



THE FORUM
For Collaborative ResearchSM

U.S. Food and Drug Administration Regulatory Update

Lara Dimick-Santos

U.S. Food and Drug Administration

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Regulatory Update

Disclaimer

- The views and opinions expressed here are my own and do not represent official FDA position.
- I have nothing to disclose

Decreasing Histopathologic Progression to Cirrhosis

There is a large body of literature to support that slowing the 'rate of' or 'time to' progression to cirrhosis (F4) in a precirrhotic NASH population on histopathology predicts a decrease in adverse clinical outcomes

Histopathological Resolution of Cirrhosis



Inversely, the histopathologic reduction of fibrosis from a level of F4 (Brunt/Kleiner scale) to F3 has not been shown to predict clinical benefit, or better liver function.

Changes in Histopathology Seen with Improvements in Fibrosis/Cirrhosis



- Decreasing thickness of septa seen in treated HBV patients¹
- Hepatitis C virus (HCV) patients with fibrosis/cirrhosis who underwent treatment showed disappearance of fibrosis, regeneration and ductular proliferation, restoration of metabolic lobular zonation with persistence of portal inflammation and markers of stellate cell activation²
- Cases reported where HCV treated patients had liver stiffness but histopathology still showed cirrhosis³

1 – Sun, et al., New Classification of Liver Biopsy Assessment for Fibrosis in Chronic Hepatitis B Patients Before and After Treatment, *Hepatology*, Vol 65:5, 2017

2 – D'Ambrosio, et al., A Morphometric and Immunohistochemical Study to Assess the Benefit of a Sustained Virological Response in Hepatitis C Virus Patients With Cirrhosis, *Hepatology*, Vol 56:2, 2012

3 – personal communication Guadalupe Garcia-Tsao



Multiple different assessments of improvements in fibrosis and in the synthetic function of the liver (e.g., TB, platelets, INR, albumin) should be used in clinical trials in a cirrhosis population where improvement in fibrosis is the endpoint



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