Liver Forum 7
October 19th, 2017

Division of Gastroenterology and Inborn Errors of Metabolism
(DGIEP)
Lara Dimick-Santos, MD

The Liver Team at the FDA

- Donna Griebel, MD – Division Director
- Dragos Roman, MD – Deputy Director
- Lisa Soule, MD – Acting Associate Director
- Stephanie O. Omokaro, MD – Team Leader
- Kathleen Donohue, MD – Team Leader
- Capt. Anissa Davis, BSN, MPH, CPHM, GWCPM – Project Manager
- CDR Cheronda Cherry-France, RN, BSN, MPH – Acting Chief Project Manager

The Liver Team at the FDA (cont.)

- Lara Dimick-Santos, MD - Medical Reviewer
- Ruby Mehta, MD - Medical Reviewer
- Anil Nayyar, MD - Medical Reviewer
- Veronica Pei, MD - Medical Reviewer
- Suna Seo, MD - Medical Reviewer

New Applications

- Spectrum of Fatty Liver Disease
  - NAFL – Research INDs
  - NASH – in all phases of clinical trials
  - Compensated cirrhosis – in all phases of clinical trials
  - Decompensated cirrhosis – in phase 2 trials

Compensated Cirrhosis

- What is the best way to stage cirrhosis?
  - Child-Pugh, MELD, cirrhosis stages, stages of Portal HTN
- Compensated cirrhosis secondary to NASH – in all phases of clinical trials
  - Surrogate endpoints - Improvement in fibrosis by one stage be supported by evidence of clinical benefit such as total bilirubin and other biomarkers of disease
  - Clinical benefit – all cause mortality, transplant and decompensation events

Decompensated Cirrhosis

- Staging Cirrhosis
  - Compensated - include presence of varices?
  - Decompensated - how to stage?
    - Ascites vs. bleeding and HE
  - Child-Pugh Score
  - MELD/PELD Score
- Endpoints?
  - Death only?
  - Decompensation events, how to define what new events are meaningful in this diverse population
  - MELD score changes?

Quality Control for Histology

- Interobserver variability
  - central reader or group of readers with adjudication of discordance
  - calculate inter-rater reliability coefficient

- Intraobserver variability
  - a stratified random subset of readings are later repeated in a blinded fashion
  - calculate an intra-rater reliability coefficient

Ethical Considerations for Clinical Trials

- We currently recommend that sponsor's obtain histopathological data in phase 2B trials to inform the design and powering of phase 3 trials to support a marketing application.
  - Is it ethical to proceed with large phase 3 trials with less than histopathological data?

Thank you from the Liver Team