Dipeptidyl Peptidase-4 Inhibitors and Risk of Inflammatory Bowel Disease among Patients with Type 2 Diabetes Mellitus

First published: 24/10/2018

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Study Ongoing

Administrative details

EU PAS number

EUPAS26245

Study ID

26246

DARWIN EU® study

No

Study countries

☐ United States

Study description

To evaluate the association between new use of dipeptidyl peptidase-4 inhibitor (DPP4i) and inflammatory bowel disease (IBD) risk, we will implement an active comparator, new user (ACNU) cohort design using MarketScan® Commercial Claims and Encounters Database (2007-2015) and 20% random sample of Medicare fee-for-service data (2007-2015). We will compare DPP4i with therapeutic alternatives, sulfonylureas (SU) and thiazolidinediones (TZD), respectively. The primary outcome is incident IBD, defined by IBD diagnosis (ICD-9-CM codes 555.x and 556.x) preceded by colonoscopy and biopsy within 30 days before diagnosis, and followed by IBD treatment within 30 days after diagnosis. We will start follow-up for the outcome 180 days after the second prescription (latency period) and exclude patients with the outcome within 180 days after their second prescription. Similarly, follow-up for IBD events will continue 180 days (the “carry-over” period) after treatment changes or discontinuation. Covariates include demographics, comorbidities (diabetes, pre-existing autoimmune, gastroenterological, and cardiovascular diseases), medications, and health care utilizations.We will perform propensity score and standardized mortality/morbidity ratio (SMR) weighting to control for measured baseline confounding, estimate adjusted hazard ratios (aHRs 95% CI) using weighted Cox proportional hazards models and pool aHRs across cohorts with the use of random-effects meta-analysis models. We will perform multiple sensitivity analyses to examine the robustness of our primary results, including changing latency and carry-over periods, initial treatment analysis, using modified outcome definitions, using a modified exclusion criteria, censoring patients received medications that could potentially induce or progress IBD during follow-up.

Study status

Ongoing

Research institutions and networks

Institutions

University of North Carolina at Chapel Hill

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Institution

Department of Epidemiology

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: 31/12/2018

Study start date
Planned: 01/08/2018

Actual: 22/08/2018

Date of final study report
Planned: 30/06/2019

Sources of funding

- Other

More details on funding

Unfunded

Study protocol

DPP4i_IBD protocol_ENCePP_22Oct18.pdf(449.34 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:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

To evaluate the association between the initiation of Dipeptidyl peptidase-4 inhibitors versus the initiation of clinically relevant second-line glucose lowering therapies (thiazolidinediones and sulfonylureas) and the short-term risk of inflammatory bowel disease, 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

Medical condition to be studied

Inflammatory bowel disease

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)

Estimated number of subjects

916285

Study design details

Outcomes

Primary outcome is incident inflammatory bowel disease (IBD), will be defined by the first IBD diagnosis (ICD-9-CM codes 555.x and 556.x), during follow-up which is preceded by a colonoscopy/sigmoidoscopy and biopsy within 30 days before diagnosis, and followed by a prescription claim for IBD medication treatment within 30 days after diagnosis. Chrohn's disease (CD) and ulcerative colitis (UC), respectively, which will be identified by the first diagnosis for CD or UC, respectively, with a colonoscopy/sigmoidoscopy and biopsy within 30 days before diagnosis and an inflammatory bowel disease treatment within 30 days after diagnosis.

Data analysis plan

We will assess this balance by looking at the crude distribution of claims data based covariates across treatment cohorts from ACNU design, will then use propensity scores and standardized mortality/morbidity ratio weighting to remove remaining imbalances in measured potential confounders between study cohorts. 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 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. If the estimates in MarketScan and Medicare are compatible (I2 >75%), we will perform a meta-analysis using random-effects models with inverse variance weighting and the DerSimonian and Laird method to pool both estimates from MarketScan and Medicare data.

Data management

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