INTRODUCTION

• Teduglutide is the only GLP-2 analog licensed for the treatment of short-bowel syndrome (SBS) in patients requiring parenteral support
• Apraglutide is a new GLP-2 analog with an extended half-life in development for SBS in patients requiring parenteral support
• Glepaglutide is also in development for SBS
• Here we report direct comparisons of the three agents with respect to intestinotrophic effects in rat.

OBJECTIVE

To compare the extent and duration of intestinotrophic effects in a rat model of SBS with apraglutide, teduglutide and glepaglutide

METHODS

• Two studies were conducted; one comparing apraglutide with teduglutide, and one comparing apraglutide, teduglutide and glepaglutide
• The three GLP-2 analogs were administered by subcutaneous (sc) injection at a range of equivalent doses (3 to 1,000 nmole/kg)
• Dosing frequencies of 24, 48 and 72 h were studied (Table 1)
• Each dosing regimen was tested in 6 Sprague-Dawley rats
• Intestinal wet weight was normalized to body weight and was expressed as % increase over a control group run in the same study
• A third study determined pharmacokinetic parameters after single intravenous bolus injection of apraglutide, teduglutide and glepaglutide at a dose of 0.2 free bases/kilogram in Sprague-Dawley rats

RESULTS

Intestinotrophic effects

• Apraglutide induced a greater intestinotrophic effect than identical doses of teduglutide and glepaglutide at 24-, 48- and 72-hour dosing intervals (Figure 1)
• With a 96-hour dosing interval (not tested with glepaglutide), apraglutide significantly increased intestinal wet weight compared with teduglutide, which decreased intestine weight (Figure 2)

Figure 1. Apraglutide Induced a Greater Intestinotrophic Effect Compared to Teduglutide or Glepaglutide

Figure 2. Dose Response with 96-hour Dosing Interval: Apraglutide vs Teduglutide

Pharmacokinetics

• Apraglutide had a longer elimination half-life and lower clearance than teduglutide and glepaglutide after a single intravenous dose (Figure 3)
• Half-life of apraglutide was ~30 hours compared with ~2-3 hours for teduglutide

Figure 3. Pharmacokinetic Profiles GLP-2 Analogs after Single IV Injection in Rats

CONCLUSIONS

• Apraglutide induced a greater intestinotrophic effect than teduglutide and glepaglutide in rats at the same dose and dosing intervals
• Apraglutide showed a prolonged duration of effect, most likely due to its extended half-life of ~30 hours
• These data indicate that apraglutide has the most robust and longest lasting pharmacodynamic effect of the compounds tested

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CONFLICT OF INTEREST

VD is a consultant to Therachon AG; RP, LS and CM are employees of Therachon AG; DH, RL, AP and PR are employees of Ferring Pharmaceuticals