Comparison of Canagliflozin vs. Alternative Antihyperglycemic Treatments on Risk of Below Knee Lower Extremity Amputation for Patients with Type 2 Diabetes Mellitus and the Subpopulation with Established Cardiovascular Disease

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Study Finalised

Administrative details

EU PAS number

EUPAS27670

Study ID

34314

DARWIN EU® study

No

Study countries

United States

Study status

Finalised

Research institutions and networks

Institutions

Johnson & Johnson

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Patrick Ryan

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 18/12/2018

Actual: 18/12/2018

Study start date
Planned: 09/01/2019

Actual: 09/01/2019

Date of final study report
Planned: 24/07/2019

Actual: 15/07/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Janssen Research & Development, LLC

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

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

Disease epidemiology

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The main objective of this study is to assess in healthcare databases whether Canagliflozin and other sodium-glucose co-transporter 2 inhibitors (SGLT2i) are associated with the risk of below-knee lower extremity (BKLE) amputation compared to non-SGLT2i antihyperglycemic agents (AHAs) and whether the risk of BKLE amputation is different between patients treated with Canagliflozin and other SGLT2i.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

INVOKANA

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

CANAGLIFLOZIN

Anatomical Therapeutic Chemical (ATC) code

(A10BK02) canagliflozin

canagliflozin

Medical condition to be studied

Amputation

Population studied

Short description of the study population

Patients who are new users of anti-hyperglycemic agent (AHA) of interest with at least 365 days of prior observation and a diagnosis of T2DM, but no diagnosis of type 1 DM (T1DM) or “secondary diabetes”, prior to the pre-specified AHA exposure.

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

Type 2 diabetes mellitus patients

Estimated number of subjects

714.582

Study design details

Outcomes

below-knee lower extremity (BKLE) amputation, lower extremity osteomyelitis, lower extremity ulcer, gangrene, peripheral occlusive disease

Data analysis plan

Crude incidence rates of BKLE amputation in each exposure cohort and pre-defined subgroups will be estimated. Baseline patient characteristics including risk factors for amputation will be summarized for those treated with target drugs versus comparator drugs. Cox proportional hazards model will be used to estimate Hazard Ratio (HR) for new user patients treated with target drugs versus comparator drugs. Exposure propensity-score (PS) will be estimated through large-scale regularized regression using all available data and used to control for confounding by imbalanced baseline covariates. Both PS matching and PS stratification will be used for adjustment. P-values in comparative analyses will be calibrated using negative control outcomes to address residual bias. Data source-specific HRs, 95% CIs, pre- and post- calibration p values will be generated for each comparison in each database. Meta-analytic estimates across 4 databases will be generated when there is sufficient homogeneity.

Documents

Study results

CSR Synopsis_RRA-21410_EUPAS27670.pdf (129.84 KB)

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 sources (types)

Administrative healthcare records (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