THE FORUM
For Collaborative Research℠

The Intercept Experience

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Two Issues for Today's Discussion

1. "What is the Optimal Number of Hepatopathologists?"
   - How do we reduce discordance in liver histology assessments in clinical trials?
   - With a panel (odd number) of pathologists, can we align on "consensus" of binary assessments?
   - In non-binary assessments (e.g., fibrosis grade) how is the grade decided?

2. Liver biopsies: Glass vs Digital
   - With thousands of slides requiring review, the transport of glass slides is impractical and risks catastrophe for sponsors
   - Inadequate peer-reviewed data exist to make conclusions about interpretation of disease severity on glass vs digitized slides
   - Sponsors are encouraged to have consistent slide methods within a study

Ongoing Issues with Dependence on Liver Histology

FDA Communications

- Concern regarding inter- and intra-observer variability
- Consider using a pre-specified adjudication histopathology committee
- Reread biopsy results by at least 3 histopathologists with expertise in NASH; include potential strategies to resolve discordant readings

Draft FDA guidance[1]

- Standardize procedure for processing biopsy slides
- Prespecified details of liver biopsy interpretation
- Improved pathologists' training both before and during the study
- A minimum of 2 pathologists; 3rd pathologist if discordant

1. Anania 2020, Matsubayashi 2021.