**S1 Table. Other Secondary and Additional Efficacy Results During the 12-week Treatment Period (ITT Population)**

|  | **Placebo(N=171)** | **Linaclotide** |
| --- | --- | --- |
| **145 µg(N=153)** | ***P* value** | **290 µg(N=159)** | ***P* value** |
| **Abdominal Bloating** (11-point NRS) |  |  |  |  |  |
| Distribution of % change from baseline at week 12 a | N/A | N/A | 0.0054\*\* | N/A | 0.0012\*\* |
| % of patients with ≥ 1-point weekly mean decrease in bloating for ≥ 6/12 weeks b | 36.8 | 53.6 | 0.0023\* | 50.9 | 0.0107\* |
| Change from baseline in % of days with abdominal bloating < 3, mean c,d | 15.6 | 25.3 | 0.0092\* | 25.6 | 0.0055\* |
| **CSBMs** |  |  |  |  |  |
| Change from baseline in CSBMs/week at week 1, mean e | 0.6 | 2.0 | <0.0001\*\* | 1.7 | 0.0004\* |
| Change from baseline in CSBMs/week at week 4, mean e | 1.0 | 2.7 | <0.0001\*\* | 2.6 | <0.0001\* |
| Change from baseline in CSBMs/week at week 8, mean e | 1.2 | 2.7 | 0.0001\*\* | 2.2 | 0.0099\* |
| Change from baseline in CSBMs/week at week 12, mean e | 1.0 | 2.2 | 0.0002\*\* | 2.4 | <0.0001\* |
| **SBMs** |  |  |  |  |  |
| Change from baseline in SBMs/week at week 1, mean e | 1.9 | 4.2 | <0.0001\*\* | 4.1 | <0.0001\* |
| Change from baseline in SBMs/week at week 4, mean e | 1.5 | 4.1 | <0.0001\*\* | 3.9 | <0.0001\* |
| Change from baseline in SBMs/week at week 8, mean e | 1.6 | 3.6 | <0.0001\*\* | 3.7 | <0.0001\* |
| Change from baseline in SBMs/week at week 12, mean e | 1.4 | 3.1 | <0.0001\*\* | 3.0 | <0.0001\* |
| **Stool Consistency** (7-point BSFS) |  |  |  |  |  |
| Change from baseline at week 12, mean e | 0.8 | 2.1 | <0.0001\*\* | 2.3 | <0.0001\* |
| **Straining** (5-point ordinal scale) |  |  |  |  |  |
| Change from baseline at week 12, mean e | -0.9 | -1.6 | <0.0001\*\* | -1.7 | <0.0001\* |
| **Abdominal Discomfort** (11‑point NRS) |  |  |  |  |  |
| Mean abdominal discomfort score c | 5.0 | 4.1 |  | 4.3 |  |
| Change from baseline, mean c,e | -1.7 | -2.5 | 0.0002\* | -2.4 | 0.0013\* |
| % change from baseline, mean c,e | -26.2 | -38.1 | 0.0009\* | -36.0 | 0.0057\* |
| **Abdominal Pain** (11‑point NRS) |  |  |  |  |  |
| Mean abdominal pain score c | 4.0 | 3.3 |  | 3.3 |  |
| Change from baseline, mean c,e | -1.6 | -2.4 | 0.0008\* | -2.3 | 0.0027\* |
| % change from baseline, mean c,e | -33.1 | -39.6 | 0.2656\* | -42.7 | 0.0976\* |
| **Abdominal Fullness** (11‑point NRS) |  |  |  |  |  |
| Mean abdominal fullness score c | 5.6 | 4.7 |  | 4.8 |  |
| Change from baseline, mean c,e | -1.6 | -2.6 | <0.0001\* | -2.5 | 0.0003\* |
| **Abdominal Cramping** (11‑point NRS) |  |  |  |  |  |
| Mean abdominal cramping score c | 3.8 | 3.1 |  | 3.2 |  |
| Change from baseline, mean c,e | -1.5 | -2.2 | 0.0018\* | -2.1 | 0.0035\* |
| **Adequate Relief of CIC Symptoms** |  |  |  |  |  |
| % of patients reporting adequate relief for ≥ 9/12 weeks b | 16.4 | 33.3 | 0.0005\* | 35.2 | <0.0001\* |
| **Degree of Relief of Constipation Symptoms** (7-point balanced scale) |  |  |  |  |  |
| % of patients reporting degree of relief ≤ 3 for all weekly scores *or* ≤ 2 for ≥ 6/12 weeks b | 19.9 | 36.6 | 0.0008\* | 37.1 | 0.0005\* |

ANCOVA = analysis of covariance; BSFS = Bristol Stool Form Scale; CIC = chronic idiopathic constipation; CSBM = complete SBM; ITT = intent to treat; NRS = numerical rating scale; SBM = spontaneous bowel movement.

\*\* Secondary endpoint (nominal *P* value); \* Additional endpoint

a *P* values were based on a comparison of linaclotide vs. placebo using a Kolmogorov-Smirnov test for equality of distribution.

b *P* values were based on a comparison of linaclotide vs. placebo using a Cochran‑Mantel‑Haenszel test controlling for geographic region.

c Means are over the 12-week treatment period.

d Changes from baseline are the arithmetic means; *P* values were based on a comparison of linaclotide vs. placebo using rank-transformed normal scores in an ANCOVA model with treatment group and geographic region as factors and corresponding baseline value as a covariate.

e Changes from baseline are the least-squares means from an ANCOVA model; *P* values were based on a comparison of linaclotide vs. placebo using an ANCOVA model with treatment group and geographic region as factors and corresponding baseline value as a covariate.