Comparative Effectiveness and Safety of Angiotensin-Converting Enzyme Inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) in Older Adults with Type 2 Diabetes

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Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/44900

EU PAS number
EUPAS44899

Study ID
44900

DARWIN EU® study
No

Study countries
United States

Study description
Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are widely used blood pressure lowering drugs which work by inhibiting the renin-angiotensin system. There are several head-to-head trials assessing the relative effectiveness of these two drug classes. However, the available evidence is limited by small sample size and real-world evidence is conflicting. Therefore, it is necessary to perform a high-quality real-world study to assess the comparative effectiveness of ACEIs to ARBs. More than one-third of the adults with diabetes are currently aged 65 years or older

and both ACEIs and ARBs are recommended as first line therapy in type 2 diabetes with hypertension. Thus, to reduce bias and achieve better baseline comparability in real-world study, we propose to assess the comparative effectiveness of ACEIs to ARBs in older adults with type 2 diabetes. We aim to 1) estimate absolute and relative rate and risk of in cardiovascular outcomes and all-cause mortality in Medicare beneficiaries with type 2 diabetes (T2D) initiating ACEIs or ARBs. 2) identify subgroups of Medicare beneficiaries with T2D that are more likely to benefit from ACEI's or ARBs to prevent cardiovascular outcomes and all-cause mortality using machine learning-based heterogeneous treatment effect analysis. We will conduct active-comparator, new-user cohort using a 20% random sample of Medicare data including patients with ?1 prescription dispensing claim for ACEI or ARB between January 01, 2007, and December 30, 2019. We will assess the following outcome: (i) hospitalization of Heart failure (HHF) (ii)composite endpoint of inpatient myocardial infarction (MI), inpatient stroke or all-cause mortality (Major Cardiovascular Events, MACE outcome) (iii) the composite of MACE plus HHF. (iv) All-cause mortality. (v) end stage renal disease and dialysis.

Study status
Finalised

Research institution and networks

Institutions

University of North Carolina at Chapel Hill
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Institution

Contact details

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Study timelines

Date when funding contract was signed
Planned:
01/08/2017
Actual:
01/08/2017

Study start date
Planned:
29/12/2021
Actual:
29/12/2021

Date of final study report
Planned:
29/12/2021
Actual:
29/12/2021

Sources of funding

- Other

More details on funding

National Institute on Aging at NIH

Study protocol

ACEI v ARB_RWE protocol_30DEC2021.pdf(594.66 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:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Drug utilisation
Effectiveness study (incl. comparative)
Safety study (incl. comparative)

Data collection methods:
Secondary data collection

Main study objective:
1. To estimate absolute and relative rate and risk of in cardiovascular outcomes and all-cause mortality in Medicare beneficiaries with type 2 diabetes (T2D) initiating ACEIs or ARBs. 2. To identify subgroups of Medicare beneficiaries with T2D that are more likely to benefit from ACEI’s or ARBs to prevent cardiovascular outcomes and all-cause mortality using machine learning-based analysis.

Study Design

Non-interventional study design
Cohort
Other

Non-interventional study design, other
Active-comparator, new-user (ACNU) design

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(C09AA) ACE inhibitors, plain
(C09CA) Angiotensin II receptor blockers (ARBs), plain

Medical condition to be studied
Type 2 diabetes mellitus

Population studied

Short description of the study population
1. Medicare FFS enrollees ?65 years of age with T2D having continuous coverage in fee-for-service Medicare plans A (inpatient services), B (physician and outpatient services) and D (prescription drugs)
2. The base population for the analysis will consist of all beneficiaries with ?1 prescription dispensing claim for ACEI or ARB between January 01, 2007, and December 30, 2019.
We will exclude the following patients:
1) To ensure new use of either ACEIs or ARBs, we will exclude all individuals who do not have at least 12 months of continuous enrollment (inpatient, outpatient, and prescription coverage) in the appropriate insurance database prior to the first prescription dispensing claim (12-month baseline period), during which no use of any of the study drug classes compared is detected.

Age groups
Adults (65 to < 75 years)
Adults (75 to < 85 years)
Adults (85 years and over)

Special population of interest
Hepatic impaired
Immunocompromised
Other
Renal impaired

Special population of interest, other
Type 2 diabetes mellitus patients

Estimated number of subjects
100000

Study design details

Outcomes
The primary outcomes are (i) Hospitalization of Heart failure (HHF) (ii) composite endpoint of inpatient myocardial infarction (MI), inpatient stroke or all-cause mortality (Major Cardiovascular Events, MACE outcome) (iii) the composite of MACE plus HHF. (iv) All-cause mortality (v) end stage renal disease or dialysis, Secondary outcomes include individual components of the MACE outcome (non-fatal MI, stroke, and HHF), and MACE plus invasive cardiac procedures (stents, revascularization, bypass surgery).

Data analysis plan
We will estimate 2-year risks of outcomes of interest, risk differences (RD) and ratios (RR) for ACEIs vs. ARBs after weighting by IPTW and IPCW. Confidence intervals will be derived from 2.5th and 97.5th percentiles of estimates from 500 bootstrap resamples of the

study population (random resampling with replacement). When estimating risks of cardiovascular outcomes in older Medicare patients, censoring those who died prior to having the outcome of interest, as commonly done in survival analyses, could bias the risks. To avoid this, we will use Aalen Johansen (AJ) estimators to estimate risks.

Data management

Data sources

Data source(s), other
Medicare Fee-for-Service (FFS) Database

Data sources (types)
Administrative data (e.g. claims)

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