FUNCTIONAL IMPROVEMENT MEASURED BY A REDUCTION IN HEPQUANT’S DISEASE SEVERITY INDEX (DSI) AFTER SUSTAINED VIRAL RESPONSE (SVR) IN ADVANCED HEPATITIS C IS RELATED TO SEVERITY OF HEPATIC IMPAIRMENT AS DETERMINED BY BASELINE DSI

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2. Background
Patients with HCV and advanced fibrosis or cirrhosis (advanced HCV) exhibit a broad spectrum of hepatic impairment. SVR is achievable in most cases of advanced HCV, but despite SVR and biochemical improvement, a subset of patients continue to exhibit signs or symptoms of portal hypertension or cirrhosis and are at risk for clinical outcomes. In this report baseline hepatic function and change in function were measured by the HepQuant SHUNT test to identify patients with persistent hepatic impairment despite achieving SVR.

3. Subjects
Adult subjects with advanced HCV who achieved SVR and had both baseline and serial testing with HepQuant SHUNT to determine DSI were selected from both DAA-based studies (HALT-C, N = 24), and direct acting antiviral (DAA) based studies (TURQUOISE CP B (Child-Pugh B), N = 7; SOLAR 1, N = 28; and a Janssen-sponsored investigator-initiated study, N = 4). Subjects exhibited a clinical spectrum ranging from well-compensated fibrosis to CP class C cirrhosis. All subjects had measurement of DSI at baseline and at variable time points from 36 to 192 weeks post-SVR. Subjects in the HALT-C study had lower fibrosis stage and lower DSI at baseline compared to subjects in the DAA-based studies.

4. Methods
The HepQuant SHUNT test involves simultaneous administration of labeled cholates both IV and PO, timed collection of 5 blood samples over 90 minutes, and LC/MS quantification of labeled cholates. The Disease Severity Index (DSI) is a proprietary algorithm defined from the cholate clearances reflecting total effective hepatic perfusion. The DSI score ranges from 0 = the best possible liver function to 50 = the most severe dysfunction. Change in hepatic function, ∆DSI, was defined from the difference in DSI from baseline to the last measurement of DSI in each study and categories of response were defined as: Improved Function: DSI reduced (↓) by >2
Worsened Function: DSI increase (↑) by >2
Stable Function: DSI either (↓) or (↑) by ≤2

5. Results:
Subjects in HALT-C had lower fibrosis stage and lower DSI at baseline compared to subjects in the DAA-based studies. Based on ∆DSI, 28 improved (44%), 8 worsened (12%), and 28 remained stable (44%). Of the subjects who improved, 82% had baseline DSI 15 to 35; and of the subjects who worsened, 50% had baseline DSI >35 (see ∆DSI Figure).

6. Results:

Functional Changes (∆DSI) after SVR in Advanced HCV

- Worsened Function
- Stable Function
- Improved Function

∆ DSI
Baseline DSI
HALT-C Wk96
TURQUOISE CPB Wk60
SOLAR 1 Wk48
Janssen IIS Wk36
HALT-C Wk192

7. Conclusions
➢ The blood-based minimally invasive ∆DSI can monitor hepatic improvement in response to therapeutic interventions.
➢ Baseline DSI <15 may define a subset with good hepatic function that improves minimally despite effective therapy.
➢ Baseline DSI >35 may define a subset with severely impaired function, some improve but others remain at risk for decompensation and clinical outcome.

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