

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

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

QUESTIONS

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?