EudraCT 2015-001334-21 (350A , Study of the Effect of Vildagliptin versus Dapagliflozin on Glucagon Response to Mixed Meal in Metformin-treated Subjects with Type 2 Diabetes)

AIMS:
Previous studies have shown that dipeptidyl peptidase (DPP)-4 inhibition lowers glucagon levels whereas sodium-glucose co-transporter 2 (SGLT-2) inhibition increases them. This study evaluated the extent of these opposite effects in a direct comparative head-to-head study.

METHODS:
In a single-centre, randomized study with a cross-over design, 28 metformin-treated patients with type 2 diabetes (T2D) (mean age, 63 years; baseline HbA1c, 6.8%) were treated with vildagliptin (50 mg twice daily) or dapagliflozin (10 mg once daily) for 2 weeks, with a 4-week wash-out period between the two separate treatments. After each treatment period, a meal test was undertaken, with measurements of islet and incretin hormones and 4-hour area under the curve (AUC) levels were estimated.

RESULTS:
Fasting glucagon (35.6 ± 2.5 vs 39.4 ± 3.4 pmoL/L; P = .032) and postprandial glucagon (4-hour $AUC_{glucagon}$, 32.1 ± 2.3 vs 37.5 ± 2.7 nmoL/L min; P = .001) were ~15% lower after vildagliptin compared to dapagliflozin treatment. This was associated with stronger early (15 minute) C-peptide response and higher 4-hour $AUC_{C\text{-}peptide}$ (P < .010), higher 4-hour AUC of the intact form of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) (P < .001) and lower 4-hour AUC of total GIP and GLP-1 (P < .001).

CONCLUSION:
Treatment with DPP-4 inhibition with vildagliptin results in 15% lower fasting and postprandial glucagon levels compared to SGLT-2 inhibition with dapagliflozin. DPP-4 inhibition also induces more rapid insulin secretion and higher levels of intact incretin hormones, resulting in stronger feedback inhibition of incretin hormone secretion than SGLT-2 inhibition.