BI 685509 improves hepatic function in subjects with Child–Pugh A cirrhosis and a liver stiffness measurement of >15 kPa: Results from the HepQuant SHUNT test

**Background and aims:**

- BI 685509 is a nitrilo side (NS)-independent activator of soluble guanylate cyclase (sGC), which catalyzes production of cyclic guanosine monophosphate (cGMP).
- cGMP stimulates hepatic vasodilation, thereby increasing sinusoidal perfusion.
- The HepQuant SHUNT test measures effective sinusoidal perfusion as a result of the flow-dependent hepatic clearance of cholate (CA) from the systemic and portal circulations.
- The test quantifies portal systemic shunting (SHUNT) and hepatic clearance of intravenously (IV) administered d4-Cholate.
- The reduction in SHUNT and increase in first-pass extraction of d4-Cholate (1-SHUNT) in subjects treated with BI 685509 compared to placebo was measured.

**Methods:**

- A randomized, placebo-controlled, double-blind (within dose groups), parallel-group, 28-day study (n=18 each in 1 mg BID and 3 mg BID groups)
- Subjects with Child-Pugh A cirrhosis (Cirrhosis etiology, n (%) for 28 days included: ALD 2 (33.3%), Hemochromatosis 2 (33.3%), Chronic viral hepatitis 1 (16.7%), and NAFLD 2 (40.0%)
- BMI, kg/m², mean (SD) 30.9 (5.1) 32.9 (5.7) 33.3 (5.7) 28.1 (3.4) 31.4 (5.2)
- MAP, mmHg, (SD) 95.5 (10.9) 100.8 (14.7) 99.2 (8.2) 94.9 (15.0) 97.7 (11.8)
- ALD 2 (33.3) 0 1 (16.7) 2 (40.0) 5 (21.7)

**Results:**

- Subject demographics were similar between dose groups
- All patients included in analysis
- Two subjects progressed from CP-A to CP-B by Day 28 (n=1 each in the 1 mg BID and 3 mg BID groups)
- BI 685509 selectively lowered the portal venous concentration of orally administered d4-Cholate, consistent with a selective effect of enhanced uptake of cholate by the liver from the portal circulation

**Conclusions:**

- The reduction in SHUNT and increase in first-pass extraction of d4-Cholate (1-SHUNT) in subjects treated with BI 685509 was due to enhanced clearance of cholate from the portal circulation (increase in portal hepatic filtration rate, Port HFR).

**Disclosures:**

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