

# 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:** 07/01/2025

Study

Finalised

## Administrative details

### PURI

<https://redirect.ema.europa.eu/resource/48711>

### EU PAS number

EUPAS43556

### Study ID

48711

### DARWIN EU® study

No

## Study countries

- ☐ Italy
  - ☐ Netherlands
  - ☐ Spain
  - ☐ United Kingdom
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## 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.

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## 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:** 23/02/2024

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:** 05/11/2024

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

ENCePP partner

## Contact details

### Study institution contact

Cristina Rebordosa

Study contact

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### Primary lead investigator

Cristina Rebordosa

Primary lead investigator

### ORCID number:

0000-0002-8064-5997

## Study timelines

**Date when funding contract was signed**

Planned: 09/08/2021

Actual: 07/09/2021

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**Study start date**

Planned: 17/02/2022

Actual: 18/02/2022

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**Date of interim report, if expected**

Planned: 22/04/2022

Actual: 26/04/2022

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**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

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## 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

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#### **Study type:**

Non-interventional study

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#### **Scope of the study:**

Drug utilisation

Safety study (incl. comparative)

Validation of study variables (exposure outcome covariate)

**Data collection methods:**

Secondary use of data

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**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

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**Name of medicine, other**

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

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**Anatomical Therapeutic Chemical (ATC) code**

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

covid-19, viral vector, non-replicating

(J07BX03) covid-19 vaccines

covid-19 vaccines

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**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.

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**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)

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**Special population of interest**

Immunocompromised

Pregnant women

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**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.

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## **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.

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## Outcomes

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

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## 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)

## Data management

## 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

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**Data sources (types)**

[Administrative healthcare records \(e.g., claims\)](#)

[Disease registry](#)

[Drug dispensing/prescription data](#)

[Electronic healthcare records \(EHR\)](#)

## Use of a Common Data Model (CDM)

**CDM mapping**

Yes

**CDM Mappings****CDM name**

ConcepTION CDM

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**CDM website**

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

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**CDM release frequency**

6 months

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## Data quality specifications

**Check conformance**

Yes

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**Check completeness**

Yes

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**Check stability**

Yes

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**Check logical consistency**

Yes

## Data characterisation

**Data characterisation conducted**

Yes