BACKGROUND & AIM

- Due to the need for parenteral support, metabolic disturbances and changes in gut-liver axis signaling, patients with short bowel syndrome (SBS) are at risk of developing hepatobiliary disorders including hepatic steatosis, cholestasis, fibrosis, cirrhosis and even liver failure. Glucagon-like peptide (GLP)-2 increases portal blood flow and may ameliorate SBS-associated hepatic damage.
- We have previously presented that 3 weeks of treatment with daily subcutaneous injections of 1 mg and 10 mg glepaglutide resulted in significant reduction in fecal output and improvement in intestinal wet weight and macronutrient absorption in SBS patients.
- As exploratory endpoints, we aimed to assess effects of glepaglutide on hepatic function as measured by transient elastography (TE, FibroScan) and indocyanine green (ICG) clearance.
- FibroScan is a noninvasive method to measure the degree of liver stiffness, and it has been proposed as an alternative to liver biopsy analysis for assessment of the progression of hepatic fibrosis.
- Indocyanine Green (ICG) is a water-soluble, tricarbocyanine dye which is taken up from the plasma almost exclusively by the hepatic parenchymal cells and is secreted entirely into the bile. It is considered to be a helpful index for hepatic function.

RESULTS

Eighteen adult patients with SBS were randomized; 16 patients completed the trial. Results are shown in Table 1 and Figure 1.

- In the 10 mg, the TE baseline value (8V) of 7.3±3.1 increased by 1.4 kPa (p=0.039). Moreover, the 10 mg increased ICG-PDR (BV 19±6 %/min) by 4 %/min (p=0.0006) and reduced ICG-R15 (8V 6±5 %) by 2 % (p=0.024).
- In addition, only decreases in alkaline phosphatase (ALP; BV 189±216 U/L) of 33 U/L (p=0.032) and bilirubin (BV 4±2 µmol/L) of 2 µmol/L (p=0.016) after 10 mg, was observed.
- Liver transaminases and INR did not change.
- No significant effects were seen in the 0.1 mg dose group.

CONCLUSION

- Treatment with glepaglutide induced changes in the hepatic function, as demonstrated by increased clearance of ICG, increased TE as well as reduction in plasma ALP and bilirubin.
- While increases in clearance of ICG, and reductions in ALP and bilirubin may imply an improvement of the hepatic function, the increase in TE could be suggestive of increased hepatic stiffness. However, postprandial increase in portal blood flow has been shown to improve TE in healthy subjects and since exogenous GLP-2 administration has been demonstrated to increase intestinal and portal blood flow, a postprandial-like flow-situation may be established even in a fasting condition which most likely explains the increase in TE seen in this trial.
- Since we did not measure portal blood flow and the acute changes in TE after glepaglutide administration and since TE was performed at least 3 weeks after baseline TE, future studies addressing this subject would be of interest.

STATISTICS

Estimates are presented as adjusted means and [95% CI] in an ANCOVA model including treatment period, parenteral support and total oral intake at baseline as covariates.

REFERENCES