GB1211, an oral galectin-3 inhibitor, in decompensated cirrhotic patients: initial findings from the Phase 2 randomized, placebo-controlled GULLIVER-2 trial

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Abstract category: Liver fibrogenesis and non-parenchymal cell biology: RO4 Clinical and Translational Fibrosis Research

Background: Galectin-3 (Gal-3) is a beta-galactoside binding lectin which regulates fibrosis, inflammation and coagulation in the liver. GB1211 is a novel oral Gal-3 inhibitor which has shown potential in preclinical studies for reducing fibrosis. The GULLIVER-2 trial (NCT05009680) is an innovative, hybrid-design, 3-part study investigating safety, pharmacokinetics (PK), and exploratory efficacy of GB1211 in patients (pts) with hepatic impairment (Child-Pugh B and C). Here, we report the findings from Part 2.

Methods: Part 2 of this trial is a Phase 2, randomized, double-blind, placebo-controlled, repeat dose study of GB1211 in pts with Child-Pugh B (CP-B) liver cirrhosis. Pts were randomized 1:1 to GB1211 100 mg twice daily for 12 weeks, or matched placebo. Primary endpoints were safety and PK of GB1211. Secondary endpoints included GB1211 effect on clinical parameters, as well as liver stiffness and steatosis, measured by vibration controlled transient elastography (VCTE), and model for end-stage liver disease (MELD) score.

Results: Thirty pts were randomized to GB1211 (n = 15) or placebo (n = 15). Seventeen treatment-emergent adverse events (TEAEs) were reported (9 with GB1211 and 8 with placebo). Three serious TEAEs were observed in one patient on GB1211 but were deemed unrelated to GB1211. Steady-state PK was reached by Day 7. GB1211 reduced markers of liver damage vs placebo (Figure 1), and this reduction deepened from Week 1 to Week 6. Furthermore, improvements in liver stiffness and the controlled attenuation parameter (CAP) were observed with GB1211 vs placebo: mean change from baseline at Week 12 of −9.66 (standard deviation [SD] 22.52) kilopascal (kPa) and −20.23 (SD 42.81) decibels per meter (dB/m) vs −7.62 (SD 11.34) kPa and 4.13 (SD 63.35) dB/m, respectively. In GB1211 treated pts, the MELD score decreased as compared to an increase in placebo-treated pts.

Conclusion: In a cohort of pts with decompensated cirrhosis, GB1211 was well tolerated with predictable PK, and showed early signs of clinical effect, demonstrating that GB1211 can be administered to pts with hepatic impairment. The observed reduction of transaminases and CAP indicate a decrease in liver inflammation and potentially steatosis which, in combination with the reduction in VCTE, prompt further exploration of anti-fibrotic effects and clinical benefit.

Author disclosures:

J Genov, R Balabanska, D Stefanova-Petrova, Z Krastev: no conflicts to disclose**; B Lindmark, D Tonev, V Aslanis, B Smith, R Slack, B Jacoby, M Gray:** employee of GalectoBiotech AB, may hold stocks or shares**; D Phung**: consultant of GalectoBiotech AB and stock shareholder

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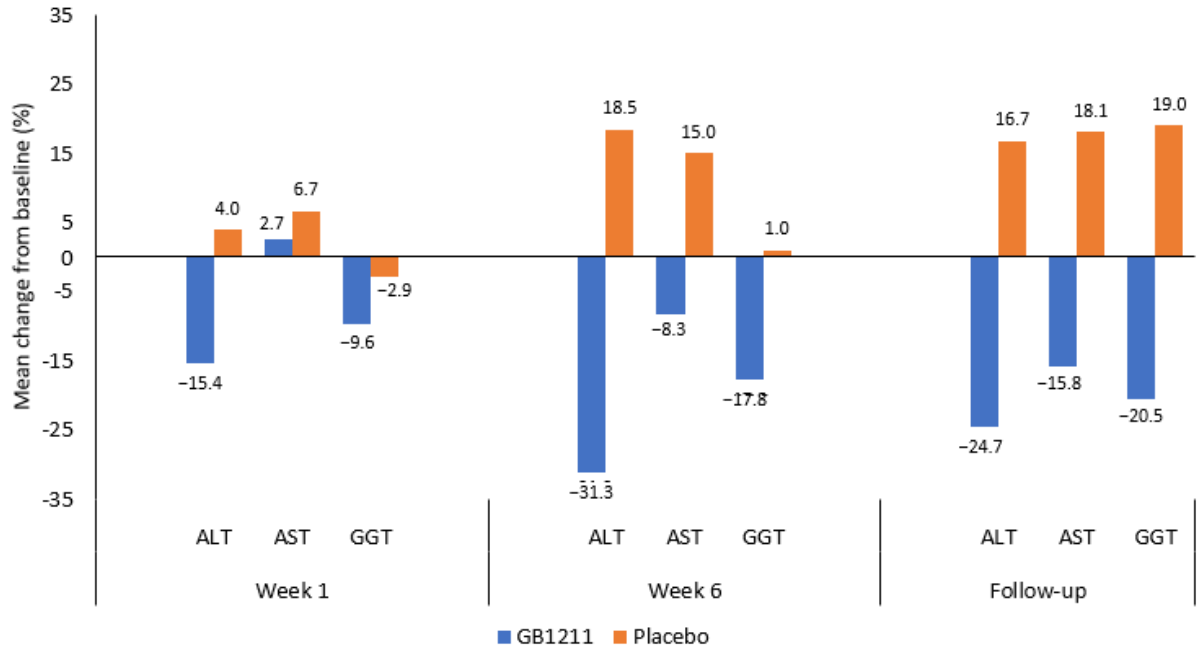
Figure 1. Mean percentage change in selected biochemistry results from baseline to Week 1, Week 6, and Follow-up



ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma- glutamyl transferase