Background

In subjects with advanced fibrosis or compensated cirrhosis, drug PK is affected by the severity of hepatic impairment. The DSI from the HepQuant SHUNT test quantifies hepatic impairment. The performance of DSI with Child-Pugh (CP) was compared in predicting the PK of 5 different classes of test compounds.

Methods

This study included data from 187 subjects enrolled in the HALT-C trial, and 31 subjects from the INTERCEPT study. Oral d4-Cholate (40 mg) + juice was used to measure cholate clearance (cytosolic transport) and oral d4-Methionine (300 mg) + juice was used to measure Methionine Breath Test (cytosolic transport). The HepQuant SHUNT test is a dual breath test with increased DSI across all 5 drug classes tested. Within each Child-Pugh Class and Score, for example A5 or A6, the DSI could discriminate different degrees of functional impairment and different degrees of PK change.

Results

Obeticholic Acid (OCA) – In NASH subjects treated with OCA, DSI strongly correlated with plasma clearance of unconjugated OCA both at baseline / Day 1 (r=0.63) and at EOT: Day 85 (r=0.85). Courtesy of Intercept Pharmaceuticals Inc.

Antipyrine, Methionine, Caffeine, Lidocaine (MEGX), Galactose – There was an association of decreased drug PK in HALT-C with increased DSI across all 5 drug classes tested. Within each Child-Pugh Class and Score, for example A5 or A6, the DSI could discriminate different degrees of functional impairment and different degrees of PK change.

Conclusions and Key Takeaways

➢ The HepQuant SHUNT test DSI provides an improved understanding of the PK of a wide spectrum of drug classes in subjects with liver disease.
➢ High or increasing DSI could potentially identify the subjects at greatest risk of decompensation should they experience drug-induced liver injury (DILI).
➢ These features of DSI could be useful in drug development programs.

References


Disclosures

Steve M. Helmke, PhD, HepQuant employee (CEO) and equity member; Gregory T. Everson, MD, HepQuant employee (CSO) and equity member.