Safety and Efficacy of Apraglutide in Patients with Short Bowel Syndrome: an Open-label Phase 2 Metabolic Balance Trial

PD-045

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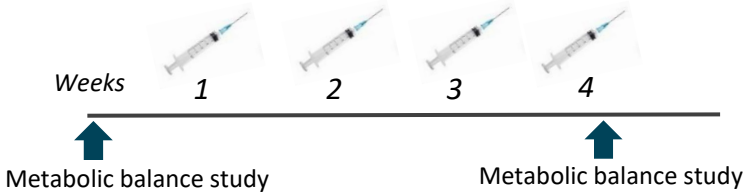
Introduction

- Patients with short bowel syndrome (SBS) and ileal or colonic resection may have impaired postprandial secretion of glucagon-like peptide-2 (GLP-2)
- Treatment with GLP-2 and its analogues improves intestinal adaptation in patients with SBS, thereby increasing fluid and nutrient absorption. This may alleviate symptoms of malabsorption and/or reduce parenteral support requirements
- **Apraglutide is a synthetic, long-acting GLP-2 analogue designed for weekly dosing with a half-life of 72-hours. This trial investigated the safety and efficacy of apraglutide in patients with SBS**

Methods

- 4 adult patients with SBS intestinal failure and 4 adult patients with SBS intestinal insufficiency were treated with weekly subcutaneous 5 mg apraglutide for four weeks
- Metabolic balance studies were performed before and after treatment (food intake was unrestricted, oral fluid intake and parenteral support were kept constant)
- Dietary and fecal energy was measured by bomb calorimetry



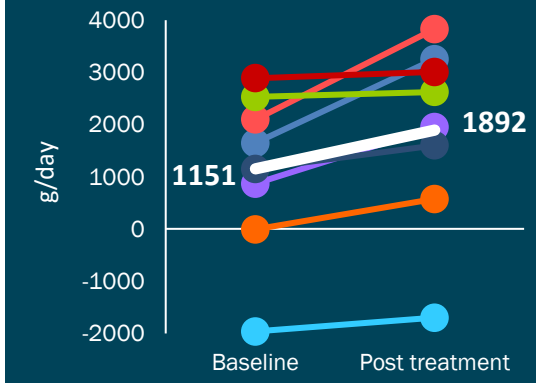
Results: safety

Common treatment-related adverse events were mostly mild to moderate and consistent with the physiological effect of GLP-2. They included stoma complication, reduced stoma output, nausea, flatulence, polyuria and abdominal pain. The only treatment related serious adverse was an event of abdominal pain which required hospitalization <24 hours and was treated conservatively with pain medication.

Results from 72-h metabolic balance studies

Estimated mean change from baseline to end of treatment was analyzed using a paired t-test.

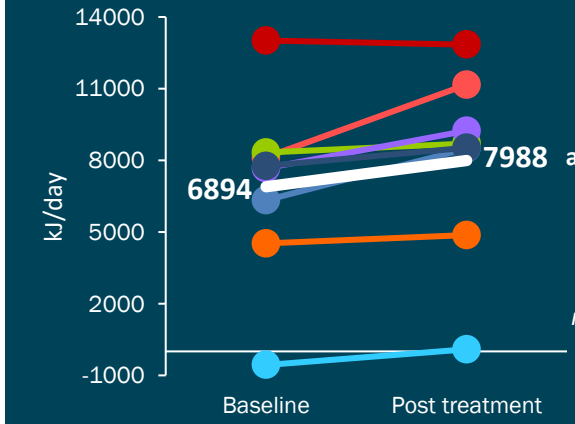
Wet weight absorption



Apraglutide increased absorption of wet weight by 741 g/day (95% CI 194 to 1287; P=.015)

White line represents mean and colored lines represents individual patients

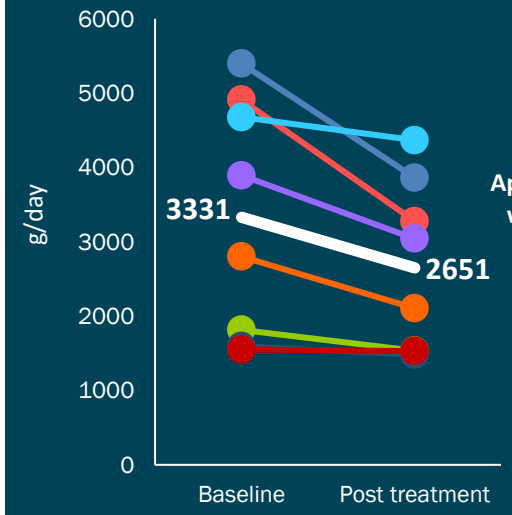
Energy absorption



Apraglutide increased absorption of energy by 1095 kJ/day (95% CI 196 to 1994, P=.024)

White line represents mean and colored lines represents individual patients

Fecal wet weight



Apraglutide decreased fecal wet weight by 680 g/day (95% CI -1200 to -159; P=.018)

White line represents mean and colored lines represents individual patients

Further results from 72-h metabolic balance studies:

	Estimated mean change from baseline
Urine production (g/day)	560 (95% CI 72 to 1048; P=.030)
Sodium absorption (mmol/day)	38 (95% CI 3 to 74; P=.039)
Potassium absorption (mmol/day)	18 (95% CI 4 to 32; P=.020)

Conclusion

5 mg apraglutide treatment was safe and well tolerated in patients with SBS intestinal failure and intestinal insufficiency. For the first time, a weekly GLP-2 analogue significantly improved absorption of wet weight, energy, electrolytes and increased urine production. A weekly dosing regimen may decrease patient burden and improve efficacy and tolerability. A phase 3 trial will be initiated to further confirm the safety and efficacy of weekly apraglutide treatment.