4)	2 (0.4)	0 (0.0)	0 (0.0)	21 (4.2)
Total	398 (78.7)	96 (19.0)	9 (1.8)	3 (0.6)	0 (0.0)	506 (100.0)	417 (83.7)	78 (15.7)	3 (0.6)	0 (0.0)	0 (0.0)	498 (100.0)
Leukocytes Decreased (White blood cell decreased)												
Grade 0	419 (82.6)	62 (12.2)	8 (1.6)	0 (0.0)	0 (0.0)	489 (96.4)	385 (77.3)	82 (16.5)	8 (1.6)	0 (0.0)	0 (0.0)	475 (95.4)
Grade 1	3 (0.6)	12 (2.4)	3 (0.6)	0 (0.0)	0 (0.0)	18 (3.6)	6 (1.2)	11 (2.2)	5 (1.0)	0 (0.0)	0 (0.0)	22 (4.4)
Grade 2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
Total	422 (83.2)	74 (14.6)	11 (2.2)	0 (0.0)	0 (0.0)	507 (100.0)	391 (78.5)	93 (18.7)	14 (2.8)	0 (0.0)	0 (0.0)	498 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Lymphocytes Decreased (Lymphocyte count decreased)												
Grade 0	314 (62.4)	87 (17.3)	32 (6.4)	6 (1.2)	1 (0.2)	440 (87.5)	339 (68.8)	57 (11.6)	22 (4.5)	5 (1.0)	0 (0.0)	423 (85.8)
Grade 1	6 (1.2)	14 (2.8)	20 (4.0)	1 (0.2)	0 (0.0)	41 (8.2)	4 (0.8)	25 (5.1)	11 (2.2)	0 (0.0)	0 (0.0)	40 (8.1)
Grade 2	3 (0.6)	1 (0.2)	12 (2.4)	2 (0.4)	0 (0.0)	18 (3.6)	0 (0.0)	4 (0.8)	13 (2.6)	3 (0.6)	0 (0.0)	20 (4.1)
Grade 3	0 (0.0)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	8 (1.6)	2 (0.4)	0 (0.0)	10 (2.0)
Total	323 (64.2)	102 (20.3)	67 (13.3)	10 (2.0)	1 (0.2)	503 (100.0)	343 (69.6)	86 (17.4)	54 (11.0)	10 (2.0)	0 (0.0)	493 (100.0)
Neutrophils Decreased (Neutrophil count decreased)												
Grade 0	428 (84.9)	38 (7.5)	20 (4.0)	3 (0.6)	0 (0.0)	489 (97.0)	417 (84.9)	43 (8.8)	18 (3.7)	3 (0.6)	0 (0.0)	481 (98.0)
Grade 1	0 (0.0)	9 (1.8)	5 (1.0)	0 (0.0)	0 (0.0)	14 (2.8)	2 (0.4)	6 (1.2)	2 (0.4)	0 (0.0)	0 (0.0)	10 (2.0)
Grade 2	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	428 (84.9)	47 (9.3)	26 (5.2)	3 (0.6)	0 (0.0)	504 (100.0)	419 (85.3)	49 (10.0)	20 (4.1)	3 (0.6)	0 (0.0)	491 (100.0)
Platelets Decreased (Platelet count decreased)												
Grade 0	455 (89.7)	43 (8.5)	0 (0.0)	0 (0.0)	0 (0.0)	498 (98.2)	454 (91.2)	25 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	479 (96.2)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Platelets Decreased (Platelet count decreased)												
Grade 1	0 (0.0)	8 (1.6)	0 (0.0)	0 (0.0)	1 (0.2)	9 (1.8)	3 (0.6)	14 (2.8)	2 (0.4)	0 (0.0)	0 (0.0)	19 (3.8)
Total	455 (89.7)	51 (10.1)	0 (0.0)	0 (0.0)	1 (0.2)	507 (100.0)	457 (91.8)	39 (7.8)	2 (0.4)	0 (0.0)	0 (0.0)	498 (100.0)
Potassium Decreased (Hypokalemia)												
Grade 0	438 (86.7)	52 (10.3)	0 (0.0)	3 (0.6)	0 (0.0)	493 (97.6)	452 (91.7)	35 (7.1)	0 (0.0)	2 (0.4)	0 (0.0)	489 (99.2)
Grade 1	3 (0.6)	5 (1.0)	0 (0.0)	3 (0.6)	0 (0.0)	11 (2.2)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	4 (0.8)
Grade 3	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	441 (87.3)	58 (11.5)	0 (0.0)	6 (1.2)	0 (0.0)	505 (100.0)	453 (91.9)	37 (7.5)	0 (0.0)	3 (0.6)	0 (0.0)	493 (100.0)
Potassium Increased (Hyperkalemia)												
Grade 0	392 (77.6)	79 (15.6)	15 (3.0)	3 (0.6)	0 (0.0)	489 (96.8)	393 (79.7)	66 (13.4)	17 (3.4)	1 (0.2)	0 (0.0)	477 (96.8)
Grade 1	5 (1.0)	8 (1.6)	1 (0.2)	0 (0.0)	0 (0.0)	14 (2.8)	5 (1.0)	7 (1.4)	2 (0.4)	0 (0.0)	0 (0.0)	14 (2.8)
Grade 2	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)
Total	399 (79.0)	87 (17.2)	16 (3.2)	3 (0.6)	0 (0.0)	505 (100.0)	399 (80.9)	74 (15.0)	19 (3.9)	1 (0.2)	0 (0.0)	493 (100.0)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Sodium Decreased (Hyponatremia)												
Grade 0	396 (78.3)	84 (16.6)	0 (0.0)	11 (2.2)	0 (0.0)	491 (97.0)	404 (81.3)	73 (14.7)	0 (0.0)	3 (0.6)	0 (0.0)	480 (96.6)
Grade 1	3 (0.6)	9 (1.8)	0 (0.0)	1 (0.2)	0 (0.0)	13 (2.6)	10 (2.0)	4 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	15 (3.0)
Grade 3	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.4)
Total	400 (79.1)	94 (18.6)	0 (0.0)	12 (2.4)	0 (0.0)	506 (100.0)	415 (83.5)	77 (15.5)	0 (0.0)	4 (0.8)	1 (0.2)	497 (100.0)
Sodium Increased (Hypernatremia)												
Grade 0	449 (88.7)	44 (8.7)	1 (0.2)	0 (0.0)	0 (0.0)	494 (97.6)	448 (90.1)	40 (8.0)	0 (0.0)	0 (0.0)	0 (0.0)	488 (98.2)
Grade 1	4 (0.8)	8 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	12 (2.4)	5 (1.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	9 (1.8)

Summary of Laboratory Toxicity Grade Shift from Baseline to Worst Post-baseline
(ASaT Population)

	Pembrolizumab (N=509)						Placebo (N=502)					
	Post-baseline Maximum Grade						Post-baseline Maximum Grade					
Baseline	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Total n (%)
Sodium Increased (Hypernatremia)												
Total	453 (89.5)	52 (10.3)	1 (0.2)	0 (0.0)	0 (0.0)	506 (100.0)	453 (91.1)	44 (8.9)	0 (0.0)	0 (0.0)	0 (0.0)	497 (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.
(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-adsl; adlbgrd]

14.4.1.1 Specific Clinically Meaningful Laboratory Abnormalities

Table 14.4-4

Subjects With Liver Function Laboratory Findings That Met Predetermined Criteria
Treatment and Follow-Up Phases
ASaT Population

Criteria	Pembrolizumab		Placebo	
	n/m	(%)	n/m	(%)
Subjects in population	509		502	
Alanine Aminotransferase				
≥3 x ULN	25/507	(4.9)	10/498	(2.0)
≥5 x ULN	14/507	(2.8)	2/498	(0.4)
≥10 x ULN	4/507	(0.8)	1/498	(0.2)
≥20 x ULN	1/507	(0.2)	0/498	(0.0)
Aspartate Aminotransferase				
≥3 x ULN	26/507	(5.1)	8/496	(1.6)
≥5 x ULN	10/507	(2.0)	2/496	(0.4)
≥10 x ULN	1/507	(0.2)	0/496	(0.0)
≥20 x ULN	1/507	(0.2)	0/496	(0.0)
Aminotransferase (ALT or AST)				
≥3 x ULN	33/507	(6.5)	14/496	(2.8)
≥5 x ULN	16/507	(3.2)	3/496	(0.6)
≥10 x ULN	4/507	(0.8)	1/496	(0.2)
≥20 x ULN	1/507	(0.2)	0/496	(0.0)

Subjects With Liver Function Laboratory Findings That Met Predetermined Criteria
Treatment and Follow-Up Phases
ASaT Population

Criteria	Pembrolizumab		Placebo	
	n/m	(%)	n/m	(%)
Bilirubin				
≥2 x ULN	10/507	(2.0)	10/498	(2.0)
Alkaline Phosphatase				
≥1.5 x ULN	26/506	(5.1)	9/494	(1.8)
Aminotransferase (ALT or AST) and Bilirubin				
AT ≥3 x ULN and BILI ≥1.5 x ULN	3/507	(0.6)	0/498	(0.0)
AT ≥3 x ULN and BILI ≥2 x ULN	1/507	(0.2)	0/498	(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	1/507	(0.2)	0/498	(0.0)

n = Number of Subjects with postbaseline test results (or combination of test results from the same day) that met predetermined criteria.

m = Number of Subjects 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.

(Data Cutoff Date: 03APR2020).

Source: [P054V02MK3475: adam-addili]

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

Vital signs and physical examinations were not part of the analysis plan.

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16.1.1.3 General Amendment No. 2

16.1.1.4 General Amendment No. 3

16.1.1.5 General Amendment No. 4

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16.1.3.2 Sample Consent Form and Written Information for Participants

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16.1.12 Important Publications Referenced in the CSR

16.1.12.1 Balch CM, Gershenwald JE, Soong S-J, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol 2009;27(36):6199-206.

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