Efficacy and Safety of Omilancor in a Phase 2 Randomized, Double-blind, Placebo-controlled Trial of Patients with Ulcerative Colitis

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Introduction. Omilancor is an oral, gut-restricted, small molecule, first-in-class LANCL2 agonist for ulcerative colitis (UC) and Crohn's disease (CD). Through LANCL2 activation, omilancor locally increases the suppressive capacity of regulatory immune cells, including regulatory CD4+ T cells (Tregs), in the intestinal mucosa. Once daily omilancor was well tolerated up to doses of 7500 mg/day in healthy volunteers in Phase 1.

Methods. In a Phase 2 study, adult patients with Mayo Clinic scores (MCS) of 4 – 10 and endoscopic subscores of 2 or more were randomly assigned to groups given omilancor 440 mg QD, omilancor 880 mg QD or placebo for 12 weeks. The primary endpoint was clinical remission after 12 weeks as defined by rectal bleeding (RB) equal to 0, stool frequency (SF) equal to 0 or 1 and endoscopic appearance (MES) equal to 0 or 1. Patients who achieved clinical response were eligible for blinded maintenance treatment in a treat-through design. A modified intent to treat (mITT) population was defined by patients with RB > 0, histological activity and elevated fecal calprotectin (FCP) at baseline.

Results. Oral omilancor was well tolerated with no trends in AE profile observed and no dose-limiting toxicities. In the mITT population, clinical remission was induced in 30.4% of omilancor treated patients relative to 3.7% of patients given placebo (Δ = 26.7, P = 0.01). Endoscopic remission, defined as a MES < 2 was induced in 39.1% of patients treated with omilancor relative to 18.5% of patients given placebo (Δ = 20.6, P = 0.11). Histological remission, defined as a Geboes score < 2b.1 with absence of neutrophils in the lamina propria, was induced in 43.5% of patients treated with omilancor relative to 22.2% of patients given placebo (Δ = 21.3, P = 0.14). In patients to enter the maintenance period, durable remission, defined as clinical remission at weeks 12 and 30, was achieved in 38.5% of patients treated with omilancor relative to 21.4% of patients given placebo (Δ = 17.1, P = 0.05). In the same population, endoscopic response was achieved in 73.1% of patients treated with omilancor relative to 53.6% of patients given placebo (Δ = 19.5, P = 0.02). PK analysis validated a gut-restricted profile with stable drug levels in stool over the treatment period, penetration into colonic biopsy tissue and limited systemic exposure.

Discussion. Once a day oral dosing with omilancor was well-tolerated and induced clinical remission in a Phase 2 UC population.

Primary Objective
- The primary objective of this proof-of-concept study was to establish the efficacy of oral BT-11 in inducing clinical remission at Week 12 in subjects with ulcerative colitis (UC).

Key Inclusion Criteria
- Male and female subjects with active UC defined by a total Mayo Score of ≥ 4 with MES ≥ 2 (confirmed by central reader); 5-aminosalicylates (max 4.8 g/day) and oral corticosteroids (max 20 mg/day prednisone or equivalent) must be stable for the 12-week induction period.

	Placebo (N = 27)	Omilancor 440 mg (N = 23)	Omilancor 880 mg (N = 19)	Pooled Omilancor (N = 42)	Total (N = 69)
Total Mayo score					
Mean (SD)	8.2 (1.3)	8.3 (1.0)	8.2 (1.4)	8.3 (1.2)	8.2 (1.3)
Median (min, max)	8.0 (6, 11)	8.0 (6, 11)	8.0 (6, 11)	8.0 (6, 11)	8.0 (6, 11)
Baseline use of corticosteroid, n (%)					
No	20 (74.1%)	17 (73.9%)	15 (78.9%)	32 (76.2%)	52 (75.4%)
Yes	7 (25.9%)	6 (26.1%)	4 (21.1%)	10 (23.8%)	17 (24.6%)
Mayo endoscopic score (MES)					
Mean (SD)	2.7 (0.5)	2.8 (0.4)	2.6 (0.5)	2.7 (0.5)	2.7 (0.5)
Median (min, max)	3.0 (2, 3)	3.0 (2, 3)	3.0 (2, 3)	3.0 (2, 3)	3.0 (2, 3)
Fecal calprotectin concentration (µg/g)					
Mean (SD)	850 (332)	885 (400)	735 (335)	817 (380)	830 (362)
Median (min, max)	890 (273, 1251)	1068 (258, 1251)	674 (254, 1251)	747 (254, 1251)	854 (254, 1251)

Table 1. Baseline patient demographics

Baseline medications and disease severity parameters (Mayo score, MES, FCP) were well balanced across treatment arms with a median Mayo score of 8 and a MES of 3 (**Table 1**).
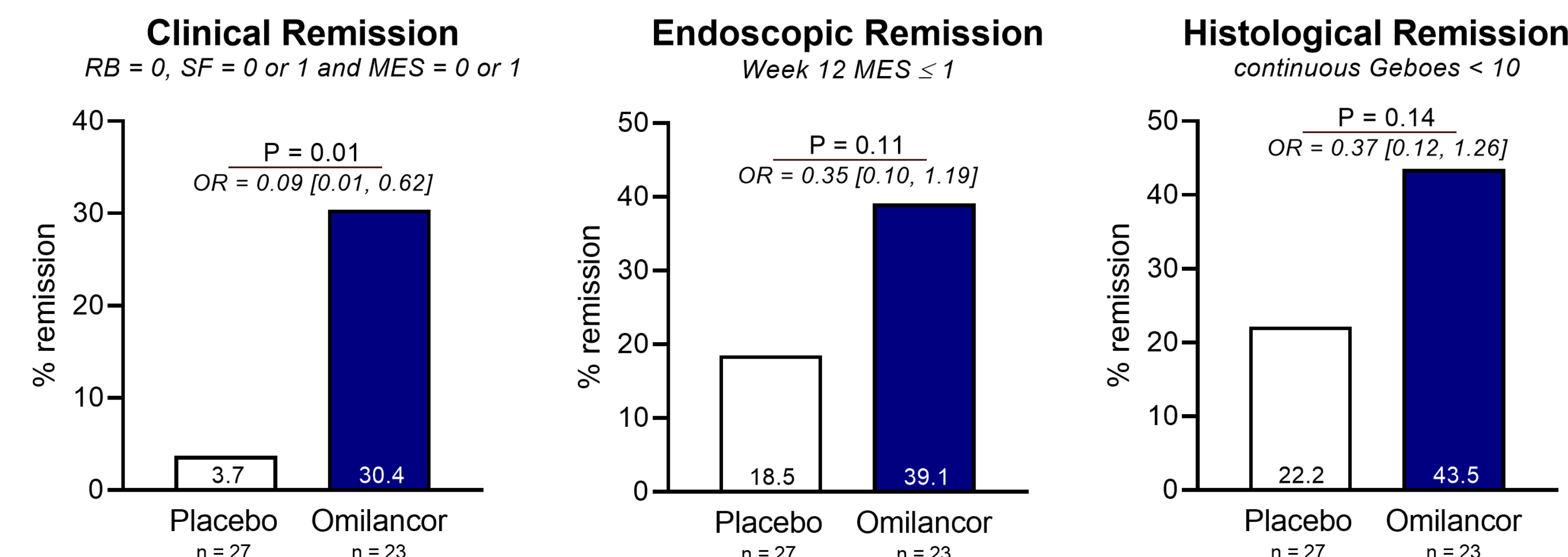

Figure 1. Primary and key secondary endpoints at Week 12

In the mITT population, the primary endpoint of induction of clinical remission at week 12 was met with 30.4% of patients treated with omilancor achieving remission (**Fig. 1**). Similar positive trends in endoscopic and histological remission were observed.
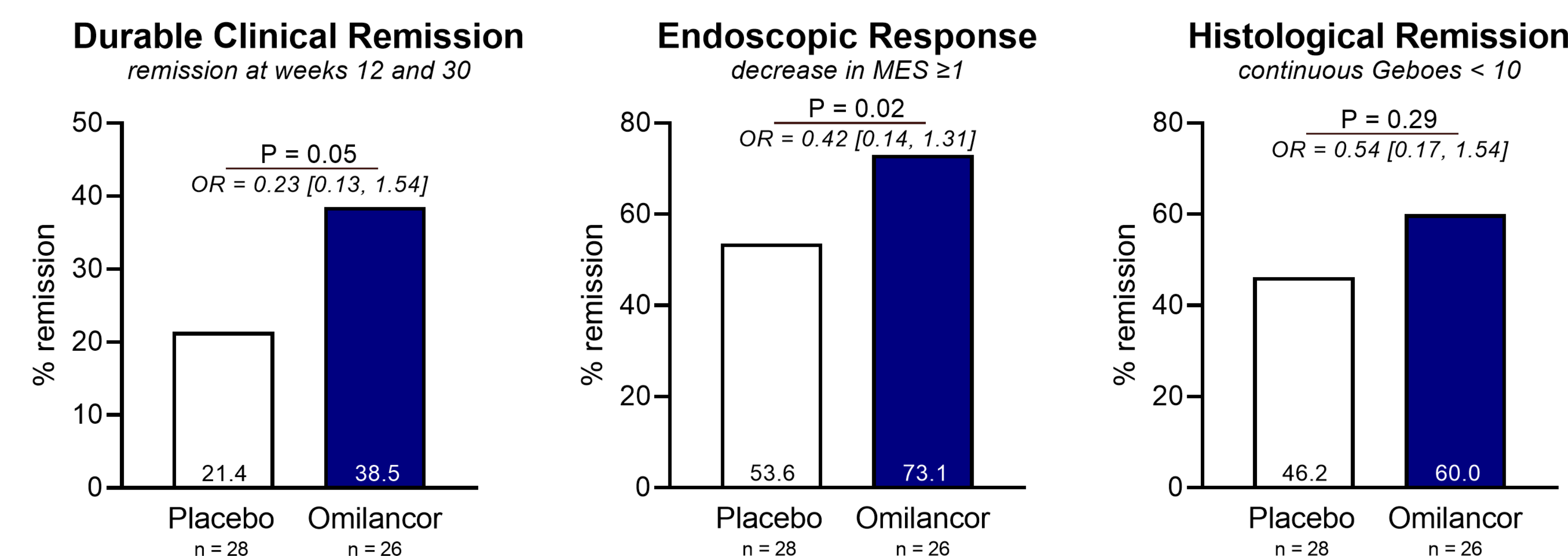

Figure 2. Key exploratory endpoints at Week 30

Maintenance clinical outcomes and biomarker assessment were key exploratory outcomes of the study. Omilancor was observed to provide statistically significant changes in durable clinical remission and endoscopic response at week 30 (**Fig. 2**). Meanwhile, a positive trend in fecal calprotectin normalization and mean change from baseline were observed as early as week 2 of the study (**Fig. 3**). Notably, normalization of fecal calprotectin was well associated with endoscopic-histologic mucosal improvement with approximately 75% of patients with fecal calprotectin normalization experiencing mucosal improvement.
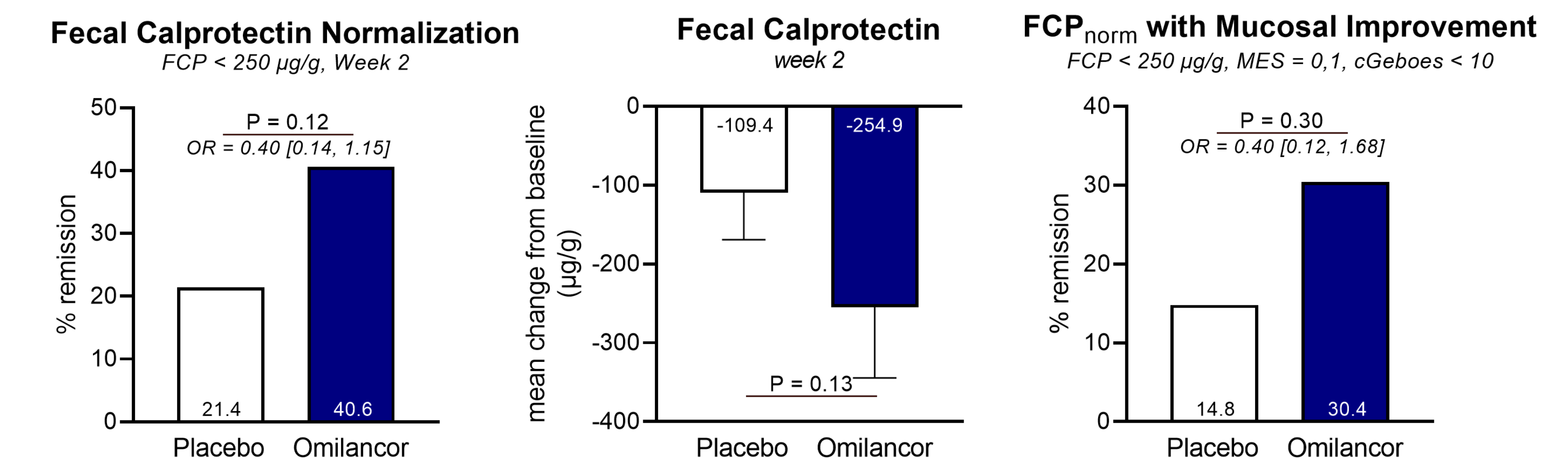

Figure 3. Fecal calprotectin normalization and change from baseline

One hundred and twenty five total TEAEs were reported in the study. 30.3% of patients in the placebo group and 25.8% of the patients in the omilancor group reported at least TEAE. The majority (52.5%) of TEAEs were considered not related to study drug. Only 4 TEAEs was considered severe, all of which were not associated with study drug. The most frequently reported TEAE was worsening of UC which occurred with equal frequency in the placebo and omilancor groups. No apparent safety findings were noted following medical review of clinical laboratory result listings.
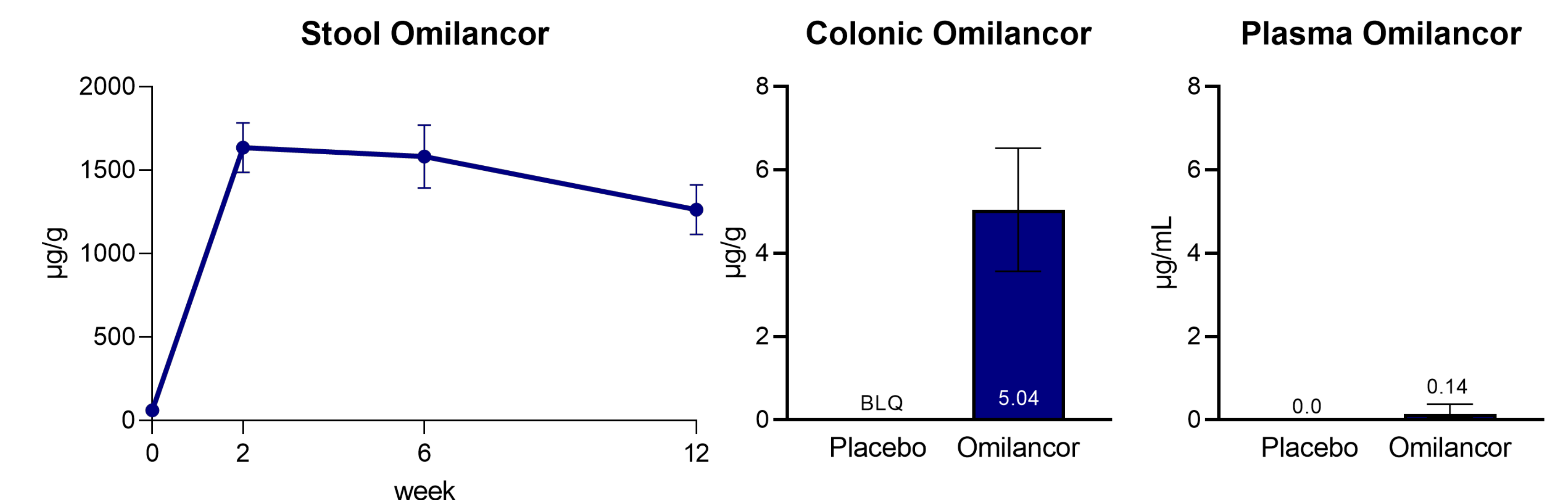

Figure 4. Pharmacokinetics of omilancor in UC patients.

Once daily oral dosing with omilancor resulted in stable stool concentrations over the 12 week induction period (**Fig. 4**). A substantial amount of omilancor was observed within colonic biopsy tissue collected at week 12. In contrast, median plasma concentrations were 0.009% of stool concentrations and 3% of colonic biopsy concentrations.

If you are interested in learning more about the omilancor mechanism of action or participating in the omilancor Phase 3 clinical program, please contact pm@nimmun.com.