A post-authorisation/post-marketing observational study to evaluate the association between exposure to AZD1222 and safety concerns using existing secondary health data sources (COVID-19)

First published: 07/10/2021

Last updated: 30/10/2025

Study Finalised

Administrative details

EU PAS number

EUPAS43556

Study ID

48711

DARWIN EU® study

No

Study countries

- ☐ Italy
- ☐ Netherlands

☐ Spain

☐ United Kingdom

Study description

AstraZeneca developed vaccine AZD1222 to prevent COVID-19 (called Vaxzevria® in Europe). Based on the EU RMP, safety concerns for AZD122 include nervous system disorders (including immune-mediated neurological conditions), vaccine-associated enhanced disease (including vaccine-associated enhanced respiratory disease), thrombocytopenia with associated bleeding, anaphylaxis, thrombosis, and ‘thrombosis with thrombocytopenia syndrome’ (TTS). This PASS will evaluate the incidence and relative risk of safety concerns and adverse events of special interest (AESIs) following immunisation in the real-world setting. The primary study objectives are to (1) describe baseline characteristics of all individuals who receive at least one dose of AZD1222 over the study period, (2) describe, among subjects who receive a first dose of AZD1222, the timing and type of second dose of any COVID-19 vaccine over the study period, (3) describe the incidence of prespecified AESIs in subjects who have received at least one dose of AZD1222 and in matched unvaccinated subjects, and (4) estimate any increased risk of prespecified AESIs following vaccination with AZD1222 using study retrospective cohort and self-controlled risk interval designs. Secondary objectives are identical to the primary, although focused on specific populations considered to have missing information, specifically (a) women who are pregnant or breastfeeding, (b) immunocompromised patients, (b) frail patients with certain comorbidities, (c) patients with autoimmune or inflammatory disorders, and (d) patients who, at cohort entry, had recently received a number of selected vaccines to prevent diseases other than COVID-19.

Study status

Finalised

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom
- [ ] United Kingdom (Northern Ireland)
- [ ] United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Drug Safety Research Unit (DSRU)

- [ ] United Kingdom

First published: 10/11/2021

Last updated: 16/02/2024

Institution | Not-for-profit | ENCePP partner

University Medical Center Utrecht (UMCU)

- [ ] Netherlands

First published: 24/11/2021

Last updated: 22/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 24/07/2024

Institution | Laboratory/Research/Testing facility | ENCePP partner

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

First published: 05/10/2012

Last updated: 23/05/2025

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Agenzia regionale di sanità della Toscana (ARS)

Italy

First published: 01/02/2024

Last updated: 12/03/2024

Institution | EU Institution/Body/Agency | ENCePP partner

The Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO)

Spain

First published: 01/02/2024

Last updated: 31/10/2025

Institution

Networks

Vaccine monitoring Collaboration for Europe (VAC4EU)

- Belgium
- Denmark
- Finland
- France
- Germany

- [ ] Italy
- [ ] Netherlands
- [ ] Norway
- [ ] Spain
- [ ] United Kingdom

First published: 22/09/2020

Last updated: 22/09/2020

Network | Outdated | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 09/08/2021

Actual: 07/09/2021

Study start date

Planned: 17/02/2022

Actual: 18/02/2022

Date of interim report, if expected

Planned: 22/04/2022

Actual: 26/04/2022

Date of final study report

Planned: 31/12/2024

Actual: 12/12/2024

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AstraZeneca AB

Study protocol

d8111r00006-pass-clinical-study-protocol_Redacted.pdf (1.35 MB)

D8111R00006_Protocol v4.0 Redacted (Apr23).pdf (1.79 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Other study registration identification numbers and links

ClinicalTrials.gov Identifier: NCT05126992

Link to Clinicaltrials.gov

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Safety study (incl. comparative)

Validation of study variables (exposure outcome covariate)

Data collection methods:

Secondary use of data

Study design:

Multinational, matched cohort design; self-controlled risk interval (SCRI) design for selected outcomes.

Main study objective:

To evaluate the incidence and relative risk of safety concerns and adverse events of special interest (AESIs) following the administration of at least one dose of the AZ COVID-19 vaccine in the real-world setting.

Study Design

Non-interventional study design

Case-only

Cohort

Study drug and medical condition

Name of medicine

VAXZEVRIA

Name of medicine, other

COVID-19 Vaccine (ChAdOx1-S [recombinant])

Anatomical Therapeutic Chemical (ATC) code

(J07BN02) covid-19, viral vector, non-replicating

covid-19, viral vector, non-replicating

Medical condition to be studied

COVID-19 immunisation

Population studied

Short description of the study population

All individuals registered in each healthcare data source during the study period.

Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Immunocompromised

Pregnant women

Estimated number of subjects

5200000

Study design details

Setting

The source population for each of the study designs will comprise all individuals registered in each healthcare data source during the study period. The study period will start on the date AZD1222 vaccination began in each country. The first vaccinations started approximately 1 week after approval date, which was 30 December 2020 in the UK and 29 January 2021 in the EU. The study period duration will be 24 months in each data source or until latest data available at the time of start of data collection. The all AZD1222 vaccinated population will include all subjects vaccinated with at least 1 dose of AZD1222 during the study period.

For each AESI, subjects who had an event of a specific AESI during the clean look-back interval were excluded from the cohort included in the analysis for the specific AESI with which they had history, but not from the analysis cohorts for other AESIs. For each AESI to be evaluated using the SCRI design, the eligible population will include subjects from the AZD1222 cohort who experienced the AESI during the study period.

Comparators

The AZD1222 cohort will be identified based on the first vaccination with AZD1222 (index date). A concurrent unvaccinated comparator cohort will be identified among subjects who have not received any vaccination for COVID-19 matched (to the extent possible) on the vaccinee’s index date, age, sex, prior diagnosis of COVID-19, and status according to each of the 5 special populations. The active comparator cohort will be initially identified based on the first vaccination with an mRNA vaccine (Comirnaty or Spikevax) matched (to the extent possible) on the vaccinee’s index date (first dose; a second matching will be done using second dose for the comparative analysis), age, sex, prior diagnosis of COVID-19, and status according to each of the 5 special populations. A historical comparator cohort will be identified among subjects who were enrolled in the study data sources at any time during 2017 and 2018

matched on age, sex, and status according to each of the 5 special populations.

Outcomes

Adverse events of special interest (AESIs) and other safety concerns listed in Table 2 of the study protocol.

Data analysis plan

Baseline characteristics will be described overall and in sequential periods overtime. For the cohort study, exposure propensity scores will be used to exclude noncomparable subjects and refine the balance between study cohorts, initially matched on calendar date of vaccination, age, and gender. Propensity scores will be used to control for confounding either by matching or by analytic methods involving stratification or weighting. For AESIs for which the risk interval is characterised, crude IRs and 95%CIs for the vaccinated population and for the comparator cohort will be estimated. Poisson regression models will be used to estimate crude and adjusted IRRs and IR differences with 95%CIs comparing vaccinated and comparator cohorts. Cox regression models will be used to estimate crude and adjusted hazard ratios and 95% CIs. For comparative analysis using the SCRI approach, conditional Poisson regression will be used to estimate IRRs and 95%CIs of specific AESIs, where appropriate.

Documents

Study report

AZD1222 PASS_Interim Report 1_Final_21Apr2022_Redacted.pdf (5.47 MB)

d8111r00006-pass-final-report_final-v1.0_12Dec2024_Redacted.pdf (14.5 MB)

Study publications

Forns J, Pajouheshnia R, Aurelius T, Bouck Z, Carreras Martínez JJ, Choi J, et …

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Clinical Practice Research Datalink

The Information System for Research in Primary Care (SIDIAP)

PHARMO Data Network

ARS Toscana

The Valencia Health System Integrated Database

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

ConcepTION CDM

CDM website

https://www.imi-conception.eu/

CDM release frequency

6 months

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes