

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

**First published:** 12/12/2023

**Last updated:** 27/03/2024

Study

Ongoing

## Administrative details

### EU PAS number

EUPAS108001

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### Study ID

108002

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### DARWIN EU® study

No

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### Study countries

 Switzerland

 United States

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## 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.

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## Study status

Ongoing

## Research institutions and networks

### Institutions

[University of North Carolina at Chapel Hill](#)

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## 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

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### Study start date

Planned: 07/12/2020

Actual: 01/12/2020

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### Data analysis start date

Planned: 01/09/2021

Actual: 01/09/2023

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### 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

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study type:**

Non-interventional study

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**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)
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## **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.

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## **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

### 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 source(s)

Clinical Practice Research Datalink

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### Data sources (types)

[Electronic healthcare records \(EHR\)](#)

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No