Session 5: Causality Assessment and the Role of Liver Biopsy as Part of the Evaluation of Suspected DILI in NASH Clinical Trials

Overview: Causality assessment for suspected drug-induced liver injury (DILI) is a major challenge during drug development, especially in studies of NASH patients presenting with elevated liver enzymes at the start of a trial.

Whether or not to obtain a liver biopsy to aid in diagnosis of suspected DILI is a subject of ongoing debate. The inherent risks of a liver biopsy must be weighed against the potential to collect useful information from the evaluation of liver tissue. Though histologic results may be nonspecific, with little impact on establishing the diagnosis of DILI or in changing the clinical assessment, histologic evaluation of liver tissue may have prognostic value and is the only way to characterize the pattern, severity, and distribution of hepatic injury.

Prior to considering a liver biopsy, other issues must be addressed, such as the extent and nature of blood tests to obtain, the phase of drug development, and the issue of rechallenge.

The goal of this session will be to address:

1. The pros and cons of obtaining a liver biopsy as part of the evaluation of new onset of elevated liver blood tests occurring during NASH clinical trials.
2. What information may be obtained from the histologic read that could assist in causality assessment.
3. Defining the spectrum of histology that can be seen with NASH to differentiate finding of NASH versus findings of DILI.
4. Best practices for assessment of unexpected or atypical findings found on histology.
5. What work-up (e.g., hepatitis E) should occur prior to obtaining a liver biopsy to assist in causality assessment.
6. Monitoring and stopping rules for DILI assessment.
7. The Phase of NASH drug development and extent of assessment.
8. The establishment of an external DILI monitoring committee prior to initiation of study.

Draft Agenda

January 28, 2022
12:00-2:00pm ET

Moderators: *Melissa Palmer, Liver Consulting LLC*
Veronica Miller, Forum for Collaborative Research

12:00 – 12:05pm	Welcoming Remarks	*Jessica Weber, Forum for Collaborative Research*
12:05 – 12:19pm	Introduction	*Veronica Miller, Forum for Collaborative Research*
12:10 – 12:25pm	Setting the Stage: Review of Issues and Recent Data	*Melissa Palmer, Liver Consulting LLC*
12:25 – 1:25pm	Panel Discussion: DILI and Regulatory Experts	*Arie Regev, Eli Lilly & Company* *David Kleiner, NCI, NIH* *Naga Chalasani, Indiana University School of Medicine* *Paul Hayashi, U.S. Food and Drug Administration* *Mark Avigan, U.S. Food and Drug Administration* *Arun Sanyal, Virginia Commonwealth University*
1:25 – 1:50pm	Group Discussion	*All*
1:55 – 2:00pm	Closing Remarks	*Veronica Miller, Forum for Collaborative Research*

Adjourn Webinar