Non-Interventional Postmarketing Safety Study to Evaluate the COMIRNATY 2024-2025 Formula (monovalent KP.2) in the United States

First published: 21/02/2025

Last updated: 28/05/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000476

Study ID

1000000476

DARWIN EU® study

No

Study countries

United States

Study description

The study will be conducted in two phases, each with its own specific objectives.
In Phase 1, the primary objective is to estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2024-2025 Formula compared to the incidence of these events during a post-vaccination control window (ie, expected rates of these events).
In Phase 2, the primary objective is to estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2024-2025 Formula compared to the incidence among individuals with no recorded vaccination with the COMIRNATY 2024-2025 Formula.
The secondary objective is to estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2024-2025 Formula compared to the incidence among individuals with no recorded vaccination with the COMIRNATY 2024-2025 Formula within subgroups of immunocompromised individuals, individuals with specific comorbidities, individuals with prior SARS-CoV-2 infection, individuals with prior COVID-19 vaccination, individuals with concomitant administration of non-COVID-19 vaccines, pregnant individuals, children, and the elderly, if sample size permits.
This is a non-interventional observational study utilizing an administrative claims database in the US.
Phase 1 will utilize a self-controlled risk interval (SCRI) design, and Phase 2 will utilize a matched comparative safety cohort design.

Study status
Ongoing

Research institutions and networks

Institutions

Pfizer

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Institution

Optum - United States

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Jenny Sun

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 23/08/2024

Actual: 23/08/2024

Study start date
Planned: 11/03/2025

Actual: 11/03/2025

Date of interim report, if expected
Planned: 30/06/2025

Actual: 30/06/2025

Date of final study report
Planned: 28/02/2027

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer

Study protocol

C4591070 PROTOCOL AND STATISTICAL ANALYSIS PLAN_28OCT2024.pdf (1.27 MB)

C4591070_PROTOCOL AND SAP V2 AMENDMENT 1_22APR2026.pdf (1.19 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This is a non-interventional observational study utilizing an administrative claims database in the US.

Main study objective:

To estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2024-2025 Formula compared to the incidence of these events during a post vaccination control window (i.e., expected rates of

these events).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

COMIRNATY KP.2

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

COVID-19 MRNA VACCINE (NUCLEOSIDE-MODIFIED)

Anatomical Therapeutic Chemical (ATC) code

(J07BN01) covid-19, RNA-based vaccine

covid-19, RNA-based vaccine

Population studied

Short description of the study population

The study population will be drawn from a nationwide healthcare insurance claims database.

It will include all eligible individuals who receive the COMIRNATY 2024-2025 Formula from 22 August 2024 (the date of product approval/authorization) through 31 March 2025.

The end date of 31 March 2025 was chosen based on the assumption that vaccine uptake will be similar to uptake during the 2022-2023 and 2023-2024 vaccine seasons.

During the 2022-2023 and 2023-2024 COVID-19 seasons, the end of March reflected the time when uptake of the COVID-19 vaccine was no longer increasing (ie, most individuals who received the COVID-19 vaccine had done so prior to March), and COVID-19 cases declined substantially from their fall/winter peak.

The source population for this study will consist of all individuals with at least one medical or pharmacy claim from 22 August 2024 through 31 March 2025.

In Phase 1, individuals age ≥ 6 months will be eligible for inclusion if they receive at least one dose of the COMIRNATY 2024-2025 Formula from 22 August 2024 through 31 March 2025, have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination date, experience a safety outcome of interest during a risk or control period, and do not experience the safety event of interest during the clean period prior to vaccination.

In Phase 2, individuals age ≥ 6 months will be eligible for inclusion in the exposed cohort if they receive a dose of the COMIRNATY 2024-2025 Formula and have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination.

Individuals age ≥ 6 months will be eligible for inclusion in the unexposed cohort if they do not receive a dose of the COMIRNATY 2024-2025 Formula but do have an outpatient physician visit with or without receipt of another vaccine and if they have continuous medical and pharmacy insurance coverage in the 365 days prior to their outpatient healthcare encounter.

Individuals in the unexposed cohort will be matched to those in the exposed cohort if their outpatient healthcare encounter is within the same 14-day calendar period as the exposed individual’s vaccination date and if they are in the same age group.

Age groups

- 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)

Study design details

Outcomes

The pre-specified safety outcomes of interest include the following: acute disseminated encephalomyelitis (ADEM), transverse myelitis (TM), encephalitis/myelitis/encephalomyelitis (not ADEM or TM), anaphylaxis, Bell’s palsy,
cerebral venous sinus thrombosis (CVST), convulsions/seizures (non-febrile), glomerulonephritis, Guillain-Barré syndrome, herpes zoster, immune-mediated myositis, immune thrombocytopenia, Kawasaki disease, multi inflammatory syndrome (in children and adults), multiple sclerosis (MS), myocardial infarction (MI),
myocarditis/pericarditis, pulmonary embolism (PE), hemorrhagic stroke, and ischemic stroke. In Phase 2 of the study, pregnancy outcomes will also be assessed among pregnant individuals and their infants, if sample size permits. The outcomes of interest include major congenital malformations, preterm birth, small for gestational age (SGA), spontaneous abortion, and stillbirth. All study outcomes will be identified through claims

indicators using published validated claims-based algorithms with high performance when available.

Data analysis plan

Phase 1: For the SCRI design, the observed incidence rates of the pre-specified AESIs will be estimated in the risk window and the control window.

Among individuals who experience an outcome of interest in either the risk window or the control window (but not both), an exact conditional Poisson regression model with the natural logarithm of the person-time as the offset will be used to calculate the relative incidence (rate ratio) and corresponding 95% confidence interval (CI) of events occurring during the risk period relative to the control period.

The results from the SCRI utilizing the Optum pre-adjudicated claims database will be presented in the interim report, while results utilizing the ORD will be presented in the final report.

Please see the protocol for a description of the data analysis plan for the phase 2 cohort 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), other

Optum pre-adjudicated claims database United States, Optum Research Database United States

Data sources (types)

Administrative healthcare records (e.g., claims)

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