Abstract Title: 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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Abstract Text:

Background: New, effective treatments are needed to combat the global diabesity pandemic. 75% of UK patients commencing GLP-1 receptor agonist therapy fail to achieve national targets for continuation1.
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 (HbA1c≥58mmol/mol, ≥7.5%) and obesity (BMI≥35kg/m2) 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 HbA1c 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 available March 2016). Groups were matched for age 50.9±12.5, 50.4±8.4, 53.7±11.6 years), BMI (40.0±4.8, 41.5±5.0, 41.4±5.0kg/m2), 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±6.0kg from 110.6±20.1kg to 99.3±22.1kg (P<0.0001), by 11.7±7.8kg from 115.3±20.5kg to 103.6±22.5kg (P<0.0001) and by 4.5±6.9kg from 120.7±15.7kg to 116.2±16.9kg (P=0.04); HbA1c fell by 22.8±15.2mmol/mol (2.1±1.4%) from 82.2±14.0mmol/mol (9.7±1.3%) to 59.4±15.3mmol/mol (7.6±1.4%) (P<0.0001), by 13.6±14.8mmol/mol (1.2±1.4%) from 78.6±19.5mmol/mol (9.3±1.8%) to 65.0±19.6mmol/mol (8.1±1.8%) (P=0.001) and by 16.2±17.1mmol/mol (1.5±1.6%) from 83.2±20.9mmol/mol (9.8±1.9%) to 67.0±17.8mmol/mol (8.3±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 HbA1c in patients with diabesity 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 GLP1-RA 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.