Natural history of coagulopathy and use of anti-thrombotic agents in COVID-19 patients and persons vaccinated against SARS-CoV-2

First published: 02/04/2021

Last updated: 02/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/45221

EU PAS number

EUPAS40414

Study ID

45221

DARWIN EU® study

No

Study countries

- [ ] France
- [ ] Germany
- [ ] Italy
- [ ] Netherlands
- [ ] Spain
- [ ] United Kingdom

Study description

Aim/s To estimate incidence rates of coagulopathy and thromboembolic events in the general population, in COVID-19 patients, and in recipients of COVID-19 vaccine/s Design We will perform a network cohort study using data mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model Population Cohorts: 1) General population, 2) Vaccinated against SARS-CoV-2 with a first dose, 3) Persons vaccinated against SARS-CoV-2 with a second dose, 4) Persons tested positive for SARS-CoV-2, 5) Persons tested positive for SARS-CoV-2 or with a clinical diagnosis of COVID-19, 6) Persons hospitalised with COVID-19, and 7) Persons requiring intensive services during a hospitalisation with COVID-19 Outcomes Venous thromboembolic events, arterial thromboembolic events, rare thrombotic and coagulopathy events, cardiovascular events, and mortality will be identified for all study populations. The occurrence of these events of interest will be identified at 7, 14, 21, and 28 days following vaccination against SARS-CoV-2, while the occurrence of venous thromboembolic and arterial thromboembolic events will be identified in the 30-, 60- and 90-days post-index date for COVID-19 patients. COVID-19 worsening will be defined as increasing care intensity (e.g. from outpatient to inpatient, from inpatient to receiving intensive care services) and/or mortality Data sources Primary care and hospital records from NL (IPCI), IT (IQVIA LPD Italy), FR (IQVIA LPD France), DE (IQVIA DA Germany), ES (SIDIAP and HM), and the UK (CPRD GOLD, CPRD AURUM, and linked HES) Analyses Background rates will be

estimated per 100,000 person-years for 2017-2019, at 7, 14, 21, and 28 days following vaccination against SARS-CoV-2, and 30, 60, and 90 days for COVID-19 patients. Rates will be stratified by socio-demographics and cohort. Post-vaccine/background rate ratios will be estimated adjusted for age and sex. Multi-state models will be fitted to study COVID-19 worsening

Study status

Finalised

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution **Educational Institution** **ENCePP partner**

Pharmacoepidemiology Research Group, Institute of Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-Universitaet Muenchen

Germany

First published: 23/04/2010

Last updated: 26/06/2014

Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

IQVIA

United Kingdom

First published: 12/11/2021

Last updated: 22/04/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

Daniel Prieto-Alhambra

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 12/11/2020

Actual: 12/11/2020

Study start date
Planned: 01/01/2017

Actual: 01/01/2017

Data analysis start date
Planned: 01/03/2021

Actual: 01/03/2021

Date of final study report
Planned: 30/09/2021

Actual: 15/10/2021

Sources of funding

- EMA

Study protocol

Coagulopathy protocol 20_04_clean.pdf(1.62 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:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Data collection methods:

Secondary use of data

Main study objective:

1-To estimate background rates of thrombo-embolic events (TEE) 2-To estimate rates of TEE in persons vaccinated against SARS-CoV-2 3-To estimate the incidence of TEE among COVID-19 patients 4-To study the risks of worsening of COVID-19 stratified by the occurrence of TEE 5-To study the risk factors for TEE in COVID-19 patients 6-To derive and externally validate prediction tools for TEE

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J07BX) Other viral vaccines

Other viral vaccines

Medical condition to be studied

SARS-CoV-2 test positive

COVID-19 immunisation

Population studied

Short description of the study population

People with a specific clinical diagnosis of COVID-19 or a positive PCR test against SARS-CoV-2 were included. People with <1 year of data visibility before index date were excluded.

The following study cohorts will be defined: 1) General population, 2) Persons vaccinated against SARS-CoV-2 with a first dose, 3) Persons vaccinated against SARS-CoV-2 with a second dose, 4) Persons tested positive for SARS-CoV-2, 5) Persons tested positive for SARS-CoV-2 or with a clinical diagnosis of COVID-19, 6) Persons hospitalised with COVID-19, and 7) Persons requiring intensive services during a hospitalisation with COVID-19.

Age groups

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

Other

Special population of interest, other

COVID-19 patients

Estimated number of subjects

6000000

Study design details

Outcomes

1.Venous thromboembolic events 2.Arterial thromboembolism 3.Rare thrombotic and coagulopathy events: disseminated intravascular coagulation, immune thrombocytopenia, thrombotic thrombocytopenia purpura, cerebral venous sinus thrombosis, and intracranial venous thrombosis 4.Other cardiovascular events 5.All-cause mortality

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Data analysis plan

Background rates will be estimated per 100,000 person-years, with individuals identified as of the 1st January in 2017, 2018, 2019, and 2020. We will estimate the incidence for all outcomes at 7, 14, 21, and 28 days following vaccination against SARS-CoV-2, and 30, 60, and 90 days for COVID-19 patients. Age-sex

adjusted incidence rate ratios for post-vaccine/background rates for all events will be estimated, stratified by age, sex, and data source. We will use a multistate model to summarise risks of worsening among COVID-19 patients stratified by those with and without thromboembolic events of interest. The impact of risk factors on risks of venous and arterial thromboembolic events among COVID-19 patients will be assessed using two approaches: 1) Cox models to estimate relative risks for pre-specified risk factors, 2) data-driven using Lasso regression and external validatio

Documents

Study results

EMAROC13_Final report.pdf(2.86 MB)

EMAROC13_report3_enceppupload.pdf(2.85 MB)

Study report

Progress_report_2_vaccinesTTS_enceppupload.pdf(1.4 MB)

Progress_report_BackgroundRates_enceppupload.pdf(980.05 KB)

Study, other information

Progress_report_BackgroundRates_enceppupload.pdf(980.05 KB)

Study publications

Burn E, Li X, Kostka K, Stewart HM, Reich C, Seager S, Duarte-Salles T, Fernand...

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other

CPRD, IPCI, SIDIAP, Longitudinal Prescription Data(LRx) -France

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Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Hospital and ambulatory electronic medical records

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