Association of angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) on coronavirus disease (COVID-19) incidence and complications

First published: 14/05/2020

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Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/35854

EU PAS number

EUPAS35296

Study ID

35854

DARWIN EU® study

No

Study countries

- ☐ Korea, Republic of
- ☐ Spain
- ☐ United Kingdom
- ☐ United States

Study description

This study will evaluate the effect of ACE inhibitor or ARB exposure on the risk of contracting COVID-19 infection and the risk of experiencing respiratory failure, pneumonia, acute kidney injury, and death in hypertensive patients following contracting COVID-19 infection. The analysis will be undertaken across a federated multi-national network of electronic health records and administrative claims from primary care and secondary care that have been mapped to the Observational Medical Outcomes Partnership Common Data Model in collaboration with the Observational Health Data Sciences and Informatics (OHDSI) and European Health Data and Evidence Network (EHDEN) initiatives.

Study status

Finalised

Research institutions and networks

Institutions

UCL School of Pharmacy, University College London

☐ United Kingdom

First published: 11/03/2010

Last updated: 21/04/2015

Institution | Educational Institution | ENCePP partner

University of Dundee

United Kingdom

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Educational Institution

Ajou University South Korea, Columbia University US, Erasmus University Medical Centre The Netherlands, Janssen Research and Development US, UCLA US, University of Dundee UK, University of Oxford UK, University of South Australia Australia

Contact details

Study institution contact

Daniel Morales

Study contact

d.r.z.morales@dundee.ac.uk

Primary lead investigator

Marc Suchard

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 02/03/2020

Actual: 02/03/2020

Study start date

Planned: 26/03/2020

Actual: 26/03/2020

Data analysis start date

Planned: 07/04/2020

Actual: 07/04/2020

Date of final study report

Planned: 26/05/2020

Actual: 16/06/2020

Sources of funding

- EU institutional research programme

More details on funding

EHDEN

Study protocol

COVID19_ACE_ARB_Protocol_Version_1_0 (1).pdf(3.9 MB)

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:

Disease /health condition

Human medicinal product

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:

To measure the risk of COVID-19 susceptibility and severity in patients exposure to ACE inhibitors and ARBs compared to patient exposed to other antihypertensive agents.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C09) AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

Medical condition to be studied

COVID-19

Population studied

Short description of the study population

Hypothesis 1, the cohort will consist of adult patients aged 18 years and over who receive at least one eligible prescription for an exposure drug between 1st November 2019 and 31st January 2020 (with index date set as the last prescription in this window) and are observable in each database for at least one year prior to the index date. Patients are required to have a history of hypertension at any point prior to or including the index date and to be prescribed antihypertensive treatment recommended for first line or initial pharmacological treatment of hypertension at the index date as either monotherapy in one analysis or in combination with other hypertensive treatments that do overlap with the comparison cohort in a second analysis. Cohort exit will be the earliest of: the occurrence of an outcome event; the end of exposure; death; loss or deregistration from the database; or date of last data collection.

Hypothesis 2,We will identify adult patients aged 18 years or over who have an incident diagnosis of COVID19 occurring after 1st December 2019 and assign the date of diagnosis as the index date. Patients will be required to be registered or observable in each database for at least 180 days prior to index date, have a history of hypertension at any point prior to the index date and be a prevalent user of antihypertensive treatment recommended for first line treatment of hypertension as monotherapy at the index date. The end of follow-up will be the earliest occurrence of either: the outcome event, discharge, date of last data collection, end of follow-up (30 days) or death.

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

100000

Study design details

Outcomes

COVID-19 susceptibility and severity, Major acute cardiovascular events (MACE)

Data analysis plan

We will use a prevalent user cohort design to estimate the relative risk of each outcome associated with monotherapy only and monotherapy or combo-therapy comparisons among patients prescribed ACE inhibitors and ARBs compared to patients with diuretics and calcium channel blockers. We will measure the risk of incident COVID-19 diagnosis and also outcomes following hospitalization with COVID-19. Data driven approaches will be used to identify potential covariates for inclusion in matched or stratified propensity score models identified using regularized logistic regression that allow balancing on a large number of baseline potential confounders. Cox regression analysis will be used to calculate hazard ratios. In addition negative control outcomes will allow for evaluating residual bias in the study design.

Documents

Study publications

Morales DR, Conover MM, You SC, Pratt N, Kostka K, Duarte-Salles T, Fernández-B…

Data management

Data sources

Data source(s), other

South Korea: Health Insurance and Review Assessment (HIRA), Columbia University Irving Medical Center

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

Unknown