Newer glucose-lowering agents versus thiazolidinediones on risk of incident cirrhosis and clinical decompensation events in patients with diabetes (Second-line GLDs and liver complications)

First published: 26/09/2019

Last updated: 08/11/2020

Study Finalised

Administrative details

EU PAS number

EUPAS31539

Study ID

37964

DARWIN EU® study

No

Study countries

United States

Study description

Aim 1) To estimate the effects of newer glucose-lowering agents versus TZD on risk of incident cirrhosis in patients with diabetes. Newer glucose-lowering agents to be examined are SGLT2 inhibitors and the incretin therapies, dipeptyl peptidase-4 (DPP4) inhibitors and GLP-1 receptor agonists. Aim 2) To estimate the effect of newer glucose-lowering agents (described above) versus TZD on risk of clinical decompensation events in patients with cirrhosis and diabetes.

Study status

Finalised

Research institutions and networks

Institutions

University of North Carolina at Chapel Hill

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Institution

Contact details

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Primary lead investigator

Jeff Yang

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 25/09/2019

Actual: 25/09/2019

Study start date

Planned: 25/09/2019

Actual: 25/09/2019

Data analysis start date

Planned: 25/09/2019

Actual: 25/09/2019

Date of final study report

Planned: 25/08/2020

Actual: 06/11/2020

Sources of funding

- Other

More details on funding

NIH T32 DK007634, Royster Society of Fellows

Study protocol

Study protocol_cirrhosis_decompensation_9-25_submitted.pdf (530.85 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:

Human medicinal product

Disease /health condition

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 estimate the effects of newer glucose-lowering agents versus TZD on risk of incident cirrhosis and incident decompensation events in patients with diabetes. Newer glucose-lowering agents to be examined are SGLT2 inhibitors and the incretin therapies, dipeptyl peptidase-4 (DPP4) inhibitors and GLP-1 receptor agonists.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A10BK) Sodium-glucose co-transporter 2 (SGLT2) inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

(A10BH) Dipeptidyl peptidase 4 (DPP-4) inhibitors

Dipeptidyl peptidase 4 (DPP-4) inhibitors

(A10BJ) Glucagon-like peptide-1 (GLP-1) analogues

Glucagon-like peptide-1 (GLP-1) analogues

(A10BG) Thiazolidinediones

Thiazolidinediones

Medical condition to be studied

Hepatic cirrhosis

Population studied

Short description of the study population

The eligible population will consist of MarketScan enrollees aged 18-64, and Medicare enrollees aged ≥ 65 with a diagnosis of type 2 diabetes and without a diagnosis of cirrhosis in the 12 months prior to drug initiation date (index date). We will include patients with and without underlying chronic liver disease, such as known hepatitis B/C infection, alcoholism and/or nonalcoholic fatty liver disease.

We will exclude the following patients:

1. Individuals without at least 12 months of continuous enrollment in MarketScan CCAE, or in Medicare Parts A, B and D prior to the first prescription dispensing claim.
2. Patients who have received any of the study drugs part of the pairwise comparison in the 12 months preceding the first prescription dispensing claim
3. Individuals with the following conditions in the 12-month period leading up to drug initiation:

- Previous diagnosis of cirrhosis
- Previous diagnosis of hepatocellular carcinoma or cholangiocarcinoma
- Prior hepatectomy or liver transplantation

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

Diabetes mellitus patients

Estimated number of subjects

500000

Study design details

Outcomes

For Aim 1, the primary outcome of interest is the first diagnosis of cirrhosis during follow-up. For Aim 2, the primary outcome of interest for this aim is any clinical decompensation event. Codes will be obtained from prior literature and clinical guidance.

Data analysis plan

We will compare the risk of primary outcomes using pairwise comparisons with the 4 study drug classes of interest. Our primary aim is to identify active comparator drug initiators that will allow us to estimate what would have happened to the index drug initiators if they had instead initiated the comparator drug. To achieve this goal, we will estimate the average treatment effect in the treated (ATT) by reweighting the comparator drug initiators by the propensity score odds (PS/(1-PS)). We will estimate and compare the cumulative incidence of the primary outcome for each study cohort using weighted Kaplan-Meier methods. Crude and adjusted hazard ratios (HRs) for both primary and secondary outcomes will be estimated using weighted Cox proportional hazards models, controlling for age, sex, as well as any potential confounders that remain unbalanced after propensity score implementation.

Documents

Study results

Yang et al, Newer second-line GLDs vs. TZDs on cirrhosis risk among older US adult patients with T2D, J Diab Complic 2020.pdf (988.45 KB)

Study publications

Yang JY, Moon AM, Kim H, Pate V, Barritt AS IV, Crowley MJ, Buse JB, Stürmer T,...

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