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: 02/04/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/36203

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 institution and networks

Institutions

National Perinatal Epidemiology Unit (NPEU), University of Oxford

United Kingdom
First published: 15/03/2010
Last updated
19/03/2010
Institution
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
23/02/2024
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 data collection

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

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
IPCI
The Information System for Research in Primary Care (SIDIAP)
Disease Analyzer - OMOP
US Open Claims
AU EMR Data - OMOP
Longitudinal Patient Data - Belgium

Data source(s), other
Optum United States, PanTher United States, CCAE United States, MDCR, MDCD, JMDC

Data sources (types)
Administrative data (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