Risk of Inflammatory Bowel Disease in New Users of Dipeptidyl Peptidase-4 Inhibitors and New Users of Sodium Glucose Cotransporter-2 Inhibitors in the FDA Sentinel System

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Conflict of Interest and Acknowledgement Statements

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Some non-FDA co-authors on this abstract are employed at organizations which conduct work for government and private organizations, including pharmaceutical companies.
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Background

Previous studies reported inconsistent findings of the incidence of inflammatory bowel disease (IBD: Crohn's disease [CD], ulcerative colitis [UC], and indeterminate colitis) following exposure to antidiabetic agents including dipeptidyl peptidase-4 inhibitors (DPP-4i) and sodium glucose cotransporter-2 inhibitors (SGLT-2i).

Objectives

1) To describe characteristics of new users of DPP-4i and new users of SGLT-2i
2) To estimate the risk of incident IBD in a combined population of DPP-4i initiators and SGLT-2i initiators

Methods

Data Source: Claims data from six Data Partners of the U.S. FDA Sentinel System

Study Period: March 29, 2013 to December 31, 2022

Study Population: DPP-4i or SGLT-2i initiators with ≥2 dispensing records, ages ≥18 years who met all the following criteria in the year prior to the first dispensing of a study drug:

- Having ≥365 days of continuous insurance enrollment
- Presence of type 2 diabetes (T2D)
- Use of oral antidiabetic drugs
- Absence of evidence of type 1 diabetes (T1D), IBD, IBD treatment, diverticulitis, colitis, intestine or colon surgery, endoscopy
- No use of study drugs

Study Drugs Identification: National Drug Codes (NDCs) to identify the study drug exposure

Index Date: First dispending of a study drug

IBD Identification: Having an ICD-9 or ICD-10 diagnosis code, preceded by endoscopy and biopsy procedures *and* followed by IBD treatment[a]

Follow-up: Began on the index date and ended at the first occurrence of an IBD event, exposure to the other study drug, discontinuation of the cohort index drug, death, insurance disenrollment, or study end date

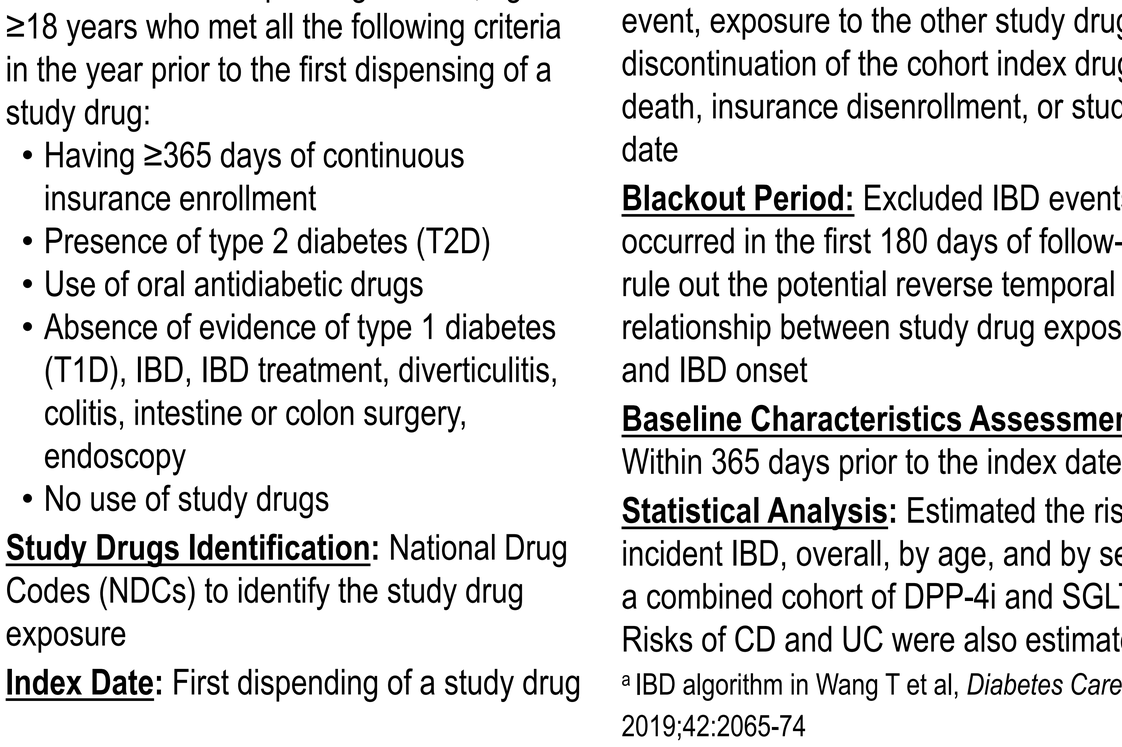
Blackout Period: Excluded IBD events that occurred in the first 180 days of follow-up to rule out the potential reverse temporal relationship between study drug exposure and IBD onset

Baseline Characteristics Assessment: Within 365 days prior to the index date

Statistical Analysis: Estimated the risk of incident IBD, overall, by age, and by sex, in a combined cohort of DPP-4i and SGLT-2i. Risks of CD and UC were also estimated

[a] IBD algorithm in Wang T et al, *Diabetes Care* 2019;42:2065-74

Figure 1. Flow Chart for Study Cohorts



Results

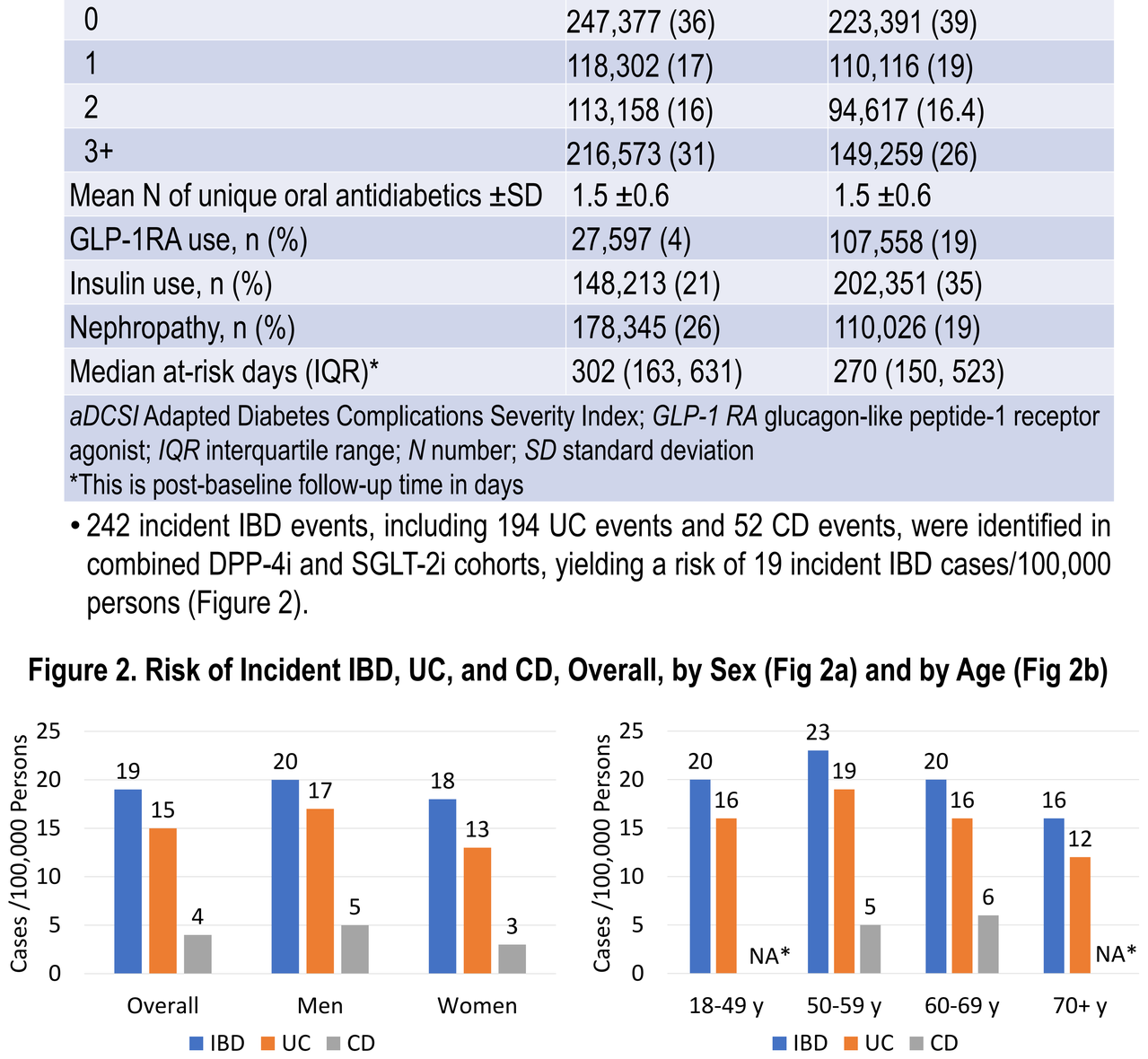
Table 1. Baseline Characteristics of Study Cohorts

Characteristics	DPP-4i (N=695,410)	SGLT-2i (N=577,383)
Mean age ±SD, (year)	66.2 ±10.9	62.6 ±9.9
Age group (year), n (%)		
18-49	85,854 (12)	92,926 (16)
50-59	128,080 (18)	132,781 (23)
60-69	188,249 (27)	179,513 (31)
≥70	293,227 (42)	172,163 (30)
Women, n (%)	360,388 (52)	248,391 (43)
Men, n (%)	335,022 (48)	328,992 (57)
Index year, n (%)		
2013-2018	476,458 (69)	220,204 (38)
2019-2022	218,952 (31)	357,179 (62)
Mean aDCSI score ±SD	1.9 ±2.0	1.6 ±1.8
aDCSI score in category, n (%)		
0	247,377 (36)	223,391 (39)
1	118,302 (17)	110,116 (19)
2	113,158 (16)	94,617 (16.4)
3+	216,573 (31)	149,259 (26)
Mean N of unique oral antidiabetics ±SD	1.5 ±0.6	1.5 ±0.6
GLP-1RA use, n (%)	27,597 (4)	107,558 (19)
Insulin use, n (%)	148,213 (21)	202,351 (35)
Nephropathy, n (%)	178,345 (26)	110,026 (19)
Median at-risk days (IQR)*	302 (163, 631)	270 (150, 523)

aDCSI Adapted Diabetes Complications Severity Index; *GLP-1 RA* glucagon-like peptide-1 receptor agonist; *IQR* interquartile range; *N* number; *SD* standard deviation
*This is post-baseline follow-up time in days

- 242 incident IBD events, including 194 UC events and 52 CD events, were identified in combined DPP-4i and SGLT-2i cohorts, yielding a risk of 19 incident IBD cases/100,000 persons (Figure 2).

Figure 2. Risk of Incident IBD, UC, and CD, Overall, by Sex (Fig 2a) and by Age (Fig 2b)



NA not available; *Y* year *Risk of CD was not available due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Conclusions

- Baseline characteristics differed between the DPP-4i and SGLT-2i cohorts. DPP-4i cohort was older, included more women and patients from earlier years, had less concurrent use of GLP-1RA or insulin, and had a higher aDCSI score.
- Risk of incident IBD in the current combined population of DPP-4i initiators and SGLT-2i initiators was 19 cases/100,000 persons. In the literature, the crude incidence of IBD ranged from 11.6 to 37.7 events/100,000 person-years in T2D populations.
- Our study did not suggest the risk of IBD in DPP-4i and SLGT-2i initiators varied substantially by sex or age.