Hydroxychloroquine safety and potential efficacy as an antiviral prophylaxis in light of potential wide-spread use in COVID-19: a multinational, large-scale network cohort and self-controlled case series study

First published: 03/04/2020

Last updated: 30/01/2025

Study Finalised

Administrative details

EU PAS number

EUPAS34497

Study ID

36203

DARWIN EU® study

No

Study countries

Germany

Japan

Netherlands

Spain

United Kingdom

United States

Study description

The overarching objective is to investigate safety and potential efficacy as an antiviral prophylaxis in light of potential wide-spread use in COVID-19

Study status

Finalised

Research institutions and networks

Institutions

National Perinatal Epidemiology Unit (NPEU), University of Oxford

United Kingdom

First published: 15/03/2010

Last updated: 19/03/2010

Institution | Outdated | Educational Institution | ENCePP partner

IQVIA

United Kingdom

First published: 12/11/2021

Last updated: 22/04/2024

Institution | Non-Pharmaceutical company | 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

Columbia University US, Erasmus MC Netherlands, SIDIAP Spain, UCLA US, Janssen Research and Development UK

Networks

Observational Health Data Sciences and Informatics (OHDSI) Network

First published: 01/02/2024

Last updated: 01/02/2024

Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Daniel Prieto-Alhambra

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 22/11/2018

Actual: 22/11/2018

Study start date

Planned: 01/09/2000

Actual: 01/09/2000

Data analysis start date
Planned: 01/03/2020

Actual: 01/03/2020

Date of interim report, if expected
Planned: 14/04/2020

Date of final study report
Planned: 30/05/2020

Actual: 30/05/2020

Sources of funding

- EU institutional research programme

More details on funding

IMI2 - EHDEN

Study protocol

PLE_HCQ_Protocol.pdf (764.57 KB)

PLE_HCQ_Protocol_1.6.pdf (849.78 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To study the safety of hydroxychloroquine and the combination of hydroxychloroquine + azithromycin in terms of severe adverse outcomes. Secondly, to study the association between the use of these medicines and the risk of viral infection/s and pneumonia.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Self-controlled case series

Study drug and medical condition

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

HYDROXYCHLOROQUINE

SULFASALAZINE

AZITHROMYCIN

AMOXICILLIN

Medical condition to be studied

Rheumatoid arthritis

Additional medical condition(s)

Coronavirus

Population studied

Short description of the study population

Participants will be identified using pre-specified concept sets reviewed by a core team of clinicians, epidemiologists, vocabulary experts, and health data scientists with extensive expertise in the use of the OMOP CDM and the OHDSI tools.

New user exposure cohorts

Exposure cohorts will be defined where treatment initiation is the index event and includes the following criteria:

• History of RA: Have a condition occurrence or observation indicating RA any time before or on the same day as the index event

• Be aged 18 years or over at index event

• Have at least 365 days of continuous observation time prior to index event.

SCCS exposure cohorts

Additional exposure populations, regardless of indication, will be included for the SCCS. For each exposure population, all prevalent users of HCQ will be included and periods of inferred persistent exposure by allowing up to 90 day gaps between dispensing/prescription records will be constructed. Individual SCCS analyses will therefore be executed separately for each of the proposed study outcomes, including both safety events and negative control outcomes.

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

Immunocompromised

Estimated number of subjects

800000

Study design details

Data analysis plan

All analyses are conducted using an international distributed data network with shared analytical tools. For the comparative cohort analyses, propensity score stratification and calibration using negative control outcomes will be used to minimise observed and unobserved confounding respectively. Cox regression models were fitted to estimate Hazard Ratios according to drug exposure. Secondly, self-controlled case series analyses were used, where Incidence Rate Ratios for on vs off-treatment risk of each of the outcomes is estimated using a modified Poisson regression model, adjusted for age and seasonality.

Documents

Study publications

Lane JC, Weaver J, Kostka K, Duarte-Salles T, Abrahao MT, Alghoul H, Alser O, A...

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.

Signed checklist for study protocols

ENCePPChecklistforStudyProtocols_HCQ.pdf (243.64 KB)

Data sources

Data source(s)

THIN® (The Health Improvement Network®)

Clinical Practice Research Datalink

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

Disease Analyzer - OMOP

US Open Claims

AU EMR Data - OMOP

IQVIA Longitudinal Patient Data - Belgium

Data source(s), other

Optum United States, PanTher United States, CCAE United States, MDCR, MDCD, JMDC

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