ASSOCIATION BETWEEN THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (TTS) OR THROMBOEMBOLIC EVENTS, AND COVID-19 VACCINES

First published: 29/11/2021

Last updated: 22/02/2024

Study Finalised

Administrative details

EU PAS number

EUPAS44469

Study ID

46886

DARWIN EU® study

No

Study countries

- ☐ France
- ☐ Germany
- ☐ Netherlands

☐ Spain

☐ United Kingdom

☐ United States

Study description

Aim/s: To quantify the association between the administration of a COVID-19 vaccine and the occurrence of TTS-1a/ thromboembolic events (TE)-2a. To quantify the comparative association of developing TTS-1b/TE-2b between the administration of different COVID-19 vaccine brands. 3) To study the association between potential risk factors and TTS/TE, 4) To characterize the treatments used in patients with TTS/TE. METHODS A multi-nation network cohort study with 8 databases across six countries. Propensity score (PS) matching cohort will be used to estimate the incidence rate of getting TTS/TE for Objective 1a-2b. Negative control outcomes will be also used to assess residual confounding. LASSO regression will be used to identify risk factors of post-vaccination TTS/TE (3). For each risk factors identified, another logistic regression will be used to estimate the size of risk and its multiplicative interaction effect with COVID-19 vaccine. Data visualisation tools will be used to describe the treatment pathways among medications in patients diagnosed with TTS/TE (4).

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

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: 23/05/2025

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

IQVIA

United Kingdom

First published: 12/11/2021

Last updated: 22/04/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Parc Salut Spain, IQVIA Germany, SIDIAP spain, EMC Netherlands, UniOxf UK

Networks

Pharmacoepidemiology Research Group

Contact details

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Primary lead investigator

Daniel Prieto-Alhambra

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 28/09/2021

Actual: 28/09/2021

Study start date

Planned: 01/12/2020

Actual: 01/12/2020

Date of final study report

Planned: 28/02/2022

Actual: 30/03/2022

Sources of funding

- EMA

Study protocol

TTSCOVID19 vaccine protocol V2.pdf(874.28 KB)

fullProtocol.pdf(874.28 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:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

1) To study the association between COVID-19 vaccine and thrombosis with thrombocytopenia syndrome/s (TTS) and thromboembolic events (VTE) 2) To quantify the association betweendifferent COVID-19 vaccine brands and the occurrence of TTS /VTE 3) To study the association between pre-specified risk factors and the occurrence of VTE/TTS 4) To characterize treatments used after post-vaccine VTE/TTS

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

Thrombosis with thrombocytopenia syndrome

Venous thrombosis

Population studied

Short description of the study population

All adult persons (aged >=18 at the index date) registered in any of the contributing databases within the study period and with at least one year of database history before the index date will be included in the target population.

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)

Estimated number of subjects

80000000

Study design details

Outcomes

VTE thrombosis with thrombocytopenia syndrome

Data analysis plan

characters The study period will cover from Dec 2020 (first vaccine users) until the latest data release available in each of the contributing databases. For objective 1a-2b, we will use propensity-score-matching to select comparable people in each two cohorts. We will report incidence rates of TTS or TE in the 14, 21 and 28 days following the index date in each PS matched cohort. Incidence Rate ratio (IRR) will be used to quantify the risk of developing TTS (Objective 1) or TE (Objective 2) via Poisson models. RRs will be stratified by 10-year age bands, sex, and vaccine type/brand (only for Objective 1a and 2a). Logistic regression will be used to identify risk factors associated with TTS/VTE/ATE among people vaccinated against SARS-CoV-2.

Documents

Study results

Obj1and2_Report_approved.pdf(4.11 MB)

Study report

Obj3and4_Report_approved.pdf(3.85 MB)

Study publications

Junqing Xie, Albert Prats-Uribe, Maria Gordillo Maranon, Victoria Y. Strauss, ...

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)

Clinical Practice Research Datalink

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other

OpenClaims United States, Hospital CDM United States, Parc Salut Mar Spain, RCGP RSC United Kingdom

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Data sources (types)

Administrative healthcare records (e.g., claims)

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