Post-Authorisation Safety Study of Comirnaty Original/Omicron BA.1 and Comirnaty Original/Omicron BA.4-5 in Europe

First published: 22/01/2024

Last updated: 02/07/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS108847

Study ID

199012

DARWIN EU® study

No

Study countries

Italy

Netherlands

Norway

Spain

United Kingdom

Study description

This study aims to answer the research question is there an increased risk of pre-specified adverse events of special interest (AESIs) after vaccination with bivalent BA.1 or bivalent BA.4-5 compared with no vaccination against COVID-19 among individuals with comparable vaccination histories? The primary study objective is to determine whether there is an increased risk of pre-specified AESIs following the administration of bivalent BA.1 or bivalent BA.4-5 compared with not receiving any COVID-19 vaccine during follow-up. A retrospective cohort design will be used to estimate the incidence of AESIs after receiving a Pfizer-BioNTech COVID-19 bivalent vaccine, and these incidences will be compared with those in a comparator group that did not receive any COVID-19 vaccine during follow-up. Exposed individuals will be matched to unexposed individuals using relevant individual characteristics. For selected AESIs a self-controlled risk interval (SCRI) study design will also be used, when appropriate. The source population will comprise all individuals registered in each of the health care data sources who are eligible to receive bivalent BA.1 or bivalent BA.4-5. The study period will start on the date of availability of the bivalent BA.1, which was the first bivalent vaccine to receive authorisation in the EU (on 01 Sep 2022), in each participating country and will end on 31 Aug 2024 or the date of the latest data availability. BA.4-5 received authorisation in the EU on 12 Sep 2022. Individuals will be evaluated for eligibility and time zero will be determined as the date of exposure (vaccination with bivalent BA.1 or bivalent BA.4-5). Matching will occur at time zero and follow-up will begin at time zero. Individuals who have received at least one dose of bivalent BA.1 or bivalent BA.4-5 will be included in the exposed cohort. Individuals who have not received a dose of any COVID-19 vaccine at time zero will be included in the unexposed cohort.

Study status

Ongoing

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

Fondaziione 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: 31/01/2024

Study start date
Planned: 31/03/2024

Actual: 13/06/2024

Date of final study report
Planned: 30/04/2026

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer

Study protocol

C4591052_PROTOCOL AMENDMENT 2_V3.0_08JAN2024.pdf (1.02 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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

To determine whether there is an increased risk of pre-specified AESIs following the administration of bivalent BA.1 or bivalent BA.4-5 compared with not receiving any COVID-19 vaccine during follow-up.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Self-controlled risk interval

Study drug and medical condition

Medicinal product name

COMIRNATY

COMIRNATY

COMIRNATY

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

(J07BX) Other viral vaccines

Other viral vaccines

Medical condition to be studied

Adverse event following immunisation

Population studied

Short description of the study population

The study size will be determined by the uptake of the bivalent BA.1 and bivalent BA.4-5 vaccines in the contributing data sources during the study period.

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

1

Study design details

Outcomes

Risk of pre-specified AESIs following the administration of bivalent BA.1 or bivalent BA.4-5 compared with not receiving any COVID-19 vaccine during follow-up.

Data analysis plan

Data from the matched cohort design will be analysed as follows: Conditional exchangeability: The pairs will be matched using several variables considered as potential confounders to ensure conditional exchangeability. Additional standard epidemiological methods, based on propensity scores, will be used to improve adjustment for confounding, if necessary. The effect estimates will be reported as risk ratios and risk differences (and their corresponding 95% confidence intervals) for those exposed to a Pfizer-BioNTech COVID-19 bivalent vaccine compared with those not exposed to any COVID-19 vaccine during follow-up. Appropriate data analysis models will be used to estimate the

incidence rate ratios of AESIs in the risk and the control windows in the SCRI study.

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)

Pedianet

PHARMO Data Network

The Information System for Research in Primary Care (SIDIAP)

Clinical Practice Research Datalink

EpiChron Cohort

Norwegian Health Registers

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

Other

Data sources (types), other

Routine primary care electronic patient registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No