An Observational Post-Authorization Safety Study to Assess the Safety of Ad26.COV2.S Using Health Insurance Databases in the United States

First published: 21/11/2022

Last updated: 25/08/2025

Study Finalised

Administrative details

EU PAS number

EUPAS49836

Study ID

49837

DARWIN EU® study

No

Study countries

United States

Study description

Retrospective observational study using health insurance claims in the United States to access the risk of developing pre-specified adverse events of special interest, following administration of Ad26.COV2.S.

Study status

Finalised

Research institutions and networks

Institutions

Harvard Pilgrim Health Care Institute

First published: 01/02/2024

Last updated: 01/02/2024

Institution

HealthCore

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Optum

Germany

First published: 03/01/2012

Last updated: 07/02/2014

Institution | Outdated | Other | ENCePP partner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

CVS Health (Aetna), Hartford, Connecticut, USA

Humana, Louisville, Kentucky, USA

Contact details

Study institution contact

Nicolas Praet ra-rndus-clnclTrlsEU@its.jnj.com

Study contact

ra-rndus-clnclTrlsEU@its.jnj.com

Primary lead investigator

Nicolas Praet

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 04/03/2021

Actual: 04/03/2021

Study start date

Planned: 01/04/2021

Actual: 01/04/2021

Date of final study report

Planned: 31/08/2025

Actual: 24/06/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Janssen

Study protocol

REDACTED_Protocol-FD-VAC31518COV4001 Amend 2_1422771.pdf (1.47 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

VAC31518COV4001

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Retrospective observational study,

Acute event: self-controlled risk interval design among the Ad26.COV2.S exposed cohort.

Non-acute events: cohort design comparing individuals exposed to Ad26.COV2. with individuals exposed to at least 1 dose of BNT 162b2 [Pfizer-BioNTech COVID-19 vaccine.

Main study objective:

To assess the potential association between the occurrence of predefined AESIs and vaccination with Ad26.COV2.S in individuals exposed to first dose of Ad26.COV2.S vaccine compared with either 1) individuals exposed to the first dose of BNT1622 vaccine for non-acute events or 2) for acute events during a control window within the same individual.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

JCOVDEN

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

COVID-19 VACCINE JANSSEN (AD26.COV2.S)

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

Population studied

Short description of the study population

First time recipients of COVID-19 vaccines (JCOVDEN or mRNA) aged ≥ 18 years with ≥ 1 year of continuous health plan enrolment with medical and prescription coverage prior to the reference date and an earliest coverage date on or before 11 December 2020 identified from claims data within four national insurers in the United States participating in the Sentinel system.

Age groups

- **Adult and elderly population (≥18 years)**

Special population of interest

Frail population

Immunocompromised

Pregnant women

Estimated number of subjects

280.000

Study design details

Setting

For the SCRI design, eligibility criteria will be applied separately for analysis of each AESI. Individuals over the age of 18 years split at the reference date will be included it they have received a first dose of Ad26.COV2.5 vaccine during the study period, experienced the AESI during the risk or control period, and have at least 1 year of continuous medical and prescription drug coverage prior to the date of vaccination until the end of the AESI-specific control interval.
For the active comparator cohort design, individuals over the age of 18 years at the reference date who have at least 1 year of continuous medical and prescription drug coverage for at least 1 year prior to the reference date, and who have not been found to be vaccinated with any COVID 19 vaccine prior to the reference date will be eligible for the overall study cohorts. Each AESI will be analyzed separately. For the analysis of each AESI, individuals with AESI-specific exclusion criteria will be excluded, and analyses will be done in the AESI-specific sub cohort.

Comparators

The SCRI design will compare the risk of the AESIs in a postvaccination risk window to a postvaccination control window within the same individual, in a cohort of individuals vaccinated with Ad26.COV2.S.
For the cohort design, the incidence of AESIs will be compared between the 1-dose Ad26.COV2.S exposed cohort and the 2-dose BNT162b2 comparator

cohort.

Outcomes

Within Janssen, a list of AESIs has been created based on current knowledge of the Ad26.COV2. vaccine and potential risks related to adeno platform vaccine. AESIs will be densified, with a date of diagnosis, using predefined validated algorithms (as possible), based on diagnosis codes (with procedure and/or pharmacy dispensing codes and/or limited to specific medical care settings if applicable to the outcome).

Data will be collected on the following AESIs using claims algorithms within disease-specific risk interval periods following the administration of Ad26.COV2.S or BNT162b2:

Nervous system: encephalitis (including acute demyelinating encephalomyelopathy and meningoencephalitis), Guillain-Barré Syndrome, transverse myelitis, Bell's palsy, Multiple sclerosis (including optic neuritis), sensorineural hearing loss, generalized convulsions (with and without epilepsy)

Immune system: autoimmune thyroiditis, immune thrombocytopenia, thrombocytopenia, Type 1 diabetes mellitus, broad arthritis, and anaphylaxis)

Cardiac system: myocarditis/pericarditis, microangiopathy, heart failure, stress cardiomyopathy, acute myocardial infarction, coronary artery disease(including acute myocardial infarction),arrhythmia

Blood and lymphatic system disorders: (Deep vein thrombosis (DVT), pulmonary embolism (PE), disseminated intravascular coagulation, non-hemorrhagic stroke, hemorrhagic stroke, composite outcome of venous thrombosis (including PE and DVT), composite outcome of arterial thrombosis (including coronary artery disease and non-hemorrhagic stroke), composite outcome of stroke (including non-hemorrhagic and hemorrhagic strokes), cerebral venous sinus thrombosis, peripheral thrombosis, and co-occurring thrombosis with thrombocytopenia,

Renal system: acute kidney failure

Hepatic system: acute hepatic failure

Data analysis plan

For the SCRI design in the Ad26.COV2.S exposed cohort, incidence rates (IRs) of each AESI during the risk period will be compared with the IRs in exposed cohort during the control period using a conditional Poisson regression model to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs).

For the cohort design comparisons of Ad26.COV2.S vaccinees versus BNT162b2 vaccinees, matching on propensity score (PS) and calendar time (within 2 weeks) will be implemented to ensure comparability between the 2 exposure groups on observed covariates. Baseline covariates including demographic characteristics, comorbidities, indicator of frailty and other factors will be used to fit the PS model.

The propensity to be vaccinated with Ad26.COV2.S will be estimated using logistic regression with vaccination received as the dependent variable and all baseline covariates as independent variables. Individuals receiving BNT162b2 will be matched on PSs to individuals receiving Ad26.COV2.S.

For continuous/ordinal variables the number of observations, mean, standard deviation, minimum, and maximum will be described. For categorical variables, the number and percent per category will be summarized. Balance of characteristics between the exposure groups will be evaluated with absolute standardized differences.

For the cohort design, IRs for each AESI will be calculated by dividing the number of events by the follow-up person-time in PS-matched exposure cohorts, and cumulative incidence curves will be estimated by exposure group. IRRs and 95% CIs will be estimated with Poisson regression models or another appropriate method to be specified in the SAP. The risk difference will be computed as the difference between the IR in the Ad26.COV2.S-exposed cohort and the IR in the active comparator, BNT162b2 exposed, cohort. IRRs will be

pooled across data sources using a random-effects model or another appropriate method to be specified in the SAP.

Documents

Study results

24Aug2025-REDACTED_CSR-Synopsis-VAC31518COV4001-1676801_1693237.pdf (290.14 KB)

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

CVS Health Clinical Trial Services United States

HealthCore United States

Humana United States

Optum United States

Data sources (types)

Administrative healthcare records (e.g., claims)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

Sentinel

CDM website

https://www.sentinelinitiative.org/methods-Data-tools/sentinel-common-Data-model

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes