Predictors of response to SGLT2-inhibitors and DPP4-inhibitors: a MASTERMIND stratified medicine study

B Shields[1], J Dennis[1], W Henley[1], M Weedon[1], M Lonergan[2], A Jones[1], N Sattar[3], R Holman[4], E Pearson[2] and A Hattersley[1]

[1]University of Exeter Medical School, Exeter, UK, [2]School of Medicine, University of Dundee, Dundee, UK, [3]Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK, [4]Diabetes Trials Unit, University of Oxford, Oxford, UK

Background: Stratified medicine targets treatment according to patient characteristics. We have shown simple criteria of sex and obesity can predict differential response to thiazolidinediones and sulfonylureas. SGLT2-inhibitors and DPP4-inhibitors are also second-line therapies used to treat Type 2 diabetes, with different mechanisms of action. We aimed to determine whether patient characteristics predicted differential responses to these two therapies.

Methods: Patients with prescription records and valid six month response (HbA1c change from baseline) for DPP4-inhibitors (n = 9,772) or SGLT2-inhibitors (n = 799) were identified from the UK Primary Care Clinical Practice Research Datalink. Regression models were used to identify predictors of response, with betas presented as the change in HbA1c per 1 unit increase in the predictor.

Results: Poor renal function (eGFR<90ml/min/1.73m^2) was associated with a worse glycaemic response to SGLT2-inhibitors (mean baseline-adjusted six month HbA1c: –12.2 vs –14.1mmol/mol, p = 0.006), but a better response to DPP4-inhibitors (–9.3 vs –8.6mmol/mol, p = 0.005). For both DPP4-inhibitors and SGLT2-inhibitors, higher baseline HbA1c (DPP4: β[SE] = –0.52[0.008]; SGLT2: β[SE] = –0.54[0.03], p < 0.0001 for both), and shorter duration of diabetes (DPP4: β[SE] = 0.13[0.02]; SGLT2: β[SE] = 0.31[0.08], p < 0.001 for both) were associated with a greater reduction in HbA1c at 6 months. Higher body mass index (BMI) (β[SE] = 0.12[0.02]) and younger age at diagnosis (β[SE] = –0.07[0.01]; p < 0.0001 for both) were associated with a worse response to DPP4-inhibitors.

Conclusion: These preliminary analyses identify simple criteria that may partly explain variability in the response to SGLT2-inhibitors and DPP4-inhibitors. The associations between eGFR and six month response to SGLT2-inhibitors and DPP4-inhibitors go in opposite directions, indicating potential criteria to aid treatment choices in Type 2 diabetes.