Dipeptidyl Peptidase-4 Inhibitors and Inflammatory Bowel Disease Risk: Impact of Study Design Differences on Comparative Safety Results

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Study Ongoing

Administrative details

EU PAS number

EUPAS108001

Study ID

108002

DARWIN EU® study

No

Study countries

- [ ] Switzerland
- [ ] United States

Study description

A recent cohort study using the British Clinical Practice Research Datalink (CPRD) database found that new use of dipeptidyl peptidase-4 inhibitors (DPP4i) was associated with an increased risk of inflammatory bowel disease (IBD) compared to other oral antidiabetic therapies (hazard ratio, HR 1.75, 95% CI: 1.22 to 2.49 during a median follow-up of 3.6 years). We implemented an active comparator, new user (ACNU) cohort design using US MarketScan and Medicare data and found that DPP4i did not increase IBD risk compared to therapeutic alternatives: pooled adjusted HRs (aHRs) for IBD were 0.87 (95% CI: 0.47-1.59) comparing to sulfonylureas (SU) and 0.76 (95% CI: 0.48 – 1.19) comparing to thiazolidinediones (TZD). We suspect that differences between results are primarily driven by different study designs. For example, our ACNU cohort included only patients who were treatment-naïve to both drugs at baseline, whereas Abrahami et al modeled DPP4i exposure as a time-varying variable (i.e. allowing the same patient to contribute both DPP4i unexposed and exposed person-time). To explore the impact and robustness of risk estimates to study design differences, this study will apply the ACNU design to CPRD data to assess the association between DPP4i use and IBD risk.

Study status

Ongoing

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

Til Stürmer

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/12/2020

Actual: 07/12/2020

Study start date

Planned: 07/12/2020

Actual: 01/12/2020

Data analysis start date

Planned: 01/09/2021

Actual: 01/09/2023

Date of final study report

Planned: 01/12/2024

Sources of funding

- Other

More details on funding

R01 AG056479 Propensity scores and preventive drug use in the elderly

Study protocol

DPP4i IBD protocol_CPRD_clean.pdf(773.64 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

Main study objective:

To evaluate the association between the initiation of DPP4i versus the initiation of clinically relevant second-line glucose lowering therapies (TZD and SU) and the short-term risk of IBD, based on an active comparator, new user study design.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A10BB) Sulfonylureas

Sulfonylureas

(A10BG) Thiazolidinediones

Thiazolidinediones

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

Dipeptidyl peptidase 4 (DPP-4) inhibitors

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

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

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)

Estimated number of subjects

100000

Study design details

Outcomes

We use the same outcome algorithm in the study by Abrahami et al 1 (Appendix 4), defined using Read codes. In this algorithm, IBD events qualify as a study outcome only if they were accompanied by at least one supporting event in the 6 months preceding or following the IBD code (Appendix 5). Secondary outcomes include Crohn’s disease (CD) and ulcerative colitis (UC), respectively.

Data analysis plan

We will assess this balance by looking at the crude distribution of CPRD data based covariates across treatment cohorts. We will then use propensity scores to remove remaining imbalances in measured potential confounders between study cohorts. Our primary aim is to identify active comparator drug initiators that will allow us to estimate what would have happened to the actual DPP4i initiators if they had, contrary to the fact, not initiated DPP4i. 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)), i.e. standardized mortality/morbidity ratio (SMR) weights 18. We will

estimate and compare the cumulative incidence of both primary and secondary outcomes 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.

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

Data sources (types)

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