

Apraglutide Has an Extended Duration and Induces a Greater Intestintrophic Effect Compared with Teduglutide, Glepaglutide and Elsiglutide.

Purpose

To assess the impact of the long (30 hour) half-life of apraglutide (FE 203799) on intestintrophic effect and duration of effect compared with teduglutide, glepaglutide and elsiglutide in a rat model.

Methods

Apraglutide was directly compared to teduglutide, glepaglutide and elsiglutide in Sprague-Dawley rats. The compounds, at equivalent dose levels of 30 or 300 nmol/kg (n=6/group), were tested at intervals of 24 hours (once daily for 5 days) or 48 hours (2 doses at times 0 and 48 hours). Rats were euthanized 96 hours after the first dose. The compounds were also tested after a single injection with the rats euthanized 72 or 96 hours post-dosing. Intestinal wet weight was normalized to body weight and was expressed as % increase over a control group run in the same study.

Results

At 24, 48 and 72 hour dosing intervals, apraglutide induced a greater intestintrophic effect compared to teduglutide, elsiglutide and glepaglutide at identical doses.

At a 96 hour dosing interval, apraglutide at 300 nmol/kg increased intestine weight over the control group. The effect of apraglutide to increase intestine weight was greater than teduglutide at identical dose.

Elsiglutide and glepaglutide were not tested at a 96 hour dosing interval.

At the 300 nmol/kg dose, 96 hour dosing interval, teduglutide treated rats had a decrease in intestine weight.

Conclusions

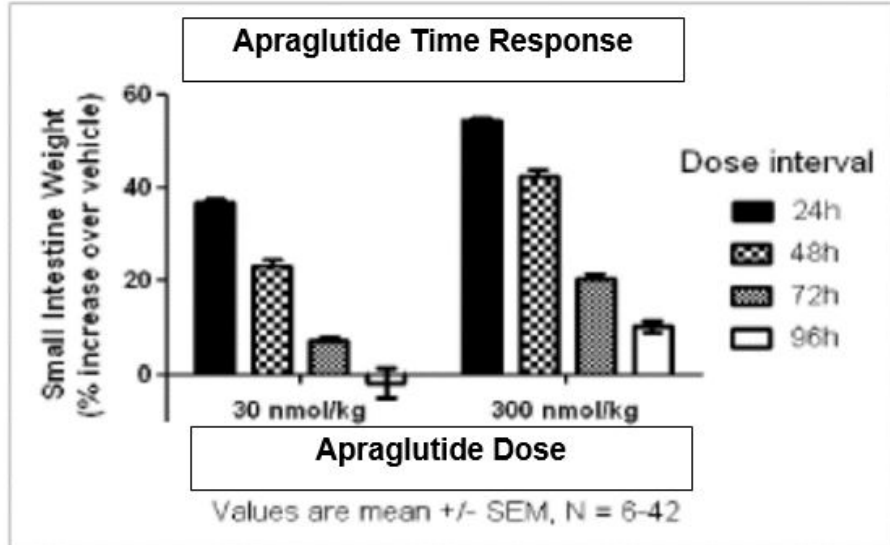
Apraglutide induces a greater intestinotrophic effect at the same dose compared to teduglutide, glepaglutide and elsiglutide in a rat model.

Apraglutide shows an extended duration of effect, most likely due to its greater half-life of 30 hours.

This is the longest half-life reported for any GLP-2 analog in development to date.

Apraglutide is currently in Phase II development for patients with short bowel syndrome requiring parenteral support.

Figure 1. Effect of apraglutide on small intestinal weight following various treatment regimens



24 h interval: 4 doses (0, 24, 48, 72 h; collection at 96 h)
 48 h interval: 2 doses (0, 48 h; collection at 96 h)
 72 h interval: 1 dose (0 h; collection at 72 h)
 96 h interval: 1 dose (0 h); collection at 96 h

Figure 2. Effect of apraglutide, elsiglutide, glepaglutide and teduglutide on small intestinal weight following various treatment regimens

