

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Gastrointestinal Drugs Advisory Committee (GIDAC) Meeting
May 19, 2023

DRAFT QUESTIONS

1. **DISCUSSION:** Discuss the strength of the available efficacy data on the histopathologic endpoint, a surrogate endpoint that is reasonably likely to predict clinical benefit, in nonalcoholic steatohepatitis (NASH) patients with Stage 2 or 3 fibrosis treated with obeticholic acid (OCA) 25 mg.
2. **DISCUSSION:** Based on the data presented concerning cholestatic drug-induced liver injury (DILI) in OCA 25 mg-treated patients, discuss:
 - a. Whether periodic liver enzyme monitoring could adequately mitigate the risk of DILI,
 - b. The frequency of such monitoring,
 - c. What stopping criteria should be developed to aid clinicians' decisions to discontinue treatment
3. **VOTE:** Given the available efficacy and safety data, do the benefits of OCA 25 mg outweigh the risks in NASH patients with Stage 2 or 3 fibrosis?
4. **VOTE:** Clinical outcome events in patients enrolled in Trial 747-303 will continue to be captured to evaluate clinical benefit in support of a future application for traditional approval. At present, which of the following would you recommend:
 - a. Approval of OCA 25 mg at this time, under the accelerated (approval) pathway, based on efficacy data on a histopathologic surrogate and available clinical safety data;
 - b. Defer approval until clinical outcome data from Trial 747-303 are submitted and reviewed, at which time the traditional approval pathway could be considered.