Large-scale evidence generation and evaluation across a network of databases for type 2 diabetes mellitus (LEGEND-T2DM)

First published: 07/10/2021

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Study Ongoing

Administrative details

EU PAS number

EUPAS43551

Study ID

44530

DARWIN EU® study

No

Study countries

Spain

United Kingdom (Northern Ireland)

United States

Study description

Therapeutic options for type 2 diabetes mellitus (T2DM) have expanded over the last decade with the emergence of sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP1) receptor agonists, which reduced the risk of major cardiovascular events in randomized controlled trials. Cardiovascular evidence for older second-line agents, such as sulfonylureas, and direct head-to-head comparisons, including with dipeptidyl peptidase 4 (DPP4) inhibitors, are lacking, leaving a critical gap in our understanding of the relative effects of T2DM agents on cardiovascular risk and on patient-centered safety outcomes. The Large-Scale Evidence Generations Across a Network of Databases for T2DM (LEGEND-T2DM) initiative is a series of systematic, large-scale, multinational, real-world comparative cardiovascular effectiveness and safety studies of all 4 major second-line anti-hyperglycemic agents including SGLT2 inhibitor, GLP1 receptor agonist, DPP4 inhibitor and sulfonylureas and leverages the Observational Health Data Science and Informatics (OHDSI) community that provides access to a global network of administrative claims and electronic health record (EHR) data sources. Across data sources, LEGEND-T2DM will identify all adult, T2DM patients who newly initiate a traditionally second-line T2DM agent, including individuals with and without established cardiovascular disease. Using an active comparator, new-user cohort design, LEGEND-T2DM will execute all pairwise class-vs-class and drug-vs-drug comparisons in each data source that meet a minimum patient count of 1,000 per arm and extensive study diagnostics that assess reliability and generalizability through cohort balance and equipoise to examine the relative risk of cardiovascular and safety outcomes. The primary cardiovascular outcomes include a 3-point and a 4-point composite of major adverse cardiovascular events, and series of safety outcomes.

Study status

Ongoing

Research institutions and networks

Institutions

University of California

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Networks

Observational Health Data Sciences and Informatics (OHDSI) Network

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Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Marc Suchard

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 01/10/2021

Study start date
Planned: 01/11/2021

Actual: 01/11/2021

Date of final study report
Planned: 01/11/2022

Sources of funding

- Other

More details on funding

US Department of Veterans Affairs, National Institutes of Health

Study protocol

Protocol_v1_0_0_EUPAS.pdf (448.23 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 type:

Non-interventional study

Scope of the study:

Drug utilisation

Effectiveness study (incl. comparative)

Main study objective:

To determine, through systematic evaluation, the comparative effectiveness and safety of traditionally second-line T2DM agents, SGLT2 inhibitors and GLP1 receptor agonists, with each other and with DPP4 inhibitors and sulfonylureas, for cardiovascular and safety outcomes.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A10) DRUGS USED IN DIABETES

DRUGS USED IN DIABETES

Medical condition to be studied

Type 2 diabetes mellitus

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

1.000.000

Study design details

Outcomes

3- and 4-point major cardiovascular events, Acute myocardial infarction, acute renal failure, glycemic control, hospitalization for heart failure, measured renal dysfunction, stroke, sudden cardiac death, and 22 other patient-centered safety outcomes

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Data analysis plan

LEGEND-T2DM will execute all pairwise class-vs-class and drug-vs-drug comparisons in each data source that meet a minimum patient count of 1,000 per arm and extensive study diagnostics that assess reliability and generalizability through cohort balance and equipoise to examine the relative risk of cardiovascular and safety outcomes. Our systematic framework will address residual confounding, publication bias and p-hacking using data-driven, large-scale propensity adjustment for measured confounding, a large set of negative control outcome experiments to address unmeasured and systematic bias, prespecification and full disclosure of hypotheses tested and their results. LEGEND-T2DM is dedicated to open science and transparency and will publicly share all our analytic code from reproducible cohort definitions through turn-key software, enabling other research groups to leverage our methods, data, and results in order to verify and extend our findings.

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)

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