P-0420 Effect of saxagliptin, with and without acarbose, on postprandial glycaemia in Chinese patients with type 2 diabetes

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Background and aim : Dipeptidyl peptidase-4 (DPP-4)

inhibitors prevent rapid inactivation of the incretin hormone glucagon-like peptide-1 (GLP-1) to improve glycaemic control in type 2 diabetes. Malabsorption of carbohydrates induced by alpha glucosidase inhibitors (e.g. acarbose) has been shown to enhance postprandial GLP-1 secretion and, according, may potentiate the lowering of blood glucose by DPP-4 inhibitors. We evaluated the effects of the DPP-4 inhibitor, saxagliptin, with or without acarbose, on the glycaemic, intact GLP-1 and insulin responses to a high carbohydrate meal in Chinese patients with type 2 diabetes.

Method : 16 patients with diet-controlled type 2 diabetes (age 57.2 ± 2.2 years; 10 males; HbA1c $6.8 \pm 0.1\%$; BMI 23.4 ± 0.6 kg/m²) were studied on 4 occasions, separated by at least 7 days each, in a randomised fashion. On each study day, patients consumed 30 mL water with 5 mg saxagliptin or water only (at $t = -60$ min), followed 50 min later by a mashed potato meal (368.5 kcal; carbohydrate 61.4 g; protein 7.4 g; fat 8.9 g) with or without 100 mg acarbose in 10 min (during $t = -50-0$ min). Accordingly, the four treatments were: (i) control + control (PLBO), (ii) control + acarbose (ACBO), (iii) saxagliptin + control (SAXA), and (iv) saxagliptin + acarbose (COMB). Arterialised venous blood was sampled at a regular interval during $t = -60-240$ min for the measurements of plasma glucose, intact GLP-1 and insulin. Incremental areas under the curves (iAUCs) during $t = -60-240$ min for these measures were calculated, and compared using two-factor repeated measures ANOVA, with ACBO and SAXA as factors.

Results : SAXA reduced plasma glucose (20.3 ± 2.2 mmol/L*h for SAXA and 15.8 ± 2.1 mmol/L*h for COMB vs. 25.1 ± 2.4 mmol/L*h for PLBO and 18.0 ± 2.1 mmol/L*h for ACBO, treatment effect: $P = 0.009$), increased plasma intact GLP-1 (58.2 ± 6.9 pmol/L*h for SAXA and 63.1 ± 7.7 pmol/L*h for COMB vs. 22.4 ± 5.7 pmol/L*h for PLBO and 30.5 ± 4.3 mmol/L*h for ACBO, $P < 0.001$), without affecting plasma insulin.

Insulin iAUC

intact GLP-1 iAUC

In contrast, ACBO was associated with lower plasma glucose ($P = 0.001$) and insulin ($P < 0.05$), without any effect on plasma intact GLP-1. In the presence of ACBO, plasma glucose was lower ($P < 0.05$), and plasma intact GLP-1 was higher ($P = 0.001$), with SAXA vs. control, without any difference in plasma insulin. In the presence of SAXA, both plasma glucose and insulin were lower ($P < 0.05$ for both) with ACBO vs. control, without any difference in plasma intact GLP-1.

Discussion : In diet-controlled Chinese patients with type 2 diabetes, saxagliptin diminished postprandial glycaemic excursion, associated with increased plasma intact GLP-1, without affecting insulin, whereas acarbose reduced both plasma glucose and insulin, probably due to inhibition of carbohydrate digestion and absorption, without affecting plasma intact GLP-1. Nevertheless, the combination of saxagliptin with acarbose reduced postprandial glycaemic excursion more effectively than either alone, supporting the use of DPP-4 inhibitors with acarbose for the management of postprandial hyperglycaemia in Chinese patients with type 2 diabetes.

Acknowledgement: This study was funded by AstraZeneca ■