Effects of apraglutide, a Glucagon-Like Peptide-2 Analog, on Patients with Short Bowel Syndrome: Preliminary Results from an Open-label Study

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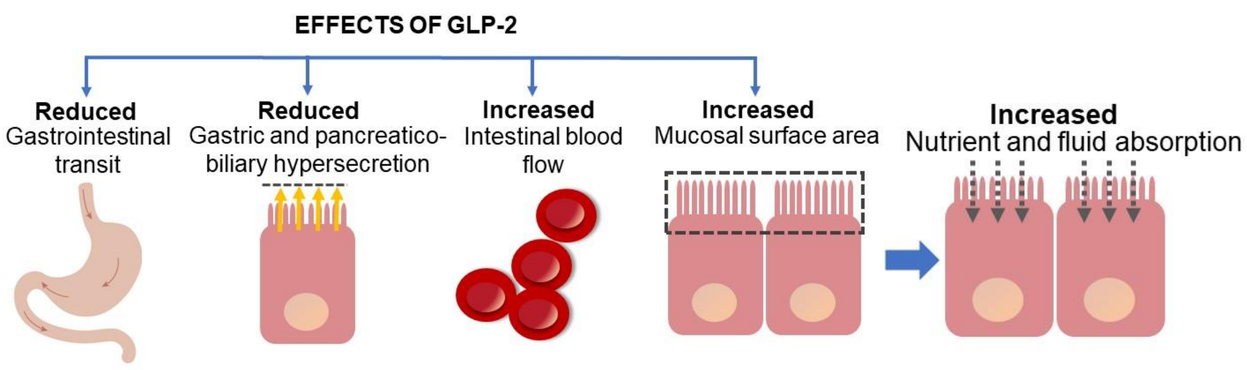
Introduction

Short bowel syndrome is a spectrum of malabsorption features following extensive intestinal resection. Glucagon-like peptide (GLP)-2 is a pro-adaptive hormone with therapeutic potential for short bowel syndrome.

Apraglutide is a novel long-acting GLP-2 analog with a longer elimination half-life compared to native GLP-2 and the already marketed GLP-2 analog teduglutide. Hence, apraglutide may improve intestinal function in patients with short bowel syndrome with a once-weekly subcutaneous injection.

We aimed to assess the safety and efficacy of apraglutide for the treatment of short bowel syndrome.



Methods

A total of 8 adult patients will be enrolled in an open-label phase 2 trial with a 5 mg once-weekly subcutaneous injection of apraglutide for 4 weeks.

Main inclusion criteria include an average fecal output ≥1,500 g/day and a urine volume <2,000 ml/day.

Metabolic balance studies were performed before and after 4 weeks of treatment. Food intake was unrestricted. Oral fluid intake and parenteral support volume were kept constant.

Safety was the primary endpoint. Secondary endpoints included changes from baseline in:

- fecal wet weight output
- absorption of wet weight
- absorption of energy

Results

We present preliminary results from the first four patients (1-4) who completed the trial. Patient 1 and 2 had jejunostomies with a short bowel length of 150 and 140 cm, respectively. Patient 3 and 4 had ileostomies with a small bowel length of 230 and 250 cm, respectively. Patient 1,2 and 3 had intestinal insufficiency and were independent of parenteral support. Patient 4 had intestinal failure and was dependent on parenteral support.

Common adverse events were peripheral edema, polyuria and stoma nipple enlargement, which were transient with a mild to moderate severity. No safety concerns were raised regarding laboratory values, vital signs and electrocardiograms.

We observed a decrease in fecal wet weight output and an increase in intestinal absorption of wet weight and energy in all four patients (Graphs 1,2,3).

Initial PK analysis supported a once-weekly injection.

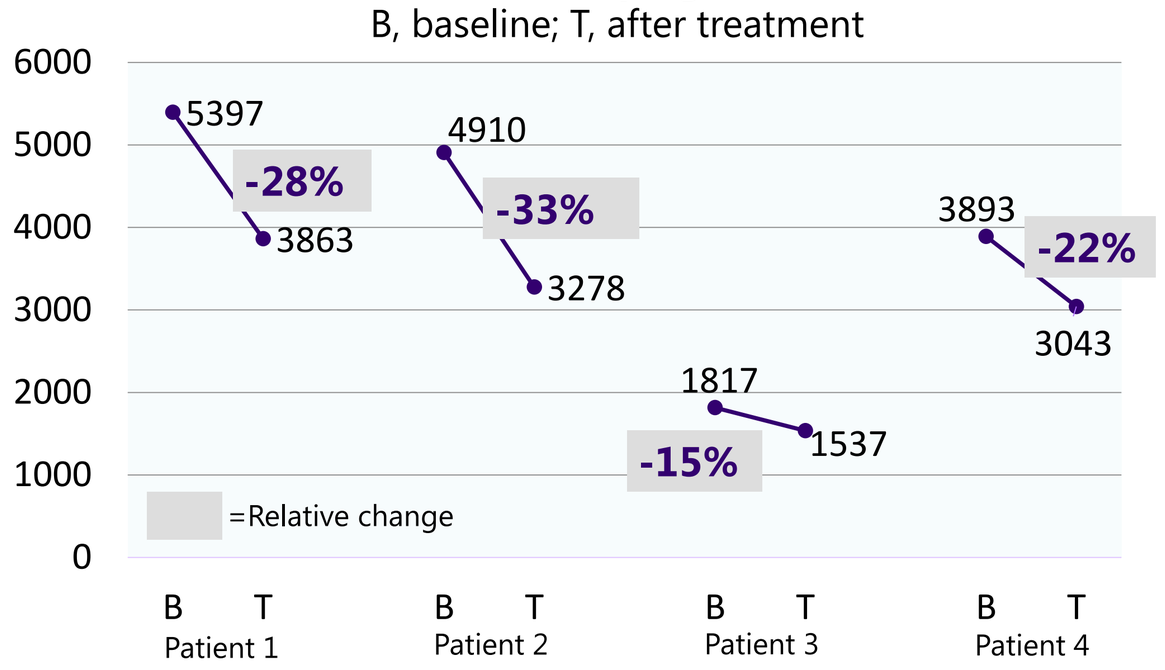
Conclusion

Preliminary results from this phase 2 trial suggest that once-weekly dosing of apraglutide is safe, well tolerated and associated with improvements in intestinal function. Apraglutide has a PK profile which enables once-weekly dosing and is therefore a potential new treatment option for patients with short bowel syndrome.

Results from 72-hour metabolic balance studies

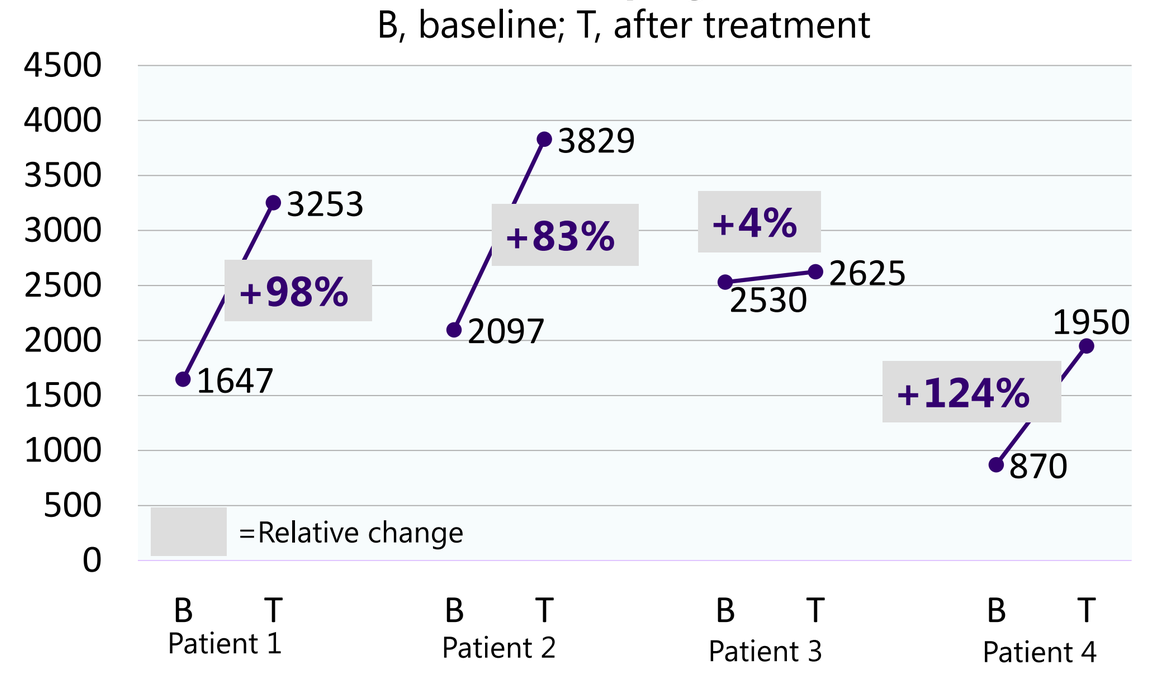
Graph 1. Fecal wet weight output (g/day) before and after 4 weeks of apraglutide

B, baseline; T, after treatment



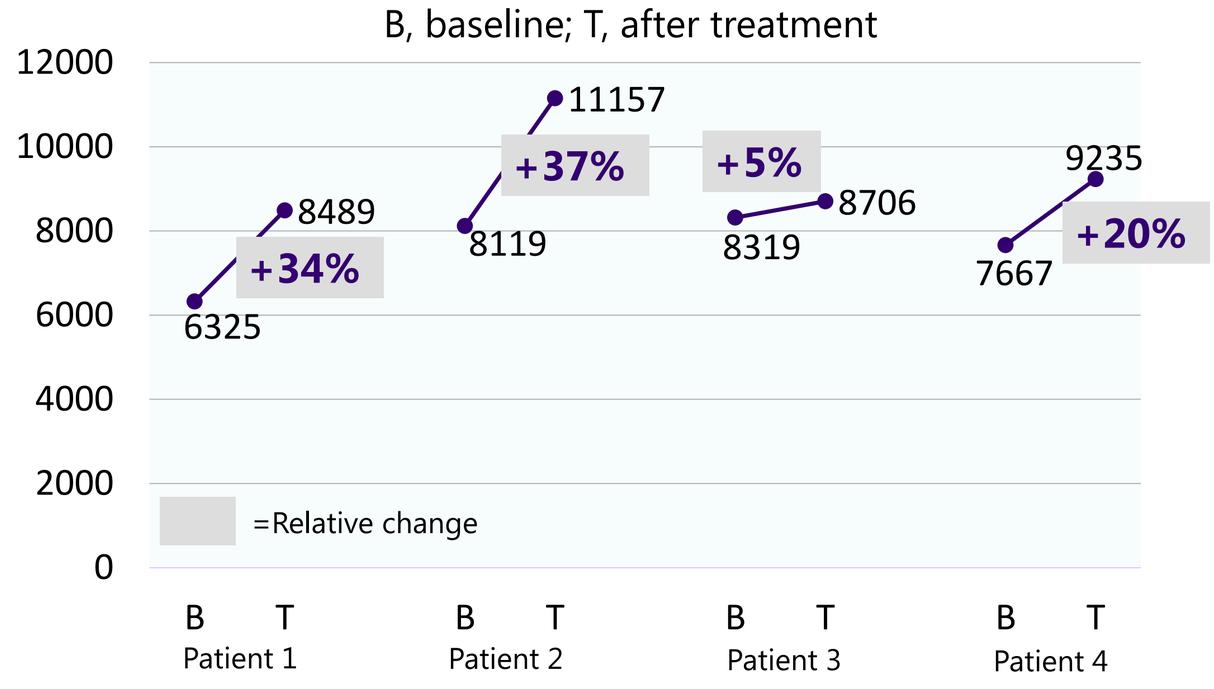
Graph 2. Wet weight absorption (g/day) before and after 4 weeks of apraglutide

B, baseline; T, after treatment



Graph 3. Energy absorption (kJ/day) before and after 4 weeks of apraglutide

B, baseline; T, after treatment



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