Efficacy and Safety of Omilancor in a Phase 2 Randomized, Double-blind, Placebo-controlled Trial of Patients with Crohn's Disease

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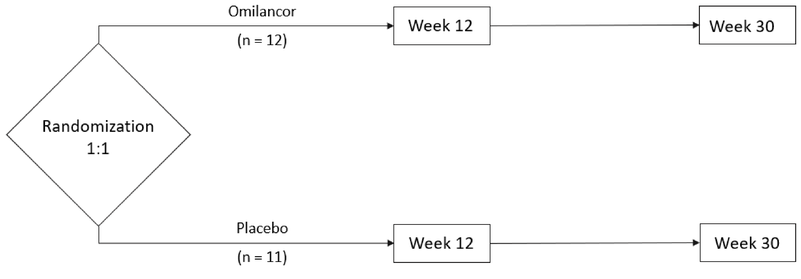
Introduction. Omilancor is an oral, gut-restricted, first-in-class LANCL2 agonist for ulcerative colitis (UC) and Crohn's disease (CD). Through LANCL2 activation, omilancor locally increases the suppressive capacity of regulatory immune cells, including regulatory CD4+ T cells (Tregs), and restores metabolic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

Methods. In a Phase 2, proof-of-concept, double-blind, parallel-group study, adult patients with moderate to severe Crohn's disease (CDAI 220 – 450; SES-CD ≥ 6 [≥ 4 for isolated ileitis]) were randomly assigned to groups given omilancor 880 mg QD (N = 12) or placebo (N = 11) for 12 weeks. The primary endpoint of the study was clinical remission defined as the proportion of patients with CDAI < 150 at Week 12. Key secondary endpoints were also assessed including clinical response (defined as CDAI decrease from baseline ≥ 100 points or CDAI < 150), PRO-2 remission (defined as an abdominal pain subscore of 0 or 1 and a stool frequency subscore ≤ 3) and fecal calprotectin normalization.

Results. Oral omilancor was well tolerated with no trends in AE profile observed and no SAEs related to study drug. Clinical remission was induced in 25.0% of patients within the omilancor group relative to 9.1% of the placebo group (Δ = 15.9). Similar effect sizes were observed within biologic experienced (Δ = 20.0) and biologic naïve (Δ = 14.3) subpopulations in clinical remission. Clinical response and PRO-2 remission were both induced in 41.7% of patients within the omilancor group relative to 9.1% of the placebo group (Δ = 32.6). Fecal calprotectin was normalized (< 250 µg/g) in 33.3% of patients within the omilancor group relative to 14.3% of the placebo group (Δ = 19.0). Mean percent change from baseline in CDAI score and fecal calprotectin were also observed to be greater in the omilancor group relative to placebo. Transcriptional analysis of ileal biopsies collected at baseline and Week 12 revealed positive trends in LANCL2 associated genes.

Discussion. Treatment with omilancor resulted in consistent improvement of patient symptoms and disease severity across multiple clinical outcomes in a first study of Crohn's disease patients. Overall patterns in biomarkers and target engagement were consistent with those previously observed in ulcerative colitis patients treated with omilancor.



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 moderate to severe Crohn's disease (CD).

Key Inclusion Criteria

- Male and female subjects with moderate to severe CD defined by a CDAI between 220 and 450 with SES ≥ 6 (≥ 4 for isolated ileitis); 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 = 11)	Omilancor (N = 12)	Total (N = 23)
CDAI			
Mean (SD)	324.5 (70.7)	288.2 (70.2)	305.6 (72.8)
Median (min, max)	317 (225, 450)	266 (224, 450)	278 (224, 450)
Abdominal pain (AP) subscore			
Mean (SD)	61.8 (19.6)	61.3 (15.4)	61.5 (17.5)
Median (min, max)	70 (35, 100)	65 (35, 95)	65 (35, 100)
Stool frequency (SF) subscore			
Mean (SD)	115.1 (39.0)	76.8 (29.1)	95.1 (39.2)
Median (min, max)	112 (50, 186)	73 (24, 118)	90 (24, 186)
Fecal calprotectin concentration (ug/g)			
Mean (SD)	675.9 (615.5)	1075.4 (1419.9)	875.7 (1112.4)
Median (min, max)	506.5 (54, 2000)	456.5 (78, 4950)	471.5 (54, 4950)
SES-CD			
Mean (SD)	12.9 (6.3)	11.2 (4.8)	12.1 (6.3)
Median (min, max)	12 (4, 27)	11 (6, 22)	12 (4, 27)
Previous biologic treatment, n (%)			
No	7 (63.6%)	7 (58.3%)	14 (60.9%)
Yes	4 (36.3%)	5 (41.7%)	9 (39.1%)
Corticosteroid use at baseline, n (%)			
No	2 (18.2%)	1 (8.3%)	3 (13.0%)
Yes	9 (81.8%)	11 (91.7%)	20 (87.0%)

Table 1. Baseline patient demographics

Clinical remission (**Fig. 1**) was induced in 25.0% of patients within the omilancor group relative to 9.1% of the placebo group (Δ = 15.9). Similar effect sizes were observed within biologic experienced (Δ = 20.0) and biologic naïve (Δ = 14.3) subpopulations in clinical remission. Clinical response and PRO-2 remission were both induced in 41.7% of patients within the omilancor group relative to 9.1% of the placebo group (Δ = 32.6).

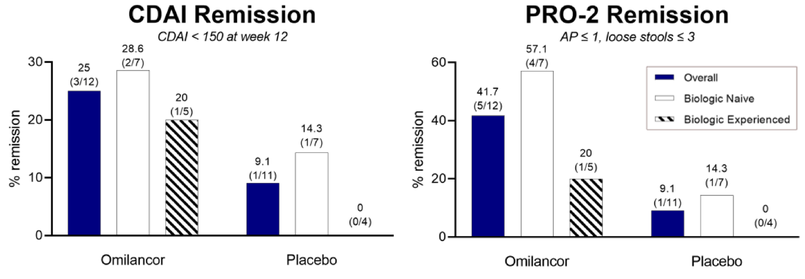


Figure 1. CDAI and PRO-2 remission

In patients with histological activity (cGeboes > 12) in at least one segment at baseline, omilancor induces remission in all segments in 42.9% of patients relative to 20.0% in the placebo group (**Fig. 2**). Omilancor treatment provided a mean decrease in Geboes score.

Twenty-eight total TEAEs were reported in the study. 58.3% of patients in the placebo group and 46.7% of the patients in the omilancor group reported at least TEAE. The majority (86.7%) of TEAEs were considered not related to study drug. Only 1 TEAE was considered severe, which was not associated with study drug. The most frequently reported TEAEs by SOC were Gastrointestinal disorders (5 of 27 subjects [18.5%]: 1 subject in the placebo group and 4 subjects in the omilancor group) and Infections and infestations (4 of 27 subjects [14.8%]: 3 subjects in the placebo group and 1 subject in the omilancor group). No subjects died during the study. No apparent safety findings were noted following medical review of clinical laboratory result listings.

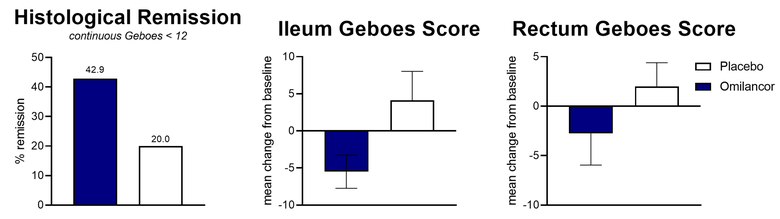


Figure 2. Histological remission and mean change in Geboes score at Week 12.

Omilancor treatment resulted in greater overall reduction of CDAI and fecal calprotectin. FCP was normalized in a 33.3% of omilancor treated patients at week 12 relative to 14.3% of placebo patients (for patients that had elevated fecal calprotectin at baseline (**Fig. 3**).

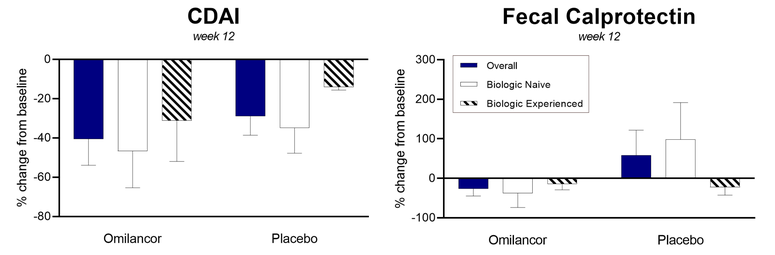


Figure 3. Percent change in CDAI and fecal calprotectin at Week 12.

Omilancor treatment resulted in reduction of multiple cytokines in the ileum relative to baseline, including Ccl3. Notable genes upregulated by omilancor treatment including those associated with endosomal, metabolic, and antimicrobial defense pathways (**Fig. 4**).

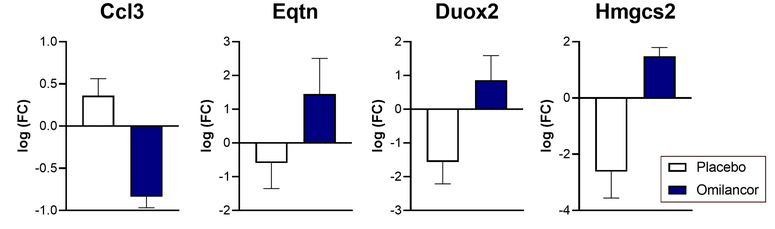


Figure 4. Percent change in CDAI and fecal calprotectin at Week 12.