

## One Year Efficacy, Safety and Tolerability Outcomes of Endoscopic Duodenal Exclusion using Endobarrier as an Adjunct to Glucagon-like Peptide-1 (GLP-1) therapy in Suboptimally Controlled Type 2 Diabetes: a Randomised Controlled Trial

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**Background:** New, effective treatments are needed to combat the global diabetes pandemic. 75% of UK patients commencing GLP-1 receptor agonist (GLP-1RA) therapy fail to achieve national targets for continuation.

**Aim:** To investigate the efficacy, safety and tolerability of adding endoscopic duodenal exclusion to GLP-1RA therapy not achieving targets, compared to either treatment alone.

**Methods:** Adults with suboptimally controlled type 2 diabetes ( $HbA_{1c} \geq 58$  mmol/mol,  $\geq 7.5\%$ ) and obesity ( $BMI \geq 35$  kg/m<sup>2</sup>) despite GLP-1RA therapy (liraglutide 1.2mg daily) were randomised to (1) additional duodenal exclusion using a novel endoscopic device, endobarrier (n24); (2) endobarrier without GLP-1RA (n24); (3) escalated dose liraglutide (1.8 mg daily) (n22). All groups underwent the same initial 2-week diet and were given the same dietary information. Those randomised to endobarrier were implanted with the device for 1-year. Participants were seen 3-monthly. The primary endpoint was change in HbA<sub>1c</sub> at 2 years compared to baseline (Registry ISRCTN00151053, NCT02055014). This 1-year analysis was by modified intention to treat.

**Results:** Of 70 patients treated, 57 have completed 1-year to date (all data will be available by April 2016). Groups were matched for age  $50.9 \pm 12.5$ ,  $50.4 \pm 8.4$ ,  $53.7 \pm 11.6$  years), BMI ( $40.0 \pm 4.8$ ,  $41.5 \pm 5.0$ ,  $41.4 \pm 5.0$  kg/m<sup>2</sup>), sex (% male 36.8, 26.1, 46.7) and ethnicity (% Caucasian 63.2, 69.6 66.7). In groups 1 (n19), 2 (n23) and 3 (n15) respectively, weight fell by  $11.3 \pm 6.0$  kg from  $110.6 \pm 20.1$  kg to  $99.3 \pm 22.1$  kg ( $P < 0.0001$ ), by  $11.7 \pm 7.8$  kg from  $115.3 \pm 20.5$  kg to  $103.6 \pm 22.5$  kg ( $P < 0.0001$ ) and by  $4.5 \pm 6.9$  kg from  $120.7 \pm 15.7$  kg to  $116.2 \pm 16.9$  kg ( $P = 0.04$ ); HbA<sub>1c</sub> fell by  $22.8 \pm 15.2$  mmol/mol ( $2.1 \pm 1.4\%$ ) from  $82.2 \pm 14.0$  mmol/mol ( $9.7 \pm 1.3\%$ ) to  $59.4 \pm 15.3$  mmol/mol ( $7.6 \pm 1.4\%$ ) ( $P < 0.0001$ ), by  $13.6 \pm 14.8$  mmol/mol ( $1.2 \pm 1.4\%$ ) from  $78.6 \pm 19.5$  mmol/mol ( $9.3 \pm 1.8\%$ ) to  $65.0 \pm 19.6$  mmol/mol ( $8.1 \pm 1.8\%$ ) ( $P = 0.001$ ) and by  $16.2 \pm 17.1$  mmol/mol ( $1.5 \pm 1.6\%$ ) from  $83.2 \pm 20.9$  mmol/mol ( $9.8 \pm 1.9\%$ ) to  $67.0 \pm 17.8$  mmol/mol ( $8.3 \pm 1.6\%$ ) ( $P = 0.004$ ). 5/42 (11.9%) of endobarrier-treated patients had serious device-related adverse events (gastrointestinal bleed, obstruction, complicated removal, liver abscess, cholecystitis) with resolution of the event in all cases. There were 5/42 (11.9%) early device removals related to gastrointestinal symptoms (3 from group 1).

**Conclusion:** At 1 year, endobarrier added to liraglutide had a superior effect in reducing both weight and HbA<sub>1c</sub> in patients with diabetes failing GLP-1RA therapy. GLP-1RA therapy substituted with endobarrier produced comparable weight reduction with less glycaemic improvement. These data suggest adding duodenal exclusion to suboptimally performing GLP-1RA therapy has clinical benefit and advantage over converting to duodenal exclusion. The endobarrier safety and tolerability profile up to 1 year was acceptable. Combination endobarrier-GLP-1RA therapy was well tolerated.

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