**Preservation of Pancreatic beta cell mass in high fat-fed STZ treated mice by the Dipeptidyl peptidase-4 inhibitors Saxagliptin and Sitagliptin.**

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**ABSTRACT**

**Background and aims:**
Glucagon-like peptide-1 promotes islet cell growth and inhibits beta cell stress. In this study we investigated the effect of saxagliptin and sitagliptin at selecting doses on pancreatic beta cell mass in a murine model of pancreatic islet cell degeneration.

**Materials and methods:**
Groups of male C57BL6J mice (n=12 per group) were placed on high fat for 3 days. Mice were treated orally with vehicle (water), saxagliptin 10mg/kg/day or saxagliptin (10mg/kg/day) and subjected to procedures as outlined below. An oral glucose tolerance test (OGTT) was undertaken following an overnight fast using a glucose dose of 2g/kg.

**RESULTS**

**Glycemic control**

Compared with the STZ vehicle-treated groups all treatments improved glycemic control (AUC baseline) during the OGTT, though no difference in insulin responses were observed (Table 1 of Abstract).

**Glycaemic control and beta cell mass following compound treatment**

Compared with the STZ vehicle-treated groups all treatments improved glycemic control (AUC baseline) during the OGTT, though no difference in insulin responses were observed (Table 1 of Abstract).

**CONCLUSION**

Both treatments were able to induce small and statistically significant improvements in beta cell endpoints, though interestingly only saxagliptin demonstrated benefits, compared to vehicle, when administered both before and after the initiation of hyperglycaemia.

**SUMMARY/CONCLUSIONS**

- Overall both saxagliptin and sitagliptin showed similar improvements in glycemic control and beta cell mass preservation in the high fat-fed, STZ mouse model of pancreatic β-cell degeneration. We have demonstrated for the first time that saxagliptin along with improving glycaemic control had a positive effect on β-cell mass effects induced by the administration of low doses of the β-cell toxin, streptozotocin (STZ), to mice with moderate insulin resistance due to exposure to a diet high in fat.

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**OBJECTIVES**

- In light of data suggesting that GLP-1 may have a role in in situ neogenesis, differentiation, and the consequent regulation of β-cell mass and preservation17, the effect of saxagliptin and sitagliptin was assessed in the present study by initiating dosing both before and immediately after induction of diabetes in the high fat fed low dose streptozotocin mouse model of Type 2 diabetes.

**INTRODUCTION**

- The primary study assessed the efficacy of saxagliptin and sitagliptin in controlling the hyperglycaemia and β-cell mass effects induced by the administration of low doses of the β-cell toxin, streptozotocin (STZ), to mice with moderate insulin resistance due to exposure to a diet high in fat.