circulation, with a median time to maximum concentration of 0.5 hour for all doses. Both Cmax and AUC of GB004 increased in a dose-dependent manner on Day 1 and 7. Concentrations of GB004 measured in colon biopsies were greater than concentrations in the plasma of biopsy. Changes in plasma GB004 or VEGF levels were similar for GB004 and placebo with no dose-related effects observed.

Conclusions: This study demonstrated that multiple daily doses of GB004 solution were safe and tolerable. The PK profile was consistent with its intended preferential exposure in the gut. In support of the gut-targeted exposure, HIF target genes EPO and VEGF were not modulated in plasma. A clinical study of GB004 is ongoing in patients with ulcerative colitis to explore safety, PK, and pharmacodynamics both systemically and within colonic tissue (NCT03860896). A tablet formulation is also being developed.

P067 IMPACT OF MIRIKIZUMAB TREATMENT ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ULCERATIVE COLITIS: A PHASE 2 STUDY ANALYSIS USING THE SF-36 V2 STANDARD
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Background: Mirikizumab (LY3074828) is a humanized monoclonal antibody directed against the p19 subunit of IL-23, and has demonstrated efficacy in psoriatic arthritis, ulcerative colitis (UC), and Crohn’s disease. The effect of miri on health-related quality of life (HRQoL) as measured by the SF-36 Item Short Form Health Survey v2 (SF-36 v2) was examined in a Phase 2, multicenter, randomized, parallel-arm, double-blind placebo (PBO)-controlled trial (NCT02891226) in patients with moderate to severe active UC.

Methods: Patients were randomized 1:1:1:1 to receive intravenous PBO, miri 50mg or 200mg with possibility of exposure-based (EB) dose increases, or fixed mini 600mg every 4 weeks (Q4W), with efficacy assessment at Week 12. Patients with clinical response to miri at Week 12 were re-randomized 1:1 to a double-blind maintenance treatment of miri 200mg subcutaneously (SC) Q4W or 12 weeks (Q12W) and were treated through Week 52. The SF-36, a 36-item patient-completed questionnaire with recall period past 4-weeks, that measures 8 domains (physical functioning, role-physical, role-emotional, bodily pain, vitality, social functioning, mental health, and general health) and two summary scores, physical component summary (PCS) and mental component summary (MCS), was assessed at baseline and at Weeks 4, 8, 12, 24, 32, and 52. Treatment comparisons were evaluated using mixed effects for repeated measures for mean improvement of PCS, MCS, and domain score changes with treatment, geographic region, and prior biologic UC therapy use as factors.

Results: The PCS was significantly higher in all mini doses at Week 12 (Least Squares Mean (LSM) ± SE: PBO: 45.4±0.8; miri 50mg: 48.2±0.9; p=0.011; 200mg: 48.0±0.8; p=0.022; 600mg: 49.0±0.9; p=0.002; Fig 1A), while the MCS was significantly higher in the miri 200mg and 600mg groups (PBO: 42.5±1.2; miri 50mg: 43.8±1.3; 200mg: 46.1±1.2; p=0.022; 600mg: 49.0±0.9, p=0.002; Fig 1B). Of the 8 SF-36 domains, 7 (physical functioning, role-physical, role-emotional, social functioning, vitality, bodily pain, and mental health) showed statistically significant improvement at Week 12 in at least one mini dose group compared to PBO, while 1 (general health) demonstrated a numerical improvement (Fig 1C). Patients who continued onto randomized maintenance treatment sustained the improved scores through Week 52 (Figure 2). These results paralleled the observed treatment associated benefits on clinical response and remission rates at Weeks 12 and 52.

Conclusion: Mirikizumab treatment results in significant improvements in patient HRQoL demonstrated by significantly improved SF-36 scores after 12 weeks of induction treatment, which were sustained during an additional 40 weeks of maintenance treatment.