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120 - CLINICAL AND ENDOSCOPIC IMPROVEMENTS WITH RISANKIZUMAB INDUCTION AND MAINTENANCE DOSING *VERSUS* PLACEBO ARE OBSERVED IRRESPECTIVE OF NUMBER OF PRIOR FAILED BIOLOGICS

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Resumen

Introduction: In phase 3 studies, risankizumab (RZB), an interleukin-23 inhibitor, was well-tolerated and superior to placebo (PBO) for inducing and maintaining clinical remission and endoscopic response in patients with moderate to severe Crohn’s disease (CD) who failed/were intolerant to conventional or biologic therapy.1.2 This post-hoc analysis examined efficacy and safety of RZB in patients with prior failure of biologic therapy (bio-failure) according to the number of prior biologics failed.

Methods: Clinical remission, endoscopic outcomes, and deep remission were assessed for RZB versus (vs) PBO following induction and maintenance dosing based on the number of prior biologics failed (1, 2, ≥ 3). Pooled induction data were reported for PBO and RZB 600 mg intravenous (IV) q4w groups at Week (Wk) 12. Data from the withdrawal (PBO SC) and RZB 360 mg subcutaneous (SC) q8w groups were reported at Wk 52 of FORTIFY. P-values for pairwise treatment comparisons were provided.

Results: At baseline, 48%, 25%, and 27% of patients failed 1, 2, and ≥ 3 prior biologics, respectively. Baseline characteristics were well balanced across subgroups, although disease duration and steroid use were slightly higher in the ‘ ≥ 3’ subgroup. Most (90%) patients who failed 1 biologic and all who failed ≥ 2 biologics were anti-TNF refractory. The proportion of patients with prior vedolizumab exposure across the 1, 2, ≥ 3 bio-failure subgroups was 6%, 27%, and 75%, respectively; prior ustekinumab exposure was 2%, 12%, and 59%, respectively. Across the bio-failure subgroups, more patients achieved the endpoints of clinical remission and endoscopic

response with RZB 600 mg IV *vs.* PBO at induction Wk 12 (p ≤ 0.019). Rates of endoscopic remission, ulcer-free endoscopy, and deep remission were also higher with RZB *vs.* PBO among the subgroups at Wk 12. In general, greater efficacy was in observed in patients failing fewer biologics. At FORTIFY Wk 52, more patients achieved endoscopic remission (p ≤ 0.001), ulcer-free endoscopy (P ≤ 0.008), and deep remission (p ≤ 0.012) in the RZB 360 mg SC treatment group *vs.* withdrawal (PBO SC) across all bio-failure subgroups; rates of clinical remission were variable across subgroups. There were no differences in treatment emergent adverse events among subgroups at induction Wk 12 or maintenance Wk 52.

Conclusions: RZB was effective and well tolerated in patients with CD irrespective of number of prior biologics failed. Achievement of endoscopic outcomes with RZB at Wk 12 and Wk 52 were lower as the number of failed biologic therapies increased. The treatment difference between RZB maintenance and withdrawal (PBO SC) for achieving clinical remission increased with the number of failed prior biologics, highlighting higher PBO rates for symptomatic improvement in less refractory patients.