Drug Safety Research Unit (DSRU)

Post-authorisation active surveillance of the Safety of COVID-19 Vaccine AstraZeneca (AZD-1222) in the UK
A consortium study

Interim 1 report

April 2021

[redacted]

PASS information

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Research question and objectives	Overall aim: To monitor the safety and utilisation of the COVID-19 Vaccine AstraZeneca (AZD-1222) administered to vaccinees under real-world use in the UK Primary objective: • To examine the safety of COVID-19 vaccine AstraZeneca (AZD-1222) through active surveillance of all vaccinee reported adverse events and assessment of incidence. Secondary objectives: • (i) To describe and characterise serious adverse events following vaccination • (ii) To describe and characterise adverse events of special interest (AESI) including AESI relevant to vaccinations in general and AESI relevant to COVID-19 vaccine AstraZeneca (AZD-1222).

	• (iii) To describe and characterise the utilisation of COVID-19 vaccine AstraZeneca (AZD-1222) in the cohort, including vaccination site, demographics of vaccinee and brand/batch of vaccine administered. • (iv) To examine use and safety in populations with missing information including pregnant and breastfeeding women and individuals with immunodeficiency disorders, treatment with immunosuppressants, concurrent medical conditions, and administration of other vaccines within previous 30 days. Quality of Life sub-study objective • (i) To describe and characterise health-related quality of life among a sub-population (n=3500) vaccinated by COVID-19 vaccine AZD1222 and to describe the effect of the COVID-19 vaccine AstraZeneca (AZD-1222) on participant's lifestyle and productivity where affected by the COVID-19 pandemic.
Country(-ies) of study	UK
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Marketing authorisation holder(s)

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1 Abstract

Title

Post-authorisation active surveillance of the Safety of COVID-19 Vaccine AstraZeneca (AZD-1222) in the UK - A consortium study

Keywords

AstraZeneca (AZD-1222) – Post-authorisation – Active-surveillance – Utilisation - Safety

Rationale and background

COVID-19 vaccines have undergone rapid development and testing due to the current global pandemic. There is a requirement to monitor the safety and effectiveness post authorisation, to supplement evidence from the pre-authorisation phase and to identify new emerging issues in a timely manner. For a COVID-19 vaccine, given the public health need for comprehensive assessment of effectiveness and safety, an active surveillance method is considered superior to passive methods of surveillance.

Research question and objectives

Overall aim:

To monitor the safety and utilisation of the COVID-19 Vaccine AstraZeneca (AZD-1222) administered to vaccinees under real-world use in the UK

Primary objective:

- To examine the safety of COVID-19 vaccine AstraZeneca (AZD-1222) through active surveillance of all vaccinee reported adverse events and assessment of incidence.

Secondary objectives:

- (i) To describe and characterise serious adverse events following vaccination.

- (ii) To describe and characterise adverse events of special interest (AESI) including AESI relevant to vaccinations in general and AESI for the COVID-19 vaccine AstraZeneca (AZD-1222).

- (iii) To describe and characterise the utilisation of COVID-19 vaccine AstraZeneca (AZD-1222) in the cohort, including vaccination site, demographics of vaccinee and brand/batch of vaccine administered.

- (iv) To examine use and safety in populations with missing information including pregnant and breastfeeding women and individuals with immunodeficiency disorders, treatment with immunosuppressants, concurrent medical conditions, and administration of other vaccines within previous 30 days.

Quality of life sub-study objective
(i) To describe and characterise health-related quality of life among a sub-population (n=3500) vaccinated by COVID-19 vaccine AstraZeneca (AZD-1222) and to describe the effect of the COVID-19 vaccine AstraZeneca (AZD-1222) on participant's lifestyle and productivity where affected by the COVID-19 pandemic.

Study design
A non-interventional post-authorisation active surveillance study. Vaccinees are recruited via the mass vaccination programme through various vaccination sites and other methods of recruitment (e.g. through social media, newspapers and local radio stations). Informed consent is obtained. Baseline information and any symptom/condition following vaccination reported by the vaccinee is collected. Further information related to serious and AESIs is captured from General Practitioners (GPs) and/or healthcare professionals (HCPs) where appropriate. Vaccinees are contacted at various time points through text message, email, or phone and asked whether they experienced an adverse event. If an adverse event is reported by the vaccinee, they are asked to provide further details via a questionnaire completed via an online portal.

Setting
Vaccination sites within the UK

Subjects and study size, including dropouts
At datalock (30th March 2021), a total of 5995 participants were eligible and signed up to the study. Of these, 3549 provided consent and 2870 completed and submitted an Enrolment/Baseline questionnaire.

Variables and data sources
Questionnaires at baseline (information from time of vaccination) and pre-defined follow up points thereafter (following first vaccination dose) collected information from vaccinees.

Results

Participants

At datalock, a total of 5995 participants were eligible and signed up to the study. Of these, 3549 provided consent and 2870 completed and submitted an Enrolment/Baseline questionnaire.

Descriptive data

The majority of participants were female (64.3%) and the majority of males and females were ages 60-69 years (48.5% and 52.1% respectively). Most participants were from White: English, Welsh, Scottish, Northern Irish or British ethnic group (92.8%). A history of allergic conditions was the most frequently reported underlying medical condition (20.3%). The majority of participants had not had any other vaccines in the month prior to their first AstraZeneca vaccination (98.8%) or an allergic reaction to any vaccine in the past (95.3%). Most participants had not been diagnosed by a healthcare professional with COVID-19 infection (96.7%) or had a positive COVID-19 test result (96.8%) at any time prior to the vaccination. No participants reported to be pregnant, three reported to be breastfeeding.

Outcome Data

A total of 1232 participants reported an event, the most frequently reported event being headache (36.9%) followed by fatigue (34.4%). No participants reported to be pregnant, one reported to be breastfeeding. Most participants had not been diagnosed by a healthcare professional with COVID-19 infection (99.2%) or had a positive COVID-19 test result (99.6%) following vaccination. A total of 803 (38.2%) participants reported taking medication to reduce their temperature in the two days following vaccination.

Discussion

This report summarises interim data for participants enrolled in the Post-authorisation active surveillance of the Safety of COVID-19 Vaccine AstraZeneca (AZD-1222) in the UK. A total of 1232 participants reported an event (58.6% of those who completed and submitted a follow up form), the most frequently reported event being headache (36.9%) followed by fatigue (34.4%).

Marketing Authorisation Holder(s)

AstraZeneca UK Limited

Names and affiliations of principal investigators

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2 List of Abbreviations

Abbreviation	Term
AE	Adverse Event
AEFI	Adverse event following immunisation
AESI	Adverse event of special interest
A and E	Accident and emergency
BMA	British Medical Association
CHMP	Committee for Medicinal Products for Human Use
CIOMS	Council for International Organisations of Medical Sciences
DSRU	Drug Safety Research Unit
EMA	European Medicines Agency
ESS	Enhanced Safety Surveillance
EU	European Union
FDA	Food and Drug Administration
FFU	Fluorescent Focus Units
GMC	General Medical Council
GP	General Practitioner
HCP	Healthcare professional
ICH	International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IRAS	Integrated Research Application System
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare Products Regulatory Agency
NHS	National Health Service
PASS	Post authorisation Safety Study
PHE	Public Health England
PIS	Participant Information Sheet
PRAC	Pharmacovigilance Risk Assessment Committee
RMP	Risk Management Plan
PS	Patient Safety
PSUR	Periodic Safety Update Report
sADR	Suspected Adverse Drug Reaction
SAE	Serious Adverse Event
SDT	Signal Detection Team
SOC	System Organ Class
SPC	Summary of Product Characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
UK	United Kingdom
US	United States

3 Investigators

Chief investigator	[redacted] DSRU Education and Research Ltd. Bursledon Hall Blundell Lane Southampton SO31 1AA UK
Co-investigators	[redacted]

4 Other Responsible Parties

Responsible party	**Appointed person(s)**
Marketing Authorisation holder contact	[redacted]
Consortium members	[redacted]

	[redacted]

5 Milestones

Milestone	Planned Date	Actual Date	Comments
Study Approval by Research Ethics Committee	February 2021	February 2021	
Start of data collection	1 March 2021	1 March 2021	
End of data collection	30 April 2023 (tbc)		
Registration in the EU PAS register	N/A		
Interim report 1	April 2021	April 2021	
Interim report 2	June 2021		
Interim report 3	September 2021		
Final report of study results	30 October 2023 (tbc)		

6 Rationale and Background

Vaccine benefit and risk evaluation is a continuum throughout the lifecycle of the vaccine, starting from pre-marketing development to post-marketing use. Whilst pre-marketing activities provide important information on vaccine safety and efficacy, post-marketing data is essential in providing evidence on post-authorisation use, short, medium and long-term safety and effectiveness of the vaccine.

The normal process for developing a vaccine is broadly similar to drug development. It is lengthy and can take 10-15 years. Animal studies follow chemical and biological development; the vaccine is then tested in humans in phase I-III clinical trials. Assessing the efficacy of a vaccine in phase III studies takes longer than medicines because the outcomes are not simply the beneficial effects of a drug on a disease but a combination of examining effects on biomarkers, e.g. antibodies, T lymphocytes and other biomarkers such as mucosal IgA in blood and saliva, and most importantly the reduction in the incidence of developing the disease in a comparable susceptible population.

In cases of urgent public health needs, such as the COVID-19 pandemic, the process of developing a vaccine is dramatically shortened; for example, developing, testing and releasing a vaccine in 12-18 months or less. Advances in genetics and biotechnology and parallel rather than sequential clinical studies are contributing to this efficiency in the case of COVID-19. To protect populations urgently, the release of a COVID-19 vaccine likely will be based on favourable effects on biomarkers and pre-marketing clinical studies with shorter observational periods compared to pre-marketing development in less urgent circumstances. Therefore, post-marketing observational studies will be vital to better understand effectiveness and safety. First, from a public health perspective, effectiveness (protecting vaccinees from the disease in real-world vaccination programmes) is different to vaccine efficacy tested in a clinical trial setting on a selected sample with inclusion and exclusion criteria. Secondly, given the limited pre-authorisation data, it is crucial to obtain near real-time notification of the safety and effectiveness signals of the vaccine when used routinely in the population so that actions to protect public health are taken promptly.

A fundamental function of the post-authorisation study is the prompted reporting by vaccinees which facilitates early identification of safety signals. The aim is to facilitate public health decisions based on findings from the study.
Also given public concerns about the novelty of some COVID-19 vaccine platforms and rapid vaccines development, transparent active vaccine surveillance that reports and evaluates signals in near real time is important to gain public trust.

In terms of safety it is important to detect any increased local and systemic adverse events, including adverse immune responses that may arise during vaccination programmes. Safety

signals can be rapidly detected in near real-time during the vaccination programme. Serious adverse events are defined by the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in the ICH E2A guidelines. Seriousness is based on patient/event outcome or action criteria and defines regulatory reporting obligations (1). An adverse event following immunisation (AEFI) will be considered serious if it results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. The ICH E2A guidelines also state that other situations, such as other important medical events that may jeopardize the patient or may require intervention to prevent one of the outcomes above, should also be considered serious after applying medical and scientific judgment. This study will comply with all these regulations.

In May 2020, the Coalition for Epidemic Preparedness Innovations (CEPI) and the Brighton Collaboration, the largest global organisation of scientific experts on vaccine safety, launched the Safety Platform for Emergency vACcines (SPEAC). SPEAC has prepared a list of potential AESI relevant to specific vaccine platforms for COVID-19 vaccines, with associated case definitions. The most recent version of the AESI list (September 2020) has been included in Appendix 1 and will be reviewed on a quarterly basis and updated as necessary. SPEAC will also develop case definitions for those AESI without existing case definitions. The AESI that still lack a case definition include enhanced disease after immunisation, multisystem inflammatory syndrome in children and acute respiratory distress syndrome. SPEAC will also review published evidence to identify the background incidence rates in target populations and the causes, risk factors and differential diagnoses and map the AESI to the corresponding codes of the International Classification of Diseases (ICD) and the Medical Dictionary for Regulatory Activities (MedDRA). We will use the case definitions and associated MedDRA codes to identify AESIs in this study, in addition to AESIs provided by AstraZeneca.

The more familiar safety evaluation methods involve comparing adverse event incidence between vaccinated and unvaccinated groups (cohort studies) or comparing rates of adverse events between infected cases and uninfected controls (case-control studies). For an active surveillance programme, in pandemics such as COVID-19 where vaccination coverage in a population is expected to be high and achieved quickly, traditional methods for evaluating vaccine safety may not be suitable due to the lack of availability of an unvaccinated comparator group for a sufficient length of time to conduct a comparative study and the

associated ethical considerations. Furthermore, if an unvaccinated group is available as a result of gradual introduction of vaccination whereby prioritisation is made for certain groups (e.g. at-risk individuals, older people, healthcare professionals) before reaching full vaccination coverage, comparison of these specific vaccinated groups to the remaining unvaccinated population may not be appropriate. This is due to the potential for significant biases, as an individual's baseline level of risk of infection and risk of developing severe disease will be different between patients in high and lower risk groups and the different demographic and biological characteristics, e.g. prevalence of underlying illnesses between the two groups. Lastly, timeliness of results from comparative studies may be longer than desired for pandemics such as COVID-19 which demand an urgent public health response.

In such scenarios, implementation of a faster and more responsive study design can provide timely information in the immediate post-marketing period with respect to safety of the vaccine in the 'real-world'. Nonetheless, single arm studies still possess methodological challenges (e.g. confounding) which require the same careful consideration in terms of statistical analyses as other study designs. Findings from post-marketing studies on vaccines can guide pharmacovigilance decisions by marketing authorisation holders and regulatory authorities.

However, it is possible to include intra-cohort comparisons within the cohort, such as nested case-control and self-controlled studies for people who develop specific adverse events such as events which have been associated with vaccines, e.g. narcolepsy, severe allergic reactions. Other analyses that can be considered include examination of secular trends, ecological and cross-sectional analyses.

The COVID-19 pandemic has potentially changed population perceptions of health, management of health by health-care professionals, lifestyle choices and behaviours (2,3). To address this emerging evidence and the impact of COVID-19 pandemics on daily lives of study participants and their response to being vaccinated against SARS-Cov-2, we aim to collect targeted information on the health-related quality of life (HRQoL) and the impact of the COVID-19 pandemic on their perception of health and productivity. A sub-study to examine quality of life outcomes will be conducted for a sample of the total cohort (Appendix 2).

For COVID-19, the urgent public health need for accelerated vaccine development has resulted in the evaluation of novel vaccine mechanisms, with animal studies and phase I human clinical

trials occurring in parallel. Fast-tracking through phase II and III clinical trials has occurred and the authorisation in the UK is for emergency use. However, the COVID-19 vaccine will be given to entire populations of healthy people. Vaccination of a very large number of people (millions) over a short period of time poses challenges compared to a gradual introduction of a product. However, the latter is not an option for a vaccine for COVID-19 for obvious reasons. While the benefit of having a vaccine available for susceptible individuals will likely be considered to outweigh the uncertainties of expedited development of a vaccine(s) for COVID-19, such scenarios merit even more rigorous post-marketing observational studies on the newly licensed vaccine. Specifically, post-marketing studies should address concerns about the safety of different vectors and adjuvants used by different COVID-19 vaccines.

Another important objective of the study is that the regular interim reports will contribute to alleviating concerns which may arise about the safety of the vaccine with a negative effect on the vaccination programme. Medical conditions, including those that have been associated with vaccines previously will occur in the population during the vaccination programme regardless of relatedness of vaccination. Publicity of some of these events will likely adversely affect the vaccination programme with serious public health consequences. Therefore, it is important that the study investigates such events to assess causality and report the results promptly. In addition rapid and transparent communication of the findings of the study is expected to build public trust and facilitate decision making by members of the public; both those who decide to be vaccinated and people with an increasingly recognised vaccine hesitancy (4).

In the UK, a vaccination strategy has been developed by the Joint Committee on Vaccination and Immunisation which is being used by the National Health Service (NHS) for implementation of COVID-19 vaccines. Phase 1 of the vaccination programme outlines specific groups which should be vaccinated first in order to prevent mortality and support the NHS and social care system. These groups are:

1. residents in a care home for older adults and their carers
2. all those 80 years of age and over and frontline health and social care workers
3. all those 75 years of age and over
4. all those 70 years of age and over and clinically extremely vulnerable individuals
5. all those 65 years of age and over

6. all individuals aged 16 years to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality
7. all those 60 years of age and over
8. all those 55 years of age and over
9. all those 50 years of age and over

This study will focus on studying those vaccinated in this first phase of the vaccination programme in the UK.

The study will build on the extensive experience of members of the consortium in conducting various types of observational studies on vaccines in the United Kingdom (UK), including both active and passive enhanced safety surveillance studies on seasonal influenza vaccines and the 2009 H1N1 (swine flu) vaccine. Study methods have included both vaccinated and unvaccinated cohorts or vaccinated individuals only. Active methods have involved organised data collection at specific time points on all individuals participating in the study, whereas passive methods relied on healthcare professionals or vaccinees completing questionnaires only if the vaccinee had experienced an adverse event. The H1N1 swine flu study monitored self-reported serious adverse events and pregnancy outcomes in patients offered swine flu vaccination (5). The seasonal influenza studies, conducted annually since 2014, have measured the incidence of suspected adverse drug reactions in children following vaccination with Fluenz Tetra (6), and compared patterns of adverse events observed with previous flu seasons. For a COVID-19 vaccine, given the public health need for comprehensive assessment of effectiveness and safety, an active surveillance method is considered necessary. However, specific characteristics of the COVID-19 pandemic require specific considerations in the study, e.g. frequency of monitoring.

This registry uses a large-scale active surveillance study, with many characteristics of a registry, to monitor the use and safety of the COVID-19 vaccination programme in near real-time in the UK. The nature of the National Health Service (NHS), Public Health England (PHE) and Public Health bodies in the devolved nations, along with the coverage of the National Institute for Health Research (NIHR) Clinical Research Networks, the accessibility of pharmacies and pharmacists nationwide will put the UK in an almost unique position to be able to lead a comprehensive, scientifically robust programme with effective capabilities to raise safety signals for rapid corrective actions.

7 Research Question and Objectives

Overall aim:

To monitor the safety and utilisation of the COVID-19 Vaccine AstraZeneca (AZD-1222) administered to vaccinees under real-world use in the UK

Primary objective:

- To examine the safety of COVID-19 vaccine AstraZeneca (AZD-1222) through active surveillance of all vaccinee reported adverse events and assessment of incidence.

Secondary objectives:

- (i) To describe and characterise serious adverse events following vaccination

To describe serious adverse events following vaccination, clinical data will be obtained and used to characterise the adverse event in detail. For example, if somebody reports weakness in a leg, characterisation includes obtaining more clinical information from the doctor and investigations such as MRI scan, nerve conduction studies etc. to enable a clinical diagnosis to decide whether this event was caused by myocitis, myopathy, transverse myelitis, a condition in the brain or any other cause. The information will then be used to help determine if the event may be linked to vaccination. An AEFI will be considered serious if it results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Other adverse events that may jeopardise the patient or may require intervention to prevent one of the outcomes above, may also be considered serious after applying medical and scientific judgment.

- (ii) To describe and characterise adverse events of special interest (AESI) including AESI relevant to vaccinations in general and AESI for the COVID-19 vaccine AstraZeneca (AZD-1222).

- (iii) To describe and characterise the utilisation of COVID-19 vaccine AstraZeneca (AZD-1222) in the cohort, including vaccination site, demographics of vaccinee and brand/batch of vaccine administered.

- (iv) To examine use and safety in populations with missing information including pregnant and breastfeeding women and individuals with immunodeficiency disorders,

treatment with immunosuppressants, concurrent medical conditions, and administration of other vaccines within previous 30 days.

Quality of life sub-study objective

(i) To describe and characterise health-related quality of life among a sub-population (n=3500) vaccinated by COVID-19 vaccine AstraZeneca (AZD-1222) and to describe the effect of the COVID-19 vaccine AstraZeneca (AZD-1222) on participant's lifestyle and productivity where affected by the COVID-19 pandemic.

8 Amendments and Updates

None

9 Research Methods

9.1 Study Design

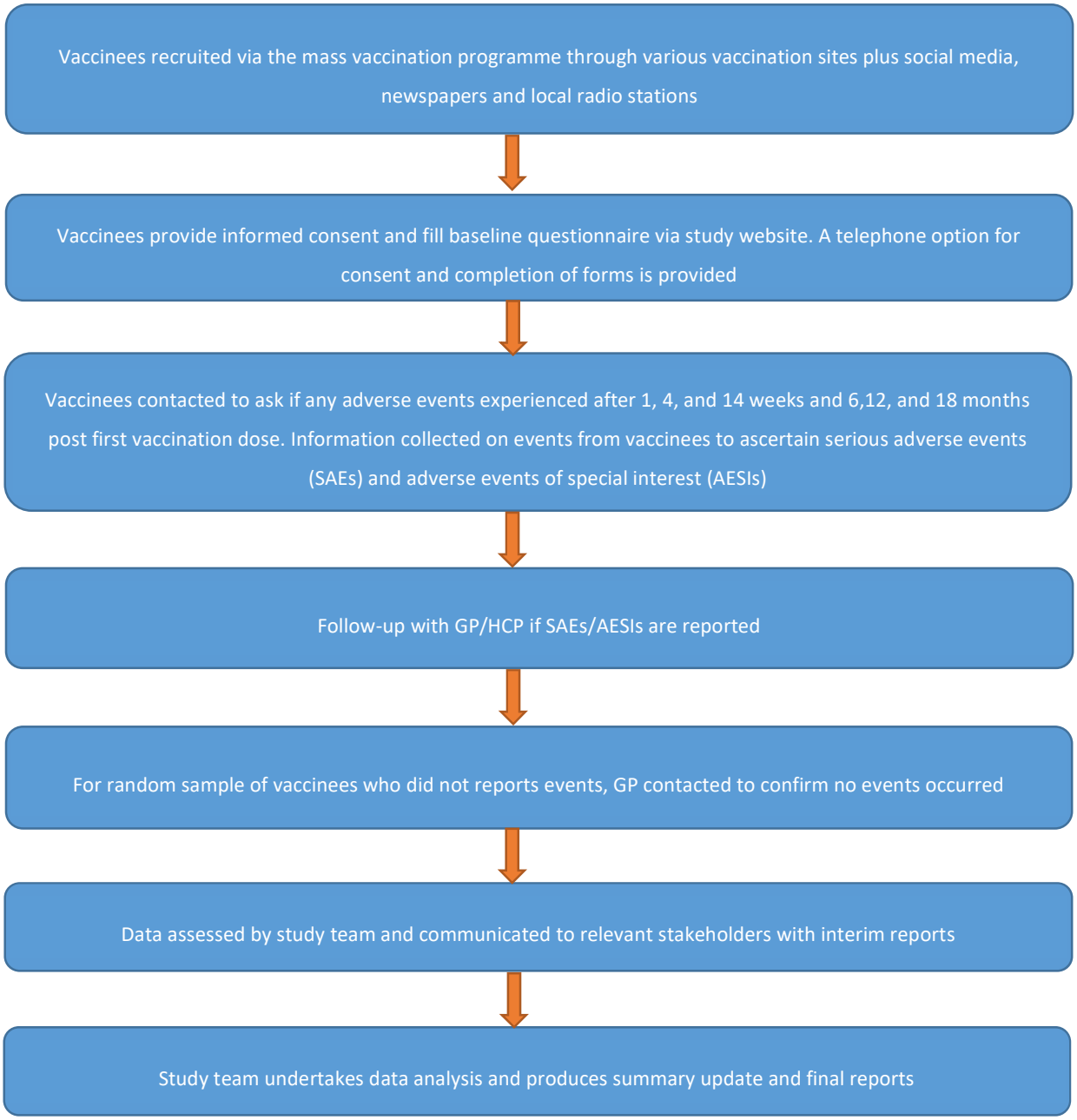
This is a prospective evaluation of data collected through active surveillance to monitor the reporting of events related to safety in COVID-19 vaccinees in the UK. There is a minimum 18-month observation period for each vaccinee. Vaccinees are eligible to consent to participate in the study up to a maximum of six weeks post first AstraZeneca vaccination dose.

Vaccinees are recruited via the mass vaccination programme through Primary care (GP practices) and other vaccination sites within the UK. Vaccinees that received the vaccine at these sites are provided with study information by immunisation staff after receiving the vaccine as part of the mass vaccination programme. In addition, further recruitment of vaccinees through social media and other direct forms of advertisement, newspapers, radio and television stations is used in order to maximise the sample size.

Vaccinees are directed by the study information provided to the portal's webpage. Vaccinees are asked to provide informed consent to participate in the study, through the secure study online portal. At time of consent, vaccinees are asked to indicate their preferred method of contact for follow up; by text message or by email (linking to secure online portal). In the scenario where vaccinees do not have internet access or cannot use text messaging, a telephone follow up is made available. Telephone consent is also possible for these vaccinees.

Figure 1 outlines the methodology used in this study.

Figure 1. Example of study flow for a COVID-19 active surveillance post-marketing study in the UK



Consent to contact vaccinees for follow up, in addition to consent to contact their GPs and other HCPs is required. Consented vaccinees are asked to provide the email address and telephone number of an emergency contact (relative, family friend or carer) who can be contacted if the study team are unable to contact the vaccinee. This is important to ensure that the study does not miss events that cause vaccinees to be too ill to respond to communications from the study.

Following consent, vaccinees are prompted to complete baseline information via the online portal (variables outlined in section 9.4.2). Vaccinees are then contacted at weeks 1, 4, and 14 then months 6, 12, and 18 following first vaccination dose (variables outlined in section 9.4.2) via their chosen communication method. A questionnaire only needs to be completed where a vaccinee has experienced events during one of these periods of contact.

For a random sample of participants who did not report events, the GP is contacted to obtain information on any events that the GP was aware the vaccinee had experienced during the observation period. This is used to validate data obtained by the vaccinee. In addition, this process is used to confirm vaccination dates (for first and second dose) and batch numbers, validating the information provided by vaccinees. Randomisation is conducted based on the cohort accrued at six months post study start and performed using simple random sampling. A sample of 10% of those who had not reported events is selected.

9.2 Setting

Vaccination sites including GP practices, health clinics etc. in the UK are invited to participate. Vaccinees and/or their representatives (parent/guardian) are provided with study information explaining the surveillance by immunisation staff after vaccination. Sites are provided with supporting information.

Recruitment via social media/advertisement (newspapers, radio and television) is also used to maximise participation. Those who have recently been vaccinated are eligible to participate by signing up directly on the online portal.

9.3 Subjects

Adults and children[1] vaccinated with COVID-19 vaccine AZD-1222, at any vaccination site throughout the UK, will be eligible for inclusion in this surveillance.

[1] Although the current guidance does not include children below the age of 16 years, we will include this group if they have received the vaccine.

9.4 Variables

9.4.1 Data from vaccinees or their representatives

Information requested from the participant at baseline (enrolment) includes:

- consent to contact vaccinee, contact details for vaccinee and relationship to vaccinee (if participant representative)
- consent to contact GP and other HCPs for follow-up if necessary and contact details for GP
- emergency contact information for participant (e.g. next of kin)
- date of birth, gender, race/ethnicity, postcode
- pregnancy status including date of last menstrual period (LMP) if pregnant
- Breastfeeding status
- vaccination details (date and brand/batch number of vaccine)
- information on specific comorbidities/conditions
- COVID-19 disease prior to vaccination

Information requested from the vaccinee at weeks 1, 4, and 14 then months 6, 12 and 18 following first vaccination dose includes:

- Any symptom(s)/condition(s) experienced following vaccination
- If yes:
    - adverse events experienced
        - Including COVID diagnosis/symptoms
        - Including AESI for example diagnosis of Guillain-Barre syndrome, idiopathic thrombocytopenia or narcolepsy (full list in Appendix 1)
    - dates of onset and resolution of reported adverse events
    - contact with GP, attendance at A & E or hospital admission
    - vaccination details (date and brand/batch number of vaccine) of second dose
    - Anti-pyretic use following vaccination with first and second dose
    - pregnancy status including date of last menstrual period (LMP) if pregnant
    - Breastfeeding status

9.4.2 Data from vaccinees' GPs or other HCPs (follow-up information about events)

Reported serious adverse events and AESI are assessed by clinical staff at the DSRU. The GP or other HCP is contacted to gather further information about the event. A standard follow-

up questionnaire is used to obtain further information and the GP or other HCP completes this via the online portal.

Data collected from GPs/other HCPs includes the following:

- confirmation of date of onset (time when first sign/symptom indicative of the adverse event) and/or first observation if date of onset unknown.
- severity of event
- contact with GP, attendance at A & E or hospital admission
- clinical details, diagnosis and relevant investigations
- management and final outcome
- seriousness of the event
- relevant medical history (including pre-existing conditions or risk factors considered to be relevant to the event) and concomitant medication

9.5 Data Sources and Measurement

Data is collected from vaccinees or their representatives. Follow-up information about vaccinee reported serious adverse events and AESI is collected from the vaccinees' GP or other HCPs.

9.6 Bias

9.6.1 Under-reporting

Under-reporting is a potential limitation where vaccinees may not report events experienced during the observation period. This is considered to be more likely to occur with mild/non-serious events, and reminders will be sent to vaccinees who do not respond to follow up requests during the observation period. In addition, we will obtain emergency contact details in the scenario where a vaccinee may have died during the observation period. However, given the perceived gravity of COVID-19 by people, it is expected that the response rate will be high among vaccinees and doctors. This will be augmented by a campaign of publicity for the study in social media and other platforms such as newspapers, radio and television.

9.6.2 Response rate

Response rate may vary by method and vaccination site. Response rates at different sites will be monitored throughout the study and steps will be taken to maximise response rate where required. In addition, we have provided multiple options for preferred methods of communication in the study to maximise response.

As with all longitudinal studies, there is the potential for loss to follow up. This will be minimised by maintaining contact with vaccinees at various time points throughout the observation period. In addition, we will obtain emergency contact information in the scenario where a vaccinee cannot be contacted due to death during the study observation period.

9.6.3 Selection bias

Selection bias is possible since those who participate may be different from those who do not take part. In addition, the participating vaccination sites are not selected at random. Rather, selection of sites is based on their willingness to participate in this surveillance, thus, the sample may not be fully representative of the general population of vaccinees in the UK. The multiple enrolment method which will mirror the vaccination programme as much as possible combined with enrolment by social media, newspapers, radio and television offer a reasonable expectation that vaccinees enrolled in the study will represent the UK vaccinees as much as possible.

9.6.4 Missing data

Due to the nature of the study design (vaccinee reported information), there is the possibility that missing data will arise for specific variables. Missingness will be examined at final report stage and an appropriate method will be used to handle missing data where appropriate. Such methods would not be used where missing values represent less than 20% of data for an individual variable.

9.7 Study Size

A cohort of at least 10,000 vaccinees is required, to provide reassurance regarding safety for vaccine AZD-1222 that will be made available in the UK. Vaccinees from a variety of age groups will be recruited, with 25% of the sample from NHS staff, social care staff and vulnerable patients below 50 years. Ages 50 years and over will form the remaining 75% and be divided into 10 year age bands for recruitment, in line with the age distribution of the UK population where possible.

A minimum sample size of 10,000 vaccinees would allow 95% certainty that events not observed in the cohort occur less frequently than one in 3333 cases. (7)

A sample size of 10,000 should allow for the detection of at least three cases of an adverse event, with 85% power, if the event occurs at a rate of at least one in 2000 persons (assuming the background rate is zero). (8)

9.8 Data Transformation

No data transformations were undertaken for the interim report.

9.9 Statistical Methods

9.9.1 Main Summary Measures

Summary descriptive statistics used for interim report.

9.9.2 Main Statistical Methods

In view of the minimal data cleaning applied to the data for this interim report, no statistical modelling was conducted.

9.9.3 Missing Values

Not applicable for interim report.

9.9.4 Sensitivity Analyses

Not applicable for interim report.

9.9.5 Amendments to the Statistical Analysis Plan

None

9.10 Quality Control

Data quality is a high priority at the DSRU and is assured through a number of methods based on staff training, validated system, error-prevention, data monitoring, data cleaning and documentation. These include:

- Staff training on data processing standard operating procedures, data entry and coding conventions, MedDRA and authorised use of the DSRU Information System (OSIRIS);
- GxP validated system to conduct pharmacovigilance research studies;
- Data management plan for every research study outlining legal basis for data collection, data flows, data access rights, data retention periods, etc.;
- On screen validation during data entry by participants, for example, setting logical limits on date values, etc.;
- Adoption of and adherence to project-specific data coding conventions for free-text events;
- Code list and algorithms for free text events to facilitate specified outcome assessments;
- Retrospective quality review of adverse event data (a minimum 15% sample), error reporting and correction of discrepancies between the entries by data entry staff.
- Routine data cleaning to screen for errors, missing values and extreme values and diagnose their cause; this being supported by bespoke software with objective, standardised logical checks and undertaken by data manager or allocated staff;
- Relevant maintenance of reference tables, e.g., Event Dictionary;
- System process logs to document staff access, etc.;
- Pilot testing of documentation.

10 Results

Data is presented up to the datalock date of 30th March 2021. This report provides information on raw data and has undergone minimal data cleaning.

10.1 Participants

At datalock, a total of 5995 participants were eligible and signed up to the study. Of these, 3549 provided consent and 2870 completed and submitted an Enrolment/Baseline questionnaire.

10.2 Descriptive Data

10.2.1 Patient demographics

Information collected on age, gender and ethnicity is presented in Tables 1 and 2.

The majority of participants were female (64.3%) and the majority of males and females were ages 60-69 years (48.5% and 52.1% respectively). Most participants were from White: English, Welsh, Scottish, Northern Irish or British ethnic group (92.8%).

Table 1. Age and gender

Age Band	Male	%	Female	%	Gender non-binary	%	Prefer not to mention	%	Missing	%	Total
10-19	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	2
20-29	5	0.5	17	0.9	1	50.0	0	0.0	0	0.0	23
30-39	14	1.4	40	2.2	0	0.0	0	0.0	0	0.0	54
40-49	37	3.7	94	5.1	0	0.0	0	0.0	0	0.0	131
50-59	116	11.5	299	16.2	1	50.0	0	0.0	0	0.0	416
60-69	490	48.5	962	52.1	0	0.0	1	100.0	0	0.0	1453
70-79	328	32.5	421	22.8	0	0.0	0	0.0	0	0.0	749
80-89	18	1.8	11	0.6	0	0.0	0	0.0	0	0.0	29
90-99	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	2
Missing	1	0.1	1	0.1	0	0.0	0	0.0	9	100.0	11
Total*	1010	35.2	1848	64.4	2	0.1	1	0.0	9	0.3	**2870**

*% of 2870

Table 2. Ethnicity

Ethnicity	Total	%
White: Any other White background	110	3.8
White: English, Welsh, Scottish, Northern Irish or British	2664	92.8
White: Gypsy or Irish Traveller	1	0.0
White: Irish	31	1.1
Mixed or Multiple ethnic groups: Any other Mixed or Multiple ethnic background	5	0.2
Mixed or Multiple ethnic groups: White and Asian	2	0.1
Mixed or Multiple ethnic groups: White and Black African	2	0.1
Mixed or Multiple ethnic groups: White and Black Caribbean	2	0.1
Asian or Asian British: Any other Asian background	5	0.2
Asian or Asian British: Bangladeshi	1	0.0
Asian or Asian British: Chinese	4	0.1
Asian or Asian British: Indian	11	0.4

Black, African, Caribbean or Black British: African	3	0.1
Black, African, Caribbean or Black British: Any other Black, African or Caribbean background	1	0.0
Black, African, Caribbean or Black British: Caribbean	5	0.2
Other ethnic group: Any other ethnic group	12	0.4
Other ethnic group: Arab	2	0.1
Missing	9	0.3
Total	**2870**	

10.2.2 Underlying medical conditions

Participants were asked to indicate whether they had any of the following chronic underlying medical conditions (Table 3). A history of allergic conditions (20.3%) was the most frequently reported condition followed by asthma (10.6%).

Table 3. Underlying medical conditions

Condition	**Total (N=2870)**	**%**
Neurological conditions	143	5.0
Bleeding disorder	14	0.5
Asthma	305	10.6
COPD (Chronic obstructive Pulmonary disease)	70	2.4
Diabetes	159	5.5
Heart disease	158	5.5
Chronic kidney disease	47	1.6
A condition which affects your immune system?	158	5.5
Auto-immune disease	172	6.0
Solid organ transplant recipient	10	0.3
Liver disease	20	0.7
History of allergic conditions	583	20.3
Cancer	137	4.8

Participants were also asked if they were currently taking immunosuppressant medication (Table 4). The majority of patients were not taking immunosuppressant medication (95.5%).

Table 4. Current immunosuppressant medication

Immunosuppressant	Total	%
Yes	104	3.6
No	2740	95.5
Don't know	17	0.6
Missing	9	0.3
Total	**2870**	

10.2.3 Prior vaccinations

Participants were asked whether they had any other vaccinations in the month prior to their first AstraZeneca vaccination (Table 5). The majority of participants had not had any other prior vaccines (98.8%); where participants specified a prior vaccination, the details of the vaccine, as reported, are presented by frequency in Table 6.

Table 5. Vaccinations one month prior

Other Vaccinations	Total	%
Yes	24	0.8
No	2836	98.8
Don't know	1	0.0
Missing	9	0.3
Total	**2870**	

Table 6. Details of vaccinations one month prior

Other Vaccinations	Total
Flu	14
B12	2
flu jab	1
Janssen trial vaccine for ENSEMBLE 2 study	1
MMR and Hepatitis B	1
Pneumococcal vaccine	1
Pneumonia	1

Psoriatic Arthritis and Psoriasis	1
Steroid injection into hip joint	1
Tetanus Booster	1
Total	**24**

Participants were also asked whether they had an allergic reaction to any vaccine in the past (Table 7). The majority of participants had not had an allergic reaction (95.3%); where participants specified an allergic reaction, the details of the vaccine, as reported, are presented by frequency in Table 8.

Table 7. Allergic reaction to any vaccine

Allergic Reaction	Total	%
Yes	86	3.0
No	2735	95.3
Don't know	40	1.4
Missing	9	0.3
Total	**2870**	

Table 8. Details of vaccine causing allergic reaction*

Vaccine	Total
TETANUS VACCINE	11
INFLUENZA VACCINE	9
IINFLUENZA, INACTIVATED, SPLIT VIRUS OR SURFACE ANTIGEN	6
Anti Tetanus	3
Flu	3
Flu Vaccine	3
Penicillins	2
TYPHOID VACCINE	2
RUBELLA VACCINE	2
Penicillin	2
CHOLERA VACCINE	2
PENICILLIN G	1
Serum by injection anti tetanus 1955	1
SMALLPOX VACCINE	1

Swine flu	1
TB	1
Tetanus	1
Unknown - pre-med for operation in 1986	1
Vaccine for allergies (personalised)	1
Whooping cough	1
Yellow Fever	1
YELLOW FEVER VACCINE	1
PNEUMOCOCCAL VACCINE	1
Pneumocyst pneumonia	1
Pneumonia	1
Primovast MRI Contrast	1
RABIES VACCINE	1
INFLUENZA and Tetanus	1
? Yellow fever	1
1960s anti-tetanus	1
Local anaesthetics,antiemetics,whooping cough,tetanus	1
MEASLES VACCINE	1
MMR VACCINE	1
Morphine [as anaesthetic]	1
Once to the flu jab.	1
Only once, to flu vaccine in 1977. Never since.	1
Pencillian	1
flu vaccine 2018	1
Hay fever	1
Hay fever desensitising injections as a student	1
HEPATITIS B VACCINE	1
Flu Pneumovax Hep B booster	1
Flu & Pneumonia	1
Flu (annual)	1
Flu jab	1
Anti tetanus serum	1
Antitetanus	1
Astra Zeneca Covid 19 vaccine	1
ASTRA ZENECCA	1
BCG as a teenager!	1
Can’t remember	1

Chicken flu	1
Childhood	1

*as reported by the participant; a small number of participants entered medicines rather than vaccines

10.2.4 COVID-19 disease prior to vaccination

Participants were asked whether they had been diagnosed by a healthcare professional (including 111) with COVID-19 infection or had a positive COVID-19 test result at any time prior to the vaccination and if so, whether they attended Accident and Emergency (A & E), were hospitalised or whether they lost any days of work or education (Tables 9 to 13).

The majority of participants had not been diagnosed by a healthcare professional (including 111) with COVID-19 infection (96.7%) or had a positive COVID-19 test result (96.8%) at any time prior to the vaccination (Tables 9 and 10). Where participants reported a positive test, this was most frequently via a nose/throat swab (93.8%) (Table 11).

Where a participant indicated a COVID-19 diagnosis and/or a positive COVID-19 test result (N=112), 8.9% attended A & E and 3.6% were hospitalised. In addition, 43.8% reported that they lost days of work or education; over a quarter of these reported losing 10 days (Tables 12-14).

Table 9. COVID-19 diagnosis

COVID-19 Diagnosis	**Total**	**%**
Yes	77	2.7
No	2776	96.7
Don't know	8	0.3
Missing	9	0.3
Total	**2870**	

Table 10. Positive COVID-19 test

Test Positive	**Total**	**%**
Yes	80	2.8
No	2779	96.8
Don't know	2	0.1
Missing	9	0.3
Total	**2870**	

Table 11. COVID-19 test method

Test Method	Total	%
Nose/throat swab	75	93.8
Blood or finger prick test	5	6.3
Total	**80**	

Table 12. Attended A & E or Hospitalised

	Attended A & E	%	Hospitalised	%
Yes	10	8.9	4	3.6
No	101	90.2	108	96.4
Don't know	1	0.9	0	0.0
Total	**112**		**112**	

Table 13. Days of work or education lost

Days of Work/Education lost	Total	%
Yes	49	43.8
No	60	53.6
Don't know	3	2.7
Total	**112**	

Table 14. Number of days of work or education lost

Number of Days Lost	Total	%
1	1	2.0
3	5	10.2
4	2	4.1
5	1	2.0
6	3	6.1
7	4	8.2
9	1	2.0
10	13	26.5
11	1	2.0
12	1	2.0

13	1	2.0
14	2	4.1
15	3	6.1
16	1	2.0
18	1	2.0
20	1	2.0
21	3	6.1
25	1	2.0
30	1	2.0
35	1	2.0
90	1	2.0
120	1	2.0
Total	49	

10.2.5 Pregnancy and Breastfeeding status

Participants were asked for their pregnancy and breastfeeding status at baseline (Table 15 and 16). No participants reported to be pregnant, three reported to be breastfeeding.

Table 15. Pregnancy status

Pregnant	**Total**	**%**
Yes	0	0.0
No	2560	89.2
Not applicable	301	10.5
Missing	9	0.3
Total	**2870**	

Table 16. Breastfeeding status

Breastfeeding	**Total**	**%**
Yes	3	0.1
No	2539	88.5
Don't know	2	0.1
Not applicable	317	11.0
Missing	9	0.3
Total	**2870**	

10.3 Outcome Data

At datalock, 2700 participants were eligible to receive their first post vaccination Follow-Up form; of these, 2101 Follow-Up forms were submitted. A total of 1232 participants reported an event. All events reported are presented in order of frequency at the MedDRA Preferred Term (PT) level in Table 17. Details as to whether the participant contacted their GP practice or attended A & E or was admitted to hospital as a result of the symptom/condition are also presented.

The most frequently reported event was headache (36.9%) followed by fatigue (34.4%). Where a participant reported headache, 3.5% contacted their GP or attended A & E and 0.7% were admitted to hospital. Where a participant reported fatigue, 3.5% contacted their GP or attended A & E and 0.5% were admitted to hospital. There was one report of COVID-19 which did not require contacted with the participant's GP or attendance at A & E or admission to hospital.

Table 17. Symptoms/conditions following vaccination*

PT	Total	%[a]	Contacted GP/Attended A & E	%[b]	Hospitalised	%[b]
Headache	455	36.9	16	3.5	3	0.7
Fatigue	424	34.4	15	3.5	2	0.5
Chills	249	20.2	8	3.2	1	0.4
Pyrexia	236	19.2	8	3.4	4	1.7
Pain in extremity	208	16.9	8	3.8	0	0.0
Influenza like illness	146	11.9	4	2.7	0	0.0
Myalgia	138	11.2	4	2.9	0	0.0
Nausea	115	9.3	6	5.2	2	1.7
Arthralgia	105	8.5	6	5.7	0	0.0
Pain	100	8.1	3	3.0	0	0.0
Injection site pain	77	6.3	1	1.3	0	0.0
Malaise	72	5.8	3	4.2	0	0.0
Feeling cold	53	4.3	1	1.9	1	1.9
Dizziness	50	4.1	5	10.0	1	2.0
Body temperature increased	38	3.1	0	0.0	0	0.0
Lethargy	36	2.9	0	0.0	0	0.0

Vaccination site pain	33	2.7	0	0.0	0	0.0
Feeling abnormal	29	2.4	3	10.3	1	3.4
Tremor	26	2.1	3	11.5	0	0.0
Decreased appetite	23	1.9	0	0.0	0	0.0
Tension headache	22	1.8	1	4.5	0	0.0
Limb discomfort	21	1.7	0	0.0	0	0.0
Migraine	18	1.5	2	11.1	0	0.0
Musculoskeletal stiffness	17	1.4	0	0.0	0	0.0
Palpitations	17	1.4	2	11.8	0	0.0
Vomiting	17	1.4	3	17.6	0	0.0
Back pain	16	1.3	1	6.3	0	0.0
Pruritus	16	1.3	8	50.0	0	0.0
Asthenia	15	1.2	1	6.7	0	0.0
Lymphadenopathy	14	1.1	5	35.7	1	7.1
Muscle fatigue	14	1.1	0	0.0	0	0.0
Diarrhoea	13	1.1	1	7.7	0	0.0
Feeling hot	12	1.0	0	0.0	0	0.0
Feeling of body temperature change	12	1.0	0	0.0	0	0.0
Hyperhidrosis	11	0.9	0	0.0	0	0.0
Nasopharyngitis	11	0.9	1	9.1	0	0.0
Abdominal discomfort	10	0.8	0	0.0	0	0.0
Injection related reaction	10	0.8	0	0.0	0	0.0
Somnolence	10	0.8	0	0.0	0	0.0
Tinnitus	10	0.8	3	30.0	0	0.0
Body temperature abnormal	9	0.7	0	0.0	0	0.0
Influenza	9	0.7	0	0.0	0	0.0
Night sweats	9	0.7	1	11.1	1	11.1
Oropharyngeal pain	9	0.7	1	11.1	0	0.0
Paraesthesia	9	0.7	1	11.1	0	0.0

Abdominal pain upper	8	0.6	0	0.0	0	0.0
Neck pain	8	0.6	1	12.5	0	0.0
Peripheral swelling	8	0.6	3	37.5	0	0.0
Rhinorrhoea	8	0.6	1	12.5	0	0.0
Adverse event	7	0.6	0	0.0	0	0.0
Chest pain	7	0.6	4	57.1	1	14.3
Dyspnoea	7	0.6	2	28.6	1	14.3
Heart rate increased	7	0.6	1	14.3	1	14.3
Injection site erythema	7	0.6	3	42.9	0	0.0
Insomnia	7	0.6	0	0.0	0	0.0
Peripheral coldness	7	0.6	0	0.0	0	0.0
Rash	7	0.6	1	14.3	0	0.0
Abdominal pain	6	0.5	2	33.3	1	16.7
Injection site swelling	6	0.5	2	33.3	0	0.0
Renal pain	6	0.5	1	16.7	0	0.0
Contusion	5	0.4	1	20.0	0	0.0
Cough	5	0.4	1	20.0	0	0.0
Ear pain	5	0.4	1	20.0	0	0.0
Head discomfort	5	0.4	0	0.0	0	0.0
Injection site warmth	5	0.4	2	40.0	0	0.0
Vaccination site swelling	5	0.4	2	40.0	0	0.0
Balance disorder	4	0.3	1	25.0	1	25.0
Bedridden	4	0.3	0	0.0	0	0.0
Bone pain	4	0.3	0	0.0	0	0.0
Chest discomfort	4	0.3	0	0.0	0	0.0
Depressed mood	4	0.3	0	0.0	0	0.0
Erythema	4	0.3	2	50.0	0	0.0
Injection site bruising	4	0.3	0	0.0	0	0.0
Post viral fatigue syndrome	4	0.3	0	0.0	0	0.0

Sinus headache	4	0.3	0	0.0	0	0.0
Sweating fever	4	0.3	1	25.0	1	25.0
Vaccination complication	4	0.3	0	0.0	0	0.0
Vertigo	4	0.3	2	50.0	0	0.0
Ageusia	3	0.2	1	33.3	0	0.0
Blood glucose increased	3	0.2	0	0.0	0	0.0
Disturbance in attention	3	0.2	1	33.3	0	0.0
Eye pain	3	0.2	0	0.0	0	0.0
Head banging	3	0.2	0	0.0	0	0.0
Illness	3	0.2	0	0.0	0	0.0
Mouth ulceration	3	0.2	0	0.0	0	0.0
Nasal congestion	3	0.2	0	0.0	0	0.0
Photophobia	3	0.2	0	0.0	0	0.0
Poor quality sleep	3	0.2	0	0.0	0	0.0
Sinus pain	3	0.2	0	0.0	0	0.0
Skin warm	3	0.2	1	33.3	0	0.0
Thirst	3	0.2	0	0.0	0	0.0
Abdominal distension	2	0.2	0	0.0	0	0.0
Abdominal pain lower	2	0.2	0	0.0	0	0.0
Application site bruise	2	0.2	0	0.0	0	0.0
Arthritis	2	0.2	0	0.0	0	0.0
Blood pressure increased	2	0.2	0	0.0	0	0.0
Body temperature normal	2	0.2	0	0.0	0	0.0
Burning sensation	2	0.2	1	50.0	0	0.0
Cellulitis	2	0.2	2	100.0	0	0.0
Condition aggravated	2	0.2	1	50.0	0	0.0
Confusional state	2	0.2	0	0.0	0	0.0
Dizziness postural	2	0.2	0	0.0	0	0.0

Drug withdrawal headache	2	0.2	0	0.0	0	0.0
Dyspepsia	2	0.2	1	50.0	0	0.0
Epistaxis	2	0.2	0	0.0	0	0.0
Flushing	2	0.2	0	0.0	0	0.0
Hot flush	2	0.2	0	0.0	0	0.0
Hypoaesthesia	2	0.2	0	0.0	0	0.0
Inflammation	2	0.2	0	0.0	0	0.0
Infusion related reaction	2	0.2	0	0.0	0	0.0
Injection site discomfort	2	0.2	0	0.0	0	0.0
Injection site hypersensitivity	2	0.2	1	50.0	0	0.0
Injection site rash	2	0.2	1	50.0	0	0.0
Injection site reaction	2	0.2	0	0.0	0	0.0
Listless	2	0.2	0	0.0	0	0.0
Muscular weakness	2	0.2	0	0.0	0	0.0
Nasal herpes	2	0.2	0	0.0	0	0.0
Neuralgia	2	0.2	0	0.0	0	0.0
New daily persistent headache	2	0.2	0	0.0	0	0.0
Paraesthesia oral	2	0.2	0	0.0	0	0.0
Photosensitivity reaction	2	0.2	0	0.0	0	0.0
Presyncope	2	0.2	0	0.0	0	0.0
Q fever	2	0.2	0	0.0	0	0.0
Rash pruritic	2	0.2	1	50.0	0	0.0
Sleep disorder	2	0.2	0	0.0	0	0.0
Sneezing	2	0.2	0	0.0	0	0.0
Swelling face	2	0.2	0	0.0	0	0.0
Syncope	2	0.2	1	50.0	0	0.0
Tachycardia	2	0.2	0	0.0	0	0.0
Tenderness	2	0.2	1	50.0	0	0.0
Vaccination site bruising	2	0.2	0	0.0	0	0.0

Vaccination site mass	2	0.2	1	50.0	0	0.0
Vaccination site rash	2	0.2	0	0.0	0	0.0
Weight decreased	2	0.2	0	0.0	0	0.0
Abnormal dreams	1	0.1	0	0.0	0	0.0
Abnormal sleep-related event	1	0.1	0	0.0	0	0.0
Anosmia	1	0.1	0	0.0	0	0.0
Arthropathy	1	0.1	0	0.0	0	0.0
Asthenopia	1	0.1	0	0.0	0	0.0
Asthma	1	0.1	0	0.0	0	0.0
Atrial fibrillation	1	0.1	1	100.0	0	0.0
Blister	1	0.1	0	0.0	0	0.0
Blood donation	1	0.1	0	0.0	0	0.0
Body temperature	1	0.1	0	0.0	0	0.0
Body temperature decreased	1	0.1	0	0.0	0	0.0
Body temperature fluctuation	1	0.1	0	0.0	0	0.0
Bronchiectasis	1	0.1	0	0.0	0	0.0
Cellulitis staphylococcal	1	0.1	1	100.0	0	0.0
Change of bowel habit	1	0.1	1	100.0	0	0.0
Chronic fatigue syndrome	1	0.1	0	0.0	0	0.0
Cluster headache	1	0.1	1	100.0	0	0.0
Cold exposure injury	1	0.1	0	0.0	0	0.0
Cold sweat	1	0.1	0	0.0	0	0.0
Constipation	1	0.1	1	100.0	0	0.0
COVID-19	1	0.1	0	0.0	0	0.0
Crying	1	0.1	0	0.0	0	0.0
Cystitis	1	0.1	1	100.0	0	0.0
Deafness	1	0.1	1	100.0	0	0.0
Dermatitis	1	0.1	0	0.0	0	0.0

Discomfort	1	0.1	0	0.0	0	0.0
Disorientation	1	0.1	0	0.0	0	0.0
Dysgeusia	1	0.1	0	0.0	0	0.0
Essential hypertension	1	0.1	0	0.0	0	0.0
Exercise tolerance decreased	1	0.1	0	0.0	0	0.0
Eye discharge	1	0.1	0	0.0	0	0.0
Eyelid disorder	1	0.1	0	0.0	0	0.0
Facial paralysis	1	0.1	1	100.0	0	0.0
Feeling of despair	1	0.1	0	0.0	0	0.0
Feeling of relaxation	1	0.1	0	0.0	0	0.0
Fibromyalgia	1	0.1	0	0.0	0	0.0
Flatulence	1	0.1	0	0.0	0	0.0
Furuncle	1	0.1	1	100.0	0	0.0
Gastrointestinal disorder	1	0.1	0	0.0	0	0.0
Gastrointestinal sounds abnormal	1	0.1	0	0.0	0	0.0
Hangover	1	0.1	0	0.0	0	0.0
Heart rate irregular	1	0.1	0	0.0	0	0.0
Herpes zoster	1	0.1	1	100.0	0	0.0
Hyperacusis	1	0.1	0	0.0	0	0.0
Hyperpyrexia	1	0.1	0	0.0	0	0.0
Hypersensitivity	1	0.1	0	0.0	0	0.0
Hypersomnia	1	0.1	0	0.0	0	0.0
Hypoaesthesia oral	1	0.1	0	0.0	0	0.0
Hypotension	1	0.1	0	0.0	0	0.0
Hypoxia	1	0.1	1	100.0	1	100.0
Idiopathic urticaria	1	0.1	1	100.0	0	0.0
Injection site inflammation	1	0.1	0	0.0	0	0.0
Injection site mass	1	0.1	1	100.0	0	0.0
Injection site paraesthesia	1	0.1	0	0.0	0	0.0

Injection site pruritus	1	0.1	0	0.0	0	0.0
Intracranial aneurysm	1	0.1	1	100.0	0	0.0
Jaundice	1	0.1	0	0.0	0	0.0
Language disorder	1	0.1	0	0.0	0	0.0
Lip swelling	1	0.1	0	0.0	0	0.0
Localised infection	1	0.1	1	100.0	0	0.0
Loss of libido	1	0.1	0	0.0	0	0.0
Migraine with aura	1	0.1	0	0.0	0	0.0
Motion sickness	1	0.1	1	100.0	0	0.0
Multiple sclerosis	1	0.1	0	0.0	0	0.0
Muscle discomfort	1	0.1	0	0.0	0	0.0
Muscle spasms	1	0.1	0	0.0	0	0.0
Musculoskeletal pain	1	0.1	1	100.0	0	0.0
Myositis	1	0.1	0	0.0	0	0.0
Nervousness	1	0.1	0	0.0	0	0.0
Neuropathy peripheral	1	0.1	1	100.0	0	0.0
No adverse event	1	0.1	0	0.0	0	0.0
Oral herpes	1	0.1	0	0.0	0	0.0
Oral pain	1	0.1	0	0.0	0	0.0
Pain of skin	1	0.1	0	0.0	0	0.0
Pelvic pain	1	0.1	0	0.0	0	0.0
Platelet count decreased	1	0.1	1	100.0	0	0.0
Post herpetic neuralgia	1	0.1	0	0.0	0	0.0
Procedural headache	1	0.1	0	0.0	0	0.0
Psoriasis	1	0.1	0	0.0	0	0.0
Pulmonary embolism	1	0.1	1	100.0	1	100.0
Pulmonary pain	1	0.1	0	0.0	0	0.0
Rash erythematous	1	0.1	1	100.0	0	0.0
Rash macular	1	0.1	0	0.0	0	0.0

Retching	1	0.1	0	0.0	0	0.0
SARS-CoV-2 test negative	1	0.1	0	0.0	0	0.0
Sedation	1	0.1	0	0.0	0	0.0
Sensitive skin	1	0.1	0	0.0	0	0.0
Sinonasal obstruction	1	0.1	1	100.0	0	0.0
Sinus bradycardia	1	0.1	0	0.0	0	0.0
Sinus congestion	1	0.1	0	0.0	0	0.0
Skin odour abnormal	1	0.1	0	0.0	0	0.0
Spinal pain	1	0.1	0	0.0	0	0.0
Swelling	1	0.1	1	100.0	0	0.0
Symptom recurrence	1	0.1	0	0.0	0	0.0
Systemic immune activation	1	0.1	0	0.0	0	0.0
Tongue discomfort	1	0.1	0	0.0	0	0.0
Type 1 diabetes mellitus	1	0.1	0	0.0	0	0.0
Upper limb fracture	1	0.1	1	100.0	0	0.0
Urticaria	1	0.1	1	100.0	0	0.0
Vaccination site discolouration	1	0.1	0	0.0	0	0.0
Vaccination site warmth	1	0.1	0	0.0	0	0.0
Vascular headache	1	0.1	1	100.0	0	0.0
Vestibular nystagmus	1	0.1	0	0.0	0	0.0
Vision blurred	1	0.1	0	0.0	0	0.0
Vitamin supplementation	1	0.1	1	100.0	0	0.0
Vitreous floaters	1	0.1	1	100.0	0	0.0
Vomiting projectile	1	0.1	1	100.0	0	0.0
Wheezing	1	0.1	1	100.0	0	0.0
Total events	3361		203		25	

* a participant could have reported more than one event

[a] % of participants who reported an event (N=1232)

[b] % of participants reporting that event

10.3.1 COVID-19 disease following vaccination

Participants were asked whether they had been diagnosed by a healthcare professional (including 111) with COVID-19 infection or had a positive COVID-19 test result following vaccination and if so, whether they attended A & E, were hospitalised or admitted to critical/intensive care, or whether they lost any days of work or education (Tables 18 to 23). Participants were also asked whether they took any medication to reduce their temperature in the two days following vaccination (Table 24 and 25). Where a participant reported a COVID-19 event as a MedDRA term when asked about any symptoms/conditions following vaccination, they were also asked the questions relating to whether they attended A & E, were hospitalised or admitted to critical/intensive care, or whether they lost any days of work or education.

The majority of participants had not been diagnosed by a healthcare professional (including 111) with COVID-19 infection (99.3%) or had a positive COVID-19 test result (99.6%) following vaccination (Tables 18 and 19). Where participants reported a positive test, this was tested by Nose/throat swab (Table 20)

Where a participant indicated a COVID-19 diagnosis and/or a positive COVID-19 test result or reported a COVID-19 event as a MedDRA term (N=14), 14.3% attended A & E and 7.1% were hospitalised. In addition, 28.6% reported that they lost days of work or education (Tables 21-23).

A total of 803 (38.2%) participants reported taking medication to reduce their temperature in the two days following vaccination (Table 24). Details of medications taken, as reported, are presented by frequency in Table 25.

Table 18. COVID-19 diagnosis

COVID-19 Diagnosis	Total	%
Yes	12	0.6
No	2086	99.3
Don't know	2	0.1
Missing	1	0.0
Total	2101	0.6

Table 19. Positive COVID-19 test

Test Positive	Total	%
Yes	4	0.2
No	2092	99.6
Don't know	4	0.2
Missing	1	0.0
Total	2101	

Table 20. COVID-19 test method

Test Method	Total	%
Nose/throat swab	4	100.0
Total	4	

Table 21. Attended A & E or Hospitalised or admitted to critical/intensive care

	Attended A & E	%	Hospitalised	%	Critical/Intensive Care	%
Yes	2	14.3	1	7.1	0	0.0
No	12	85.7	13	92.9	14	100.0
Total	14		14		14	

Table 22. Days of work or education lost

Days of Work/Education lost	Total	%
Yes	4	28.6
No	10	71.4
Total	14	

Table 23. Number of days of work or education lost

Number of Days Lost	Total	%
5	2	50.0
10	1	25.0

130	1	25.0
Total	4	

Table 24. Medication to reduce temperature

Medication	Total	%
Yes	803	38.2
No	1297	61.7
Missing	1	0.0
Total	2101	

Table 25. Details of medication to reduce temperature

Drug Name	Total
PARACETAMOL	683
IBUPROFEN	89
DIHYDROCODEINE/PARACETAMOL	24
PARACETAMOL WITH METOCLOPRAMIDE	10
CO-CODAMOL	8
ASPIRIN	7
PANADOL	7
Paracetemol	7
Paracetomol	7
ANADIN EXTRA	4
COLD/FLU REMEDY	4
NUROFEN	4
CODEINE	3
SOLPADEINE	3
ZAPAIN	3
Lemsip	2
Paracetamols	2
TRAMADOL/PARACETAMOL	2
Paracetamol	1
ANTIBIOTIC	1
Co codamol	1
CO-AMOXICLAV	1
Codiene	1

FLUCLOXACILLIN	1
HYDROCORTISONE	1
Ibroprufin	1
Ibuoprofen	1
IMODIUM	1
Jakeman's Menthol	1
LORATADINE	1
NABUMETONE	1
NAPROXEN	1
Neurofen	1
ORAMORPH	1
Panadol Extra	1
PANADOL SOLUBLE	1
PARACETAMOL & IBUPROFEN	1
Paracetamol 500mg	1
Paracetamol and Ibuprofen	1
Paracetamol and ibuprofen as a precaution	1
PARACETAMOL and Ibuprofin	1
paracetamol/IBUPROFIN	1
Paracetmol	1
paracetomol - But forgot to take it in the first six hours when I felt really chilled	1
Parcetamol	1
SOLPADOL	1
SYNDOL	1
Tesco paracetamol	1
TRAMADOL	1

10.3.2 Pregnancy and Breastfeeding status

Participants were asked for their pregnancy and breastfeeding status at follow up (Table 26 and 27). No participants reported to be pregnant and one reported to be breastfeeding.

Table 26. Pregnancy status

Pregnant	**Total**	**%**
No	1880	89.5

Not applicable	220	10.5
Missing	1	0.0
Total	2101	

Table 27. Breastfeeding status

Breastfeeding	Total	%
Yes	1	0.0
No	1868	88.9
Don't know	1	0.0
Not applicable	230	10.9
Missing	1	0.0
Total	2101	

10.4 Main Results

No Statistical analyses were conducted for this interim analysis and therefore no results are presented in this section.

10.5 Other Analyses

Not applicable

10.6 Adverse Events/Adverse Reactions

For all events refer to Section 10.3

11 Discussion

This report summarises interim data for participants enrolled in the Post-authorisation active surveillance of the Safety of COVID-19 Vaccine AstraZeneca (AZD-1222) in the UK.

11.1 Key Results

At datalock (30th March 2021), total of 5995 participants were eligible and signed up to the study. Of these, 3549 provided consent, 2870 completed and submitted an Enrolment/Baseline questionnaire and 2101 participants were eligible to receive and submitted their first post vaccination Follow-Up form.

The majority of participants were female (64.3%) and the majority of males and females were ages 60-69 years (48.5% and 52.1% respectively). Most participants were from White: English, Welsh, Scottish, Northern Irish or British ethnic group (92.8%). A history of allergic conditions was the most frequently reported underlying medical condition (20.3%). The majority of participants had not had any other prior vaccines (98.8%) or an allergic reaction to any vaccine in the past (95.3%). Most participants had not been diagnosed by a healthcare professional with COVID-19 infection (96.7%) or had a positive COVID-19 test result (96.8%) at any time prior to the vaccination. No participants reported to be pregnant at baseline, three reported to be breastfeeding. A total of 1232 participants reported an event (58.6% of those who completed and submitted a follow up form), the most frequently reported event being headache (36.9%) followed by fatigue (34.4%). Most participants had not been diagnosed by a healthcare professional with COVID-19 infection (99.2%) or had a positive COVID-19 test result (99.6%) following vaccination. A total of 803 (38.2%) participants reported taking medication to reduce their temperature in the two days following vaccination. No participants reported to be pregnant at follow up, one reported to be breastfeeding.

11.2 Limitations

Limitations mentioned in section 9.6 (Possible biases).

11.3 Interpretation

At time of interim report, there were no new safety signals raised.

11.4 Generalisability

Generalisability will be assessed at final report stage.

12 Other Information

None

13 Conclusion

This report summarises interim data for participants enrolled in the Post-authorisation active surveillance of the Safety of COVID-19 Vaccine AstraZeneca (AZD-1222) in the UK. A total of 1232 participants reported an event (58.6% of those who completed and submitted a follow

up form), the most frequently reported event being headache (36.9%) followed by fatigue (34.4%). At time of interim report, there were no new safety signals raised.

14 References

1. European Medicines Agency. Guideline on good pharmacovigilance practices (GVP): Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2) [Internet]. 2017. Available from: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vi-collection-management-submission-reports_en.pdf
2. McGinty EE, Presskreischer R, Han H, Barry CL. Psychological Distress and Loneliness Reported by US Adults in 2018 and April 2020. JAMA. 2020 Jul 7;324(1):93.
3. Stöhr E, Aksoy A, Campbell M, Zaidi MA, Öztürk C, Vorloeper J, et al. Hospital admissions during Covid-19 lock-down in Germany: Differences in discretionary and unavoidable cardiovascular events. PLOS ONE. 2020 Nov 20;15(11):e0242653.
4. Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med. 2020 Oct 20;1–4.
5. Mackenzie IS, MacDonald TM, Shakir S, Dryburgh M, Mantay BJ, McDonnell P, et al. Influenza H1N1 (swine flu) vaccination: a safety surveillance feasibility study using self-reporting of serious adverse events and pregnancy outcomes. Br J Clin Pharmacol. 2012 May;73(5):801–11.
6. McNaughton R, Lynn E, Osborne V, Coughtrie A, Layton D, Shakir S. Safety of Intranasal Quadrivalent Live Attenuated Influenza Vaccine (QLAIV) in Children and Adolescents: A Pilot Prospective Cohort Study in England. Drug Saf. 2016 Apr;39(4):323–33.
7. Strom B. Sample Size Considerations for Pharmacoepidemiology Studies. In: Pharmacoepidemiology. Third edition. John Wiley & Sons; 2000. p. 31–9.
8. Machin D, Campbell M, Fayers P, Pinol A. Table 7.1. In: Sample size considerations for clinical studies. Second edition. Oxford: Blackwell Science Ltd; 1997.

Appendices

Annex 1. List of stand-alone documents

Appendix 1: AESI list (September 2020)
Appendix 2: Quality of Life (QOL) sub-study
Appendix 3: Management of adverse events