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)

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# Administrative details

EU PAS number	
EUPAS31539	
Study ID	
37964	
DARWIN EU® study	
-	
No	
Study countries	
□ United States	
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

#### Study institution contact

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Study contact

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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  $\geq$  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

# Unknown Check completeness Unknown

## **Check stability**

**Check conformance** 

Unknown

## **Check logical consistency**

Unknown

## Data characterisation

#### **Data characterisation conducted**

No