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

Pulmonary-Allergy Drugs Advisory Committee (PADAC) Meeting
August 31, 2020

DRAFT QUESTIONS

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1. **DISCUSSION:** Discuss the persuasiveness of the data in the IMPACT trial to support the claim that fluticasone furoate, as a component of TRELEGY ELLIPTA, improves all-cause mortality in chronic obstructive pulmonary disease (COPD). Include the following elements in your discussion:

    a. The exploratory nature of the all-cause mortality (ACM) analysis, the lack of Type I error control, and the strength of evidence in IMPACT
    b. Whether the ACM results from IMPACT are persuasive in light of the additional ACM data from fluticasone comparisons provided by SUMMIT and TORCH
    c. The observed timeframe of the IMPACT results, i.e., the early separation in survival

2. **DISCUSSION**: Discuss the implications of pre-study inhaled corticosteroid (ICS) use and ICS-removal on the interpretation of the ACM data in the IMPACT trial. Include the following elements in your discussion:

    a. The clinical understanding of the contribution of ICS to COPD therapy and the effects of ICS removal in patients with uncontrolled COPD and frequent exacerbations
    b. The implications of randomization to study drugs that do not contain ICS among patients with uncontrolled COPD despite pre-study ICS therapy
    c. The observed timeframe of the IMPACT results, i.e., the early separation in survival
    d. The pre-study ICS subgroup data from SUMMIT and TORCH, in light of the differences from IMPACT in study design and patient population

3. **DISCUSSION:** Discuss the generalizability of the IMPACT ACM data to relevant clinical practice decisions about fluticasone furoate (FF) as add-on therapy in COPD. Include the following elements in your discussion:

    a. The clinical relevance and persuasiveness of the ACM results from fluticasone comparisons among the ICS-naïve subgroups of IMPACT, SUMMIT, and TORCH
    b. The clinical relevance of data from the pre-study ICS subgroup to inform decisions regarding the addition of FF
    c. The clinical relevance of the IMPACT trial design and its ability to assess the benefit of adding FF
    d. The clinical implications of the proposed labeling claim in light of the submitted data

4. **VOTE**: Do the data from the IMPACT trial provide substantial evidence of efficacy to support the claim that TRELEGY ELLIPTA improves all-cause mortality in patients with COPD?

    a. If no, what further data are needed?