BACKGROUND & AIM

• We recently reported that three weeks of daily subcutaneous injections of glepaglutide improved intestinal function, hydration level and renal function in patients with short bowel syndrome (SBS) (Figure 1).1

• Glepaglutide, primarily in the 10 mg dose group, also improved liver excretory function as demonstrated by increased clearance of indocyanine green and improvement in plasma alkaline phosphatase and bilirubin. Increase in liver stiffness by transient elastography (TE) was also observed, potentially due to the increase in portal blood flow.2

• As an exploratory endpoint, we evaluated the effects of glepaglutide on gut integrity and the activation of liver macrophages.

RESULTS

Eighteen adult patients with SBS (13 with intestinal failure and 5 with intestinal insufficiency) were randomized; 16 patients completed the trial. Results are shown in Table 1 and Figure 3.

• Compared to baseline, glepaglutide increased sCD163 by 0.44 mg/mL (P=0.0498) in the 10 mg dose group from the baseline value of 3.3 ± 2.2 mg/mL. In the same dose group, there was also a small but non-significant increase of 0.03 mg/mL (P=0.068) in sMR from the baseline value of 0.3 ± 0.2 mg/mL.

• LBP did not change following treatment with glepaglutide.

• The 0.1 mg and 1 mg groups showed no significant effect on the measured parameters.

CONCLUSION

• Increases in sCD163 and sMR may suggest activation of hepatic macrophages primarily in the 10 mg dose group with no sign of increased bacterial translocation.

• It is possible that a sudden increase in the compromised portal blood flow following treatment with glepaglutide is responsible for the activation of the liver macrophages, which now need to relate to a new-normal portal flow status.

• Our findings should be interpreted with caution due to the exploratory nature of the endpoints and the lack of statistical power.

Table 1. Changes from baseline in sCD163, sMR and LBP. N = number of patients in full analysis set.

<table>
<thead>
<tr>
<th></th>
<th>0.1 mg (N=10)</th>
<th>1 mg (N=11)</th>
<th>10 mg (N=11)</th>
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<tbody>
<tr>
<td>sCD163 (mg/L)</td>
<td>0.14 [-0.32, 0.61] P=0.513</td>
<td>0.05 [-0.40, 0.49] P=0.824</td>
<td>0.44 [0.00, 0.88] P=0.0498</td>
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<td>sMR (mg/L)</td>
<td>0.03 [-0.01, 0.07] P=0.115</td>
<td>0.00 [-0.04, 0.04] P=0.985</td>
<td>0.03 [-0.00, 0.07] P=0.068</td>
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<td>LBP (µg/mL)</td>
<td>-0.21 [-3.24, 2.82] P=0.881</td>
<td>1.33 [-1.57, 4.23] P=0.330</td>
<td>0.77 [-2.07, 3.61] P=0.561</td>
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REFERENCES


Figure 1: Changes from baseline in fecal and urine wet weight output

Figure 2: Trial Design

Figure 3. Mean and individual changes from baseline for sCD163 and sMR.