EFFECT OF APRAGLUTIDE, A LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 ANALOG, IN PATIENTS WITH SHORT BOWEL SYNDROME: PRELIMINARY RESULTS FROM AN OPEN-LABEL PHASE 2 TRIAL

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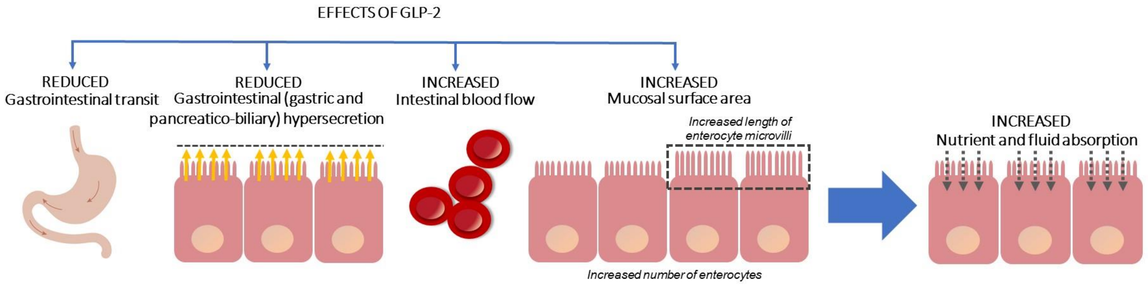
BACKGROUND & AIM

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

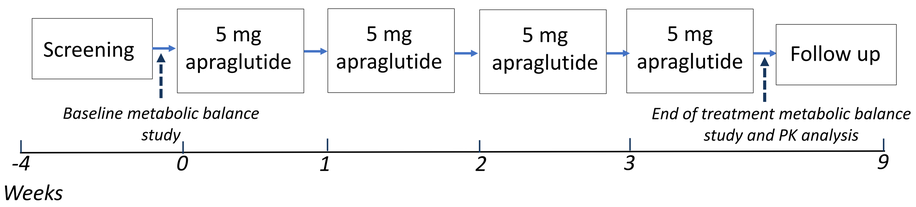
Apraglutide is a novel long-acting GLP-2 analog, with a longer elimination half-life compared to native GLP-2 and the already marketed GLP-2 analog teduglutide. Apraglutide may improve intestinal function in patients with short bowel syndrome with a once-weekly subcutaneous injection. We aimed to assess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



METHODS

- A total of 8 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.
- Safety was the primary endpoint.
- As secondary endpoints, we examined changes from baseline in: 1) stoma wet weight output as well as intestinal absorption of wet weight and energy measured by 72-hour metabolic balance studies, 2) plasma citrulline, a proposed marker for enterocyte mass and 3) drug concentration of apraglutide measured by pharmacokinetics (PK) during the post-treatment metabolic balance study.

FIGURE 1. TRIAL DESIGN

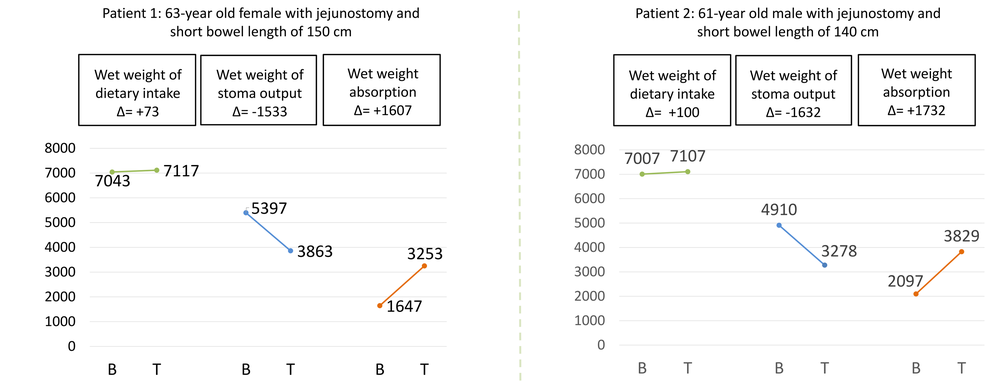


RESULTS

- We present preliminary results from the first two patients who completed the trial.
- Common adverse events (AEs) were peripheral edema, polyuria and stoma nipple enlargement. AEs 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 stoma wet weight output and an increase in intestinal absorption of wet weight and energy in both patients (Figure 2).
- Plasma citrulline increased in both patients (Table 1).
- Initial PK analysis supports once-weekly injection.

FIGURE 2. RESULTS FROM 72-HOUR METABOLIC BALANCE STUDIES BEFORE AND AFTER 4 WEEKS OF APRAGLUTIDE TREATMENT

A. CHANGES IN WET WEIGHT DIETARY INTAKE, OUTPUT AND ABSORPTION (g/day). B, baseline; T, after treatment



B. CHANGES IN ENERGY CONTENT OF DIETARY INTAKE, STOMA OUTPUT AND ABSORPTION (MJ/day), B, baseline; T, after treatment

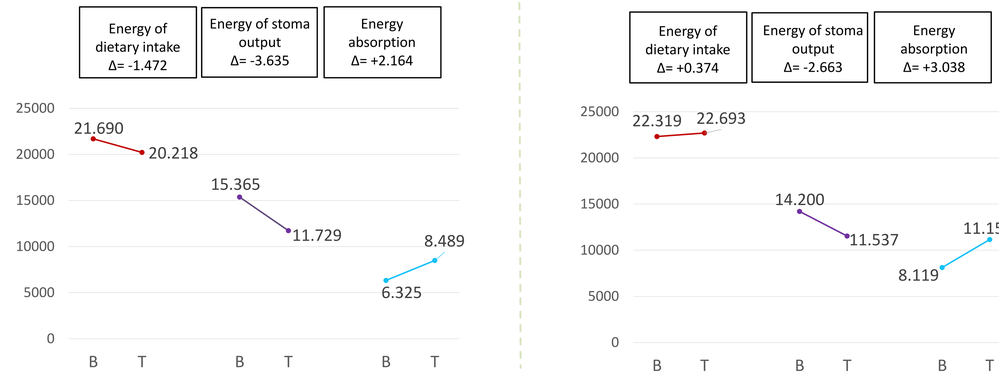


TABLE 1. PLASMA CITRULLINE BEFORE AND AFTER 4 WEEKS OF APRAGLUTIDE TREATMENT (µmol/L)

	Baseline	After 4 weeks of apraglutide treatment	Absolute change from baseline	Relative change from baseline
Patient 1	26.0	44.6	18.6	72 %
Patient 2	56.6	77.8	21.2	37 %

CONCLUSIONS

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.

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