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Sitagliptin Associated Pancreatic Carcinoma: a Review of the FDA AERS Database

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Abstract

Purpose: Sitagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor used in the treatment of type 2 diabetes mellitus in adults, as adjunct to diet and exercise to improve glycemic control. During phase III studies, sitagliptin was shown to cause toxicity to the pancreas, including pancreatitis. To date there is limited information available regarding its association with pancreatic carcinoma. Our goal was to qualitatively and quantitatively review available information in the AERS database in order to provide clinicians with a general understanding of the comparative occurrence of sitagliptin use and pancreatic carcinoma and any clinically relevant characteristics that may be useful in identifying patients at risk.

Keywords

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Disciplines

Pharmacy and Pharmaceutical Sciences

Comments

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Purpose

Sitagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor used in the treatment of type 2 diabetes mellitus in adults, as adjunct to diet and exercise to improve glycemic control. During phase III studies, sitagliptin was shown to cause toxicity to the pancreas, including pancreatitis. To date there is limited information available regarding its association with pancreatic carcinoma. Our goal was to qualitatively and quantitatively review available information in the AERS database in order to provide clinicians with a general understanding of the comparative occurrence of sitagliptin use and pancreatic carcinoma and any clinically relevant characteristics that may be useful in identifying patients at risk.

Methods

We used Empirica Signal software to query AERS from November 1968 to December 31, 2013. The software was used to calculate a disproportionality statistic, namely the Empirical Bayesian Geometric Mean (EBGM), for reports of sitagliptin -associated pancreatic carcinoma. The FDA considers an EBGM significant if the 5th percentile of the distribution is at least two (EB05 $\geq$ 2.0). With use of a disproportionality analysis, sitagliptin was compared with all agents listed in AERS. The disproportionality analysis was also performed on other medications classified as DPP-4 inhibitor and other oral hypoglycemic agents.

Figure 1: DPP-4 Inhibitors and Reports of Pancreatic Carcinoma

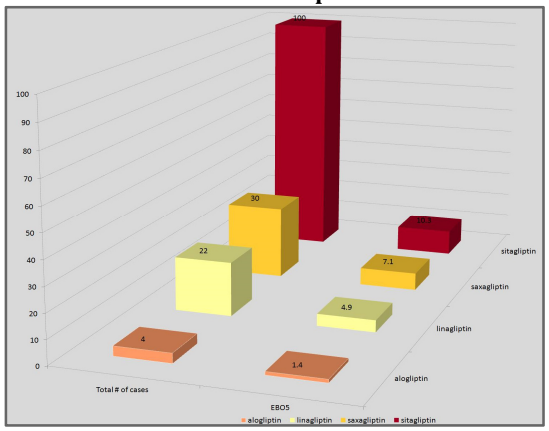

Figure 2: Oral hypoglycemic agents and Reports of Pancreatic Carcinoma

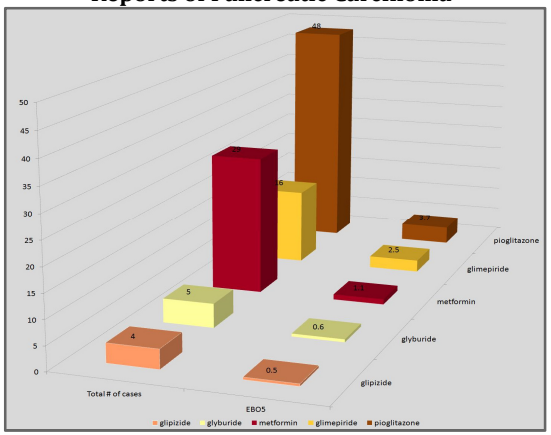

Table 1: Demographics of Study Population

Variable	Study Population (n= 105)
Mean age	70 years (range: 47-95 years)
Gender Female	56%
Duration of therapy Sitagliptin	460 days (range: 10- 1947 days)
Reported deaths	28

Results

One hundred cases of pancreatic carcinoma were reported in patients who were receiving sitagliptin. Overall 39% of the cases reported in patients receiving treatment with oral hypoglycemic agents occurred in patients receiving sitagliptin. An EB05 of 10.3 was determined for sitagliptin compared to all other agents included in AERS. All but one medication classified as a DPP-4 inhibitor were determined have an EBO5 $\geq$ 2.0. Glimepiride and pioglitazone were also determined to have an EBO5 $\geq$ 2.0, but the findings were not consistent within their associated medication classes.

Conclusions

There appears to be a statistical association between sitagliptin use and pancreatic carcinoma. Additional clinical studies are needed to further explore this statistical association.