Cancer Risks Associated With Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: A Pharmacovigilance Study Of The FDA Adverse Event Reporting System (FAERS)

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BACKGROUND

- Dipeptidyl peptidase-4 (DPP-4) inhibitors are widely used across the globe to control sugar levels in adults with Type 2 diabetes mellitus.
- Specific cancer types have been found to be associated with DPP-4 inhibitors in the literature, such as pancreatic cancer.[1-4]
- To date, very few studies have comprehensively evaluated the association between DPP-4 inhibitors and all other types of cancers.

OBJECTIVE

- The objective of this study was to comprehensively evaluate the overall cancer and specific cancer types associations with DPP-4 inhibitors using the FDA Adverse Event Reporting System (FAERS).

METHODS

Data source
- Data was sourced from the FDA Adverse Event Reporting System (FAERS).
- Data includes patient demographic information (age and sex), drug information (drug name, active ingredient, and route of administration), and reaction information through standardized preferred terms (PT).
- The adverse drug reaction data is made publicly available on a quarterly basis by the FDA.

Study design
- FAERS data from January 1, 2004 to September 30, 2022 were included in this study.
- If a report was submitted to the FDA multiple times with updated information, only the most recently submitted version was included in this study to avoid duplicate data.

Drug Exposure Definition
- Each drug was identified in FAERS by the medication's generic and brand names listed in the Drugs@FDA Database.

Reporting Odds Ratio (ROR)
- Reporting Odds Ratios and corresponding 95% confidence intervals (95% CI) were calculated for the association between DPP-4 inhibitors and cancer.
- ROR was calculated as the ratio of the odds of reporting cancer versus all other events for a given drug compared with the reporting odds for other drugs present in FAERS.
- An association was considered to be statistically significant when the lower limit of the 95%CI was greater than 1.

Statistical software
- Microsoft Excel Office 365
- SAS 9.4

RESULTS

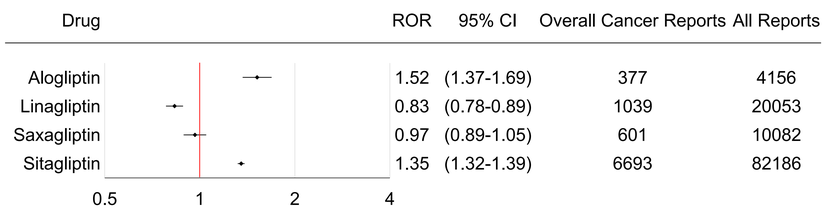

Figure 1. Reporting odds ratios of overall cancer for DPP-4 inhibitors

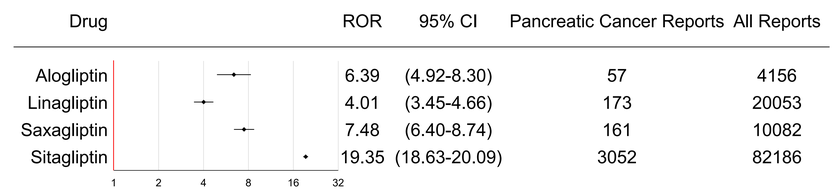

Figure 2. Reporting odds ratios of pancreatic cancer for DPP-4 inhibitors

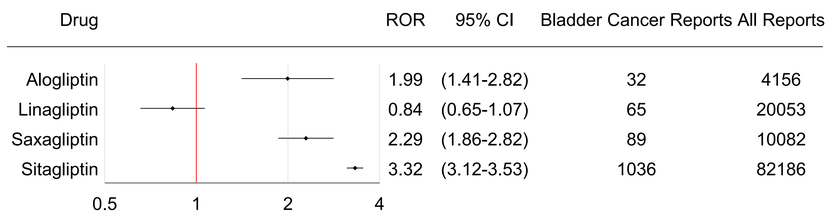

Figure 3. Reporting odds ratios of bladder cancer for DPP-4 inhibitors

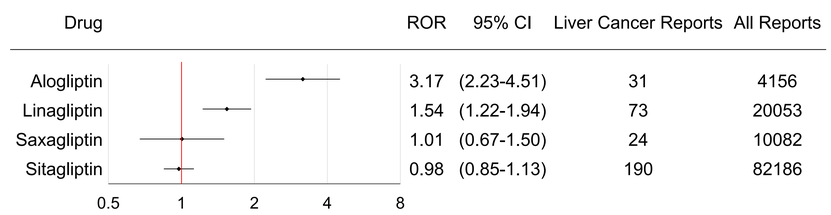

Figure 4. Reporting odds ratios of liver cancer for DPP-4 inhibitors

RESULTS

- A total of 15,598,679 reports were considered, after inclusion criteria were applied.
- Overall cancer RORs (95% CI) for DPP-4 inhibitors were (in descending order): alogliptin 1.52 (1.37-1.69), sitagliptin 1.35 (1.32-1.39), saxagliptin 0.97 (0.89-1.05), and linagliptin 0.83 (0.78-0.89).
- Pancreatic cancer RORs (95% CI) for DPP-4 inhibitors were (in descending order): sitagliptin 19.35 (18.63-20.09), saxagliptin 7.48 (6.40-8.74), alogliptin 6.39 (4.92-8.30), and linagliptin 4.01 (3.45-4.66).
- Bladder cancer RORs (95% CI) for DPP-4 inhibitors were (in descending order): sitagliptin 3.32 (3.12-3.53), saxagliptin 2.29 (1.86-2.82), alogliptin 1.99 (1.41-2.82), and linagliptin 0.84 (0.65-1.07).
- Liver cancer RORs (95% CI) for DPP-4 inhibitors were (in descending order): alogliptin 3.17 (2.23-4.51), linagliptin 1.54 (1.22-1.94), saxagliptin 1.01 (0.67-1.50), sitagliptin 0.98 (0.85-1.13).

CONCLUSIONS

- In FAERS, alogliptin and sitagliptin were significantly associated with overall cancer.
- Sitagliptin, saxagliptin, alogliptin, and linagliptin were significantly associated with pancreatic cancer.
- Sitagliptin, saxagliptin, and alogliptin were significantly associated with bladder cancer.
- Alogliptin and linagliptin were significantly associated with liver cancer.

FUNDING

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