Comparative cardiovascular and renal effectiveness and safety of Empagliflozin and other SGLT2i in patients with type 2 diabetes (T2D), with and without baseline kidney disease in the United States

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Study Ongoing

Administrative details

EU PAS number

EUPAS45682

Study ID

50338

DARWIN EU® study

No

Study countries

United States

Study description

While clear renal and cardiovascular benefits of empagliflozin have been demonstrated in randomized clinical trials, the effectiveness of this therapy in direct comparison to other anti-hyperglycemic therapies has not been shown among patients with diabetic kidney disease. We aim to use PCORnet, which is a large, national network of electronic health record data, to determine the following in a real-world population: 1. Characteristics of patients with T2D, both with and without DKD, who have been initiated on empagliflozin vs. those who have been initiated on dipeptidyl peptidate-4 inhibitor (DPP4i) or glucagon-like peptide-1 receptor agonists (GLP1RA) 2. Renal and CV effectiveness of empagliflozin compared with DPP4i and GLP1RA in these same populations, evaluated up to 24 months after treatment initiation. 3. Safety of empagliflozin compared with DPP4i and GLP1RA in these same populations, evaluated up to 24 months after treatment initiation. This is a non-interventional study using existing data from 20 US health systems participating in PCORnet. The study period will be Jan 2014 Dec 2021. The primary comparisons will be incident prescription of empagliflozin or any SGLT2 inhibitor without prior use of any sodium-glucose cotransporter-2 inhibitors or (SGLT2i) or DPP4i compared to incident prescription of any DPP4i without prior use of any DPP4i or any SGLT2i. If feasible based on patient numbers, comparisons between empagliflozin/any SGLT2i and GLP-1 RAs will also be made. The primary outcome will be a composite renal outcome including 40% decline in glomerular filtration rate, incident end stage renal disease, or all-cause mortality (ACM). Secondary outcome is a composite of hospitalization for heart failure and ACM. The primary analysis will be performed using overlap weighting to balance covariates across the two treatment arms (empagliflozin vs DPP4i) and Cox proportional hazards modelling to determine the effect of drug on outcomes.

Study status

Ongoing

Research institutions and networks

Institutions

Duke Clinical Research Institute (DCRI)

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Institution

Contact details

Study institution contact

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Primary lead investigator

Neha Pagidipati

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 08/04/2021

Study start date

Planned: 13/08/2022

Actual: 08/09/2022

Data analysis start date
Planned: 22/08/2022

Date of interim report, if expected
Planned: 30/09/2022

Date of final study report
Planned: 31/03/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim

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 type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Main study objective:

The primary purpose of this research study is to determine the cardiovascular and renal effectiveness and safety associated with initiation of empagliflozin compared to initiation of DPP4i in patients with type 2 diabetes mellitus in the • Overall patient cohort, • Patients with established diabetic kidney disease, and • Patients without established diabetic kidney disease.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Comparative effectiveness

Study drug and medical condition

Medicinal product name

JARDIANCE

Medical condition to be studied

Diabetes mellitus

Diabetic nephropathy

End stage renal disease

Cardiac death

Myocardial infarction

Acute kidney injury

Hypovolaemia

Urinary tract infection

Diabetic ketoacidosis

Additional medical condition(s)

stroke, coronary revascularization, genital mycotic infections

Population studied

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

Renal impaired

Estimated number of subjects

30400

Study design details

Outcomes

A composite outcome including 40% decline in estimated glomerular filtration rate(eGFR), incident end-stage kidney disease, or all-cause mortality. 40% decline in eGFR End-stage kidney disease Dialysis Kidney transplant Composite hospitalization for heart failure (HHF) or all-cause mortality (ACM) HHF ACM Composite: myocardial infarction, stroke, ACM or coronary revascularization procedure Diabetic ketoacidosis Severe hypoglycemia Urinary tract cancer Severe urinary tract infections Acute kidney injury Genital mycotic infections

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Data analysis plan

Propensity score modeling with post-LASSO overlap weighting will be used to generate matched patient pairs across treatment groups. The effect of empagliflozin compared to DPP4i on outcomes will be assessed using Cox proportional hazards models in a 2-arm comparison. Incidence rates will be computed as the number of first events per 100 patient years of follow-up. Analyses of time to first event will be performed using Cox proportional hazards models. Outcomes where death is a competing risk will be analyzed using cause-specific proportional hazards models, achieved by censoring follow-up at the time of death. All analyses will be adjusted for covariates that continue to be unbalanced after reweighting, with any additional covariates of medical interest identified by the clinicians. Hazard ratios comparing empagliflozin to DPP4i with 95% confidence intervals and the adjusted p-value will be presented for all outcomes.

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), other

PCORnet United States

Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

This study will utilize several types of data from inpatient and outpatient healthcare encounters from electronic medical records from approximately 20 health systems in the US with data mapped to the PCORnet Common Data Model. Data types will include renal laboratory data, prescription data, and relevant medical diagnoses.

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