Rapid Safety Assessment of SARS-CoV-2 vaccines in EU Member States using electronic health care datasources (CVM Covid19-Vaccine-Monitor-EHR)

First published: 16/08/2021
Last updated: 01/07/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/50433

EU PAS number
EUPAS42467

Study ID
50433

DARWIN EU® study
No

Study countries
Belgium
Italy
Netherlands
Norway
Spain
United Kingdom

Study description
Readiness The readiness phase will include the following objectives: • To provide an overview of the methods for identification of COVID-19 vaccine exposure in the data

sources • To monitor the number of individuals exposed to any COVID-19 vaccine and to compare this to COVID-19 vaccine exposure data • To quantitatively evaluate different algorithms to identify adverse events by provenance in electronic health care data • To conduct time-to-onset analyses for the AESI with respect to time since vaccination • To assess the association between and the vaccines of interest and negative control events using the SCRI to estimate systematic bias (unmeasured confounding) • To test the impact of different comparators in the cohort design, using the negative control outcomes • To generate information for testing of methodological questions around misclassification of events/exposure Rapid assessment studies Primary objective The primary objective for this rapid assessment study is to assess the potential association between the occurrence of specific AESIs and vaccination with COVID-19 vaccines within disease-specific risk periods in individuals exposed to the COVID-19 vaccines compared to other COVID-19 vaccine exposed individuals or compared to a control window within the same individual. Secondary objectives The secondary objectives for the rapid assessments studies are: • To assess the potential association between the occurrence of specific AESIs and vaccination with COVID-19 vaccines in the following subgroups o immunocompromised persons o persons with the presence of co-morbidities elevating the risk of serious COVID-19 o persons with a history of diagnosed COVID-19 disease o pregnant women o age groups o patients with a prior history (ever) of that event more than a year before. Study design: A retrospective, multi-database, self-controlled risk interval or cohort study

Study status
Finalised

Research institution and networks

Institutions

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

Pharmacoepidemiology Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010
Last updated
18/06/2012

Institution

Educational Institution

ENCePP partner

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands
First published: 01/03/2010
Last updated
23/05/2024

Institution

Educational Institution

ENCePP partner

Department of Epidemiology of the Regional Health Service - Lazio

Italy
First published: 23/03/2010
Last updated
22/06/2018

Institution

EU Institution/Body/Agency

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

Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina

Italy
First published: 29/11/2021
Last updated 01/12/2021

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 10/01/2022

Institution | Laboratory/Research/Testing 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 19/02/2024

Institution | Not-for-profit | 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

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain
First published: 01/02/2024
Last updated
01/07/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority

FISABIO Spain, University Oslo Norway

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

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

Netherlands
First published: 01/02/2024
Last updated 23/05/2024

Network

Contact details

Study institution contact
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Primary lead investigator
Miriam Sturkenboom
Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
06/04/2021
Actual:
06/04/2021

Study start date
Planned:
31/08/2021
Actual:
31/08/2021

Date of final study report
Planned:
08/05/2023
Actual:
08/05/2023

Sources of funding

- EMA

Study protocol

CVM_WP3_Protocol_v2.2_20210825.pdf(1.41 MB)

CVM_WP4_Protocol_v2.1_20210825.pdf(792.38 KB)

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:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness
Drug utilisation

Data collection methods:
Secondary data collection

Main study objective:

The objective of the COVID-Vaccine Monitor study is to rapidly assess signals of potential safety concerns emerging from active surveillance and identified by PRAC.

Study Design

Non-interventional study design
Cohort
Other

Non-interventional study design, other
Retrospective, multi-database, self-controlled risk interval study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(J07BX03) covid-19 vaccines

Medical condition to be studied
Guillain-Barre syndrome

Additional medical condition(s)
All COVID-19 AESI

Population studied

Short description of the study population
The study involved three cohorts: readiness, rapid assessment, and methodological assessment. Readiness cohort included subjects in the source population who were in follow-up for at least 365 days or were born during the study period. Rapid assessment cohort included subjects with the outcome of interest and a COVID-19 vaccination, while methodological assessment cohort included vaccinated subjects and different matched comparisons.
Inclusion Criteria:
Readiness study:
For the readiness study, the person will be included if there is at least one day of follow-up and the person has at least 12 months of data in the data source at the start of follow-up.
SCRI Design:
For analyses of outcomes assessed with the SCRI design, the following criteria must be met. Note that the study population for each outcome-specific analysis will thus be different.
• Received a dose of COVID-19 vaccine during the study period.

• Have experienced a specific event of interest during the predefined observation period.
• Have at least 12 months of data/registration in the data sources at study entry.
Cohort design:
Individuals must meet all the following inclusion criteria to be eligible for inclusion in the cohort study:
• At time zero, being in the underlying population of the data source for at least 12 months; or, being born in the previous 12 months in the underlying population.
• Study participants must be eligible (eg, lack of contra-indications) to receive the COVID-19 vaccines at time zero.
Exclusion Criteria:
For the readiness study, there will be no exclusion criteria.
Individuals will be excluded from the rapid assessment studies if:
• They have a recorded diagnosis for the specific event in the one year prior to cohort /SCRI entry. Persons with such acute diagnoses more than a year ago will be maintained to allow for subgroup analyses. Upon investigation of one event, we do not exclude any history or prevalence of other groups of events (AESIs).
• They have a contra-indicati

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)

Estimated number of subjects
59000000

Study design details

Data analysis plan
Risk estimation: IRR

Documents

Study results
D4.2_CVM_ExecutiveSummary_WP3-4_20230714.pdf(512.3 KB)
D4.2_CVM_FinalReport_WP3-4_14082023_ExSumm.pdf(589.48 KB)

Study, other information
FollowUp_version_CVM_WP3_Protocol_v2.1.pdf(1.3 MB)

Study publications
Bots SH, Riera-Arnau J, Belitser SV, Messina D, Aragón M, Alsina E, Douglas IJ,…
Durán, Carlos E., Messina, Davide, Gini, Rosa, Riefolo, Fabio, Aragón, María, B…

Data management

Data sources

Data source(s)
Clinical Practice Research Datalink
The Information System for Research in Primary Care (SIDIAP)
Caserta claims database
ARS Toscana
Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)
PHARMO Data Network

Data source(s), other
ARS Toscana (Agenzia Regionale di Sanità della Toscana), Pedianet (Societa Servizi Informatici), Caserta local health database (INSPIRE srl), PHARMO Database Network (PHARMO Institute for Drug Outcomes Research), CPRD (Clinical Practice Research Datalink) & HES data (UK), SIDIAP (Sistema d'Informació per el Desenvolupament de la Investigació en Atenció Primària), BIFAP (Base de Datos para la Investigación Farmacoepidemiológica en Atención Primaria)

Data sources (types)
Administrative data (e.g. claims)
Disease registry
Drug dispensing/prescription data
Electronic healthcare records (EHR)

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