The Disease Severity Index (DSI) from the HepQuant SHUNT Test
Sets the Stage for Predicting Drug Pharmacokinetics (PK) in Chronic Liver Disease

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1. Premise
Drug PK in subjects with advanced fibrosis or compensated cirrhosis (advanced HCV) is affected by the severity of hepatic impairment. The DSI from the HepQuant SHUNT test quantifies hepatic impairment.

2. Conclusion
- The DSI, from the HepQuant SHUNT test, is a functional score that quantifies global liver function and parallels Child-Pugh Class and Score.
- The DSI may provide an improved understanding and distinction of changes in PK and risk of DILI for diverse classes of drugs within and across Child-Pugh Class and Score.

3. Subjects
This study included data from subjects enrolled in the HALT-C trial (N=187) and the INTERCEPT 747-117 obeticholic acid (OCA) trial (N=31). In HALT-C, the rates were measured of antipyrine clearance (N=150), methionine oxidation (N=183), caffeine elimination (N=168), lidocaine→MEGX oxidation (N=171), and galactose elimination (N=183).

4. Methods
The HepQuant SHUNT test is a dual cholate clearance test involving co-administration of 20 mg 13C-cholate intravenously and 40 mg d4-cholate orally with peripheral venous blood sampling at 5, 20, 45, 60, and 90 minutes and LCMS quantification of labeled cholates. The Disease Severity Index (DSI) is a proprietary algorithm defined from the cholate clearances reflecting total effective hepatic perfusion. DSI ranges from 0 (healthy) to 50 (severe dysfunction).

5. Results
- **DSI Parallels Child-Pugh Class and Score**
- **Diverse Drugs have Diverse PK Pathways**

6. Conclusion
- The DSI is associated with risk of outcomes (Aliment Pharmacol Ther. 2021;53:928–938) and drug clearance, elimination, and metabolism. Therefore, DSI would be predicted to be associated with risk for DILI and risk for poor outcomes in DILI.