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Session A32 - ASTHMA: CLINICAL STUDIES II

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A1320 / P711 - Oral Corticosteroid Tapering During Benralizumab Treatment of Severe, Uncontrolled Eosinophilic Asthma: PONENTE Phase IIIb Clinical Trial

May 19, 2019, 11:15 AM - 1:00 PM | Area E (Hall F, Level 2), KBHCCD

Participant

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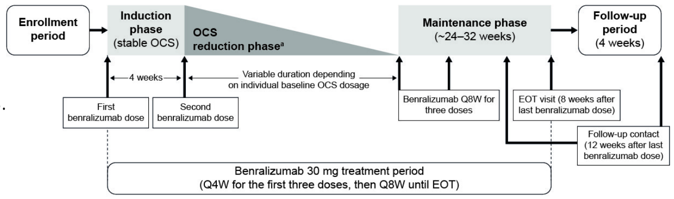
Abstract

Rationale: In the Phase III ZONDA trial (NCT02075255), benralizumab produced a median 75% reduction from baseline in oral corticosteroid (OCS) dosage (vs. 25% for placebo) while maintaining asthma control for patients with OCS-dependent severe asthma. The OCS tapering speed in ZONDA with its relatively short trial duration (28 weeks) perhaps did not provide enough time for patients receiving baseline prednisone >12.5 mg/day to eliminate OCS use. The PONENTE (NCT03557307) trial builds on ZONDA and other OCS-sparing studies. PONENTE has a more aggressive steroid reduction schedule for prednisone doses ≥7.5 mg/day than previous studies, and it includes an evaluation of adrenal insufficiency (AI) and an algorithm to specifically taper OCS dosage when prednisone is ≤5 mg/day. It also has a longer maintenance phase to assess OCS reduction up to 6 months after completing OCS tapering. **Methods:** PONENTE is an open-label study divided into three phases (figure). Patients will receive benralizumab 30 mg subcutaneously (first three doses every 4 weeks, then every 8 weeks [Q8W]). OCS reduction is initiated after the second benralizumab dose and will be dependent on baseline OCS use/loss of asthma control until reaching ≤5 mg/day OCS. Following 4 weeks at ≤5 mg/day, further OCS reduction will also be dependent on cortisol concentration and AI status (evaluated by hypothalamic-pituitary-adrenal axis integrity) assessed by ACTH stimulation testing. Adult patients with asthma receiving high-dosage inhaled corticosteroids/long-acting β2-agonists (≥6 months before enrollment) and OCS (≥5 mg/day prednisone stable dosage for ≥4 weeks before enrollment), and with blood eosinophil counts of ≥150 cells/μL or ≥300 cells/μL at enrollment and 12 months before, respectively. **Results:** PONENTE aims to enroll ~600 patients in ~180 clinical centers worldwide. The trial started on August 1, 2018, and planned completion is October 2020. The two primary endpoints are 1) the number of patients achieving 100% reduction in daily OCS, and 2) the number of patients achieving 100% reduction in daily OCS or achieving ≤5 mg/day dosage, if AI prevented further reduction. Safety and change from baseline in health-related quality of life will also be assessed. **Conclusions:** PONENTE will provide valuable guidance for clinicians on tapering OCS dosage following benralizumab introduction for the treatment of OCS-dependent patients with severe, uncontrolled eosinophilic asthma, including management of AI. These results aim to direct future clinical practice on OCS tapering following introduction of biologics, and potentially drive guideline changes.

Figure. PONENTE Study Flow Chart



[a]Guided by schema of OCS reduction defined in the study protocol.
EOT, end of treatment; OCS, oral corticosteriods; Q4W, every 4 weeks; Q8W, every 8 weeks.

(http://files.abstractsonline.com/CTRL/0e/8/81c/a68/a06/4ce/eac/cee/1bf/933/f43/ce/g10350_2.jpg)