Dose-Ranging Effects of Extrafine Beclomethasone Dipropionate (BDP) Delivered Via a Pressurized Metered-Dose Inhaler (PMDI) in Patients with Asthma: The Beam Study

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Rationale: As part of the US development of single-inhaler triple therapy BDP/FF/G (extrafine beclomethasone dipropionate (BDP), formoterol fumarate (FF), glycopyrronium (G)), clinical dose-confirmation of each individual component is required. The BEAM study characterized the dose-response of BDP in patients with asthma.

Methods: This was a phase II, multicenter, randomized, double-blind, placebo and active-controlled, parallel group, dose-ranging study. Patients were 18-75 years with asthma and symptomatic on low-medium ICS dose. They had an Asthma Control Questionnaire score ≥1.5, pre-bronchodilator FEV₁ 50-85% predicted normal, FEV₁ reversibility ≥12% and ≥200mL after 360µg albuterol, basal morning serum cortisol level 5-28µg/dL, and BMI between 18.5-35kg/m². Following a 2-week run-in period where prior ICS was switched to a therapeutically-equivalent dose of QVAR® (BDP HFA pMDI) 80 – 160 µg twice daily (bid), eligible patients were randomized to receive treatment with BDP 50, 200, 400µg bid corresponding to 100, 400, 800 µg total daily dose (TDD) , placebo, or open-label QVAR® 160µg bid (320 µg TDD) for 8 weeks. Albuterol could be taken as rescue throughout the study. The primary efficacy endpoint of change from baseline in pre-dose morning FEV₁ at Week 8 was performed on the intent-to-treat population (ITT) and on per protocol (PP) population for sensitivity purposes. Change from baseline in 24-hr urinary free cortisol (UFC) was assessed at Week 8, and treatment-emergent adverse events (TEAEs) were collected. Results: The ITT population included 602 patients, 62% females, 71% white, 58% on medium-dose ICS. Mean (SD) age was 48.1 years (14.5), baseline % predicted FEV₁ 68.5% (8.4), and reversibility 523mL (26.0%). Baseline characteristics were comparable across all treatment groups. The PP population included 554 patients. Statistically significant (p<0.05) improvements from baseline vs Placebo in the primary efficacy endpoint were observed with BDP 400µg TDD (113 mL; p = 0.015) in the ITT population, and BDP 400 and 800µg TDD in the PP population (149mL; p = 0.002 and 122mL; p = 0.013, respectively). TEAEs occurred in 23.5%, 25.0%, 30.6%, 34.7%, and 30.6% of patients, and change from baseline in median 24-hour UFC (nmol/d) were -3.6, -5.4, -4.1, +1.4 and -3.5 on BDP 100, 400, 800µg TDD, Placebo and QVAR® 320µg TDD, respectively. Conclusion: This dose-ranging study demonstrated that the BDP 400 µg TDD appears to offer the optimal efficacy/safety balance to include in the extrafine single-inhaler triple therapy BDP/FF/G pMDI.

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