BACKGROUND & AIM
Patients with short bowel syndrome (SBS) have impaired neuro-endocrine feedback including loss of neo-colonic "brake" mechanisms due to distal bowel resections. This results in:
- Gastric hypersecretion
- Rapid gastrointestinal transit
- Lack of intestinal adaptation
- Large intestinal outputs

We aimed to assess the effect of glepaglutide, a novel long-acting glucagon-like peptide-2 analog, on gastrointestinal transit time in patients with SBS associated intestinal failure (IF) and intestinal insufficiency (II).

RESULTS
Eighteen adult patients with SBS were randomized and 14 completed all 4 scintigraphic examinations (13 with jejunostomy; 1 without jejunostomy). The 10 mg dose group of glepaglutide prolonged time to 10% solid-phase intestinal emptying by 27 mins (p=0.024) in the 10 mg dose group. Trend towards a liquid-phase prolongation was seen in the 10 mg dose group, but not in the 1 and 0.1 mg dose groups. Time to 50% liquid-phase gastric emptying was prolonged by 40 mins (p=0.038) in the 10 mg dose group. Likewise, time to 50% solid-phase gastric emptying was prolonged by 21 mins (p=0.038) in the 10 mg dose group. Likewise, time to 50% liquid-phase gastric emptying was prolonged by 40 mins (p=0.048) in the 10 mg dose group, but was unchanged in the 1 and 0.1 mg dose groups. Time to 10% liquid-phase intestinal emptying remained unchanged in each group.

STATISTICS
Estimates are presented as adjusted means with 95% confidence interval in an ANCOVA model including treatment period, parenteral support and total oral intake at baseline as covariates.

CONCLUSION
The 10 mg dose group of glepaglutide prolonged solid-phase gastrointestinal emptying time and liquid-phase intestinal emptying measured by scintigraphy.

We speculate that the observed slowed gastrointestinal transit – along with demonstrated positive effects on intestinal growth and potential other beneficial effects (anti-secretion, blood flow, etc.) – contribute to the observed beneficial effects of glepaglutide on fecal output (primary endpoint) and associated improvement in intestinal absorption.

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Correspondence to Mark Hvistendahl, E-mail mark.hvistendahl@regionh.dk

PATIENTS

Table 1. Changes from baseline in the gastrointestinal transit time. Solid-phase: Technetium-99m; liquid-phase: Indium-111. GI = Gastrointestinal

<table>
<thead>
<tr>
<th>Time to 10% GI emptying</th>
<th>Phase</th>
<th>0.1 mg</th>
<th>1 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid</td>
<td>3</td>
<td>4.1</td>
<td>2.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Liquid</td>
<td>3</td>
<td>4.1</td>
<td>2.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Changes from baseline (minutes [95% CI])

<table>
<thead>
<tr>
<th>Time to 10% solid-phase</th>
<th>Phase</th>
<th>0.1 mg</th>
<th>1 mg</th>
<th>10 mg</th>
</tr>
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<td>1.7</td>
</tr>
</tbody>
</table>

Time to 10% and 50% gastric emptying
- Time to 10% and 50% gastric emptying
- Time to 10% gastrointestinal emptying
- Time to 10% gastrointestinal emptying minus time to 10% gastric emptying

SBS: Short Bowel Syndrome

For more results from the Glepaglutide Phase 2 trial see the oral presentation on Monday 5.4 - 6.12 pm (Morphological changes), and Tuesday 8.00 - 8.30 am (Intestinal energy absorption).