Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine

First published: 25/06/2021

Last updated: 08/05/2026

Study Finalised

Administrative details

EU PAS number

EUPAS41623

Study ID

46939

DARWIN EU® study

No

Study countries

Italy

Netherlands

Norway

Spain

United Kingdom

Study description

A retrospective cohort design will be used to estimate the incidence of adverse events of special interest (AESI) after receiving the Pfizer-BioNTech COVID-19 vaccine doses and compare this incidence with that occurring in an unvaccinated comparator group matched on relevant individual characteristics (eg, age, comorbidities). Where appropriate, the study will also use a self-controlled risk interval (SCRI) design. The source population will comprise all individuals registered in each of the healthcare data sources who are eligible to receive the Pfizer-BioNTech COVID-19 vaccine. The study period will start on the date of launch of the Pfizer-BioNTech COVID-19 vaccine and will end on the date of the latest data availability or 31 Dec 2023. It is expected that follow-up will last for 2 years for AESI. People who are pregnant at time of vaccination or who become pregnant within two years of study start and their live born infants will be followed for an additional 12 months to collect information about birth outcomes and linked infant outcomes. Exposure will be based on recorded prescription, dispensing, or administration of the Pfizer-BioNTech COVID-19 vaccine. Vaccine administration and date of vaccination should be obtained from all possible sources that capture COVID-19 vaccination. The outcomes will be based on the AESI proposed by the European Medicines Agency sponsored ACCESS project (vACcine COVID-19 monitoring readinESS). AESI will be identified based on patient profile review of electronic records by healthcare professionals. In addition, manual review of patient charts conducted by clinicians blinded to COVID-19 vaccine exposure will be performed. Confirmation of an event diagnosis will be classified against existing definitions of the Brighton Collaboration and those currently being developed. The study will be performed within select data sources from Netherlands, Italy, Spain,

United Kingdom, and Norway.

Study status

Finalised

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

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

RTI Health Solutions (RTI-HS)

France

Spain

Sweden

United Kingdom

United Kingdom (Northern Ireland)

United States

First published: 21/04/2010

Last updated: 11/08/2026

Institution | Not-for-profit | ENCePP partner

Teamit Institute

Spain

First published: 12/03/2024

Last updated: 12/03/2024

Institution | Other | ENCePP partner

Fundazione Penta ONLUS

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

Cynthia de Luise

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 15/12/2020

Actual: 15/12/2020

Study start date
Planned: 30/09/2021

Actual: 03/09/2021

Date of final study report
Planned: 30/09/2025

Actual: 30/09/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer

Study protocol

C4591021_PROTOCOL_20MAY2021____.pdf (844.83 KB)

C4591021_PROTOCOL AMENDMENT 6 V8.0_22JUL2025.pdf (1.23 MB)
C4591021_PROTOCOL AMENDMENT 5_V7.0_15MAY2024.pdf (1.22 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)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To determine whether an increased risk of prespecified AESI exists following the administration of at least one dose the Pfizer-BioNTech COVID 19 vaccine using two approaches: (a) a cohort design comparing risk in vaccinated and non-vaccinated individuals and (b) a self-controlled risk interval (SCRI) design.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Self-controlled case series

Study drug and medical condition

Medicinal product name

COMIRNATY

Study drug International non-proprietary name (INN) or common name

COVID-19 MRNA VACCINE (NUCLEOSIDE-MODIFIED)

FAMTOZINAMERAN

RAXTOZINAMERAN

RILTOZINAMERAN

TOZINAMERAN

Anatomical Therapeutic Chemical (ATC) code

(J07BN01) covid-19, RNA-based vaccine

covid-19, RNA-based vaccine

Medical condition to be studied

COVID-19 immunisation

Population studied

Short description of the study population

Individuals must meet all the following inclusion criteria to be eligible for inclusion in the
cohort study:

 Have a minimum of 12 months (or from birth if enrolled in the data source at birth) of
active enrolment and history in one of the selected data sources to ensure adequate
characterisation of medical history; this criterion may be met after the start of the study
period.

 No history of vaccination with a COVID-19 vaccine before time zero.

Age groups

- Preterm newborn infants (0 – 27 days)
- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- 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

13.225.000

Study design details

Setting

For the implementation of this study, electronic healthcare databases in Europe will be used.

Comparators

No COVID-19 vaccination

Outcomes

Risk of prespecified AESI following the administration of at least one dose the Pfizer-BioNTech COVID-19 vaccine using two approaches: (a) a cohort design comparing risk in vaccinated and non-vaccinated individuals and (b) a self-controlled risk interval (SCRI) design, Incidence rates of prespecified AESI among individuals who receive at least one dose of the Pfizer-BioNTech COVID-19 vaccine using a cohort study design and compared with a matched comparator group with no COVID-19 vaccination within subcohorts of interest, including pregnant people and their neonates. Utilization patterns of Pfizer-BioNTech COVID-19 vaccine among individuals within Europe.

Data analysis plan

The distributions of baseline characteristics at time zero by exposure group will be calculated to describe the study cohort and illustrate differences between the groups. For safety outcomes, the risk over specific time period(s), incidence rates and their corresponding 95% confidence intervals (CIs) will be computed after the receipt of first, second, and subsequent doses. Crude risks, cumulative incidence over different time periods, and measures of association for each AESI after vaccination will be estimated in the entire population overall and separately by number of doses received. Subgroup analyses will be conducted by demographic and clinical characteristics as well as other covariates of interest. To account for potential confounding, propensity score methods will be used to estimate the adjusted risk ratios and 95% CIs. Appropriate random-effects meta-analytic methods will be used to obtain a combined effect estimate. Where appropriate, the study will also use a SCRI design.

Documents

Abstract of study report

C4591021 Final Non-Interventional Study Report Abstract.pdf (170.44 KB)

Study report

C4591021_PROGRESS REPORT_27SEP2021.pdf (1.82 MB)

C4591021 NI Study Report Abstract - interim 1.pdf (1.29 MB)

c4591021-interim2-abstract.pdf (1.84 MB)

c4591021-interim3-abstract.pdf (659.37 KB)

c4591021-interim-abstract.pdf (703.59 KB)

C4591021 Interim 5 Study Report Abstract .pdf (120.38 KB)

C4591021 Final Non-Interventional Study Report.pdf (11.81 MB)

Study, other information

C4591021_PROTOCOL AMENDMENT 2_31MAR2022.pdf (4.11 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

Pedianet

EpiChron Cohort

Norwegian Health Registers

Health Search/IQVIA Health Longitudinal Patient 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

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No