**Table,** **Supplemental Digital Content 3. Additional efficacy endpoints**

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| --- | --- | --- | --- | --- |
|  | **Placebo (N = 308)** | **Linaclotide (N = 306)** | **OR (95% CI)** | ***P* value** |
| **Responder endpoints, n (%)** |  |  |  |  |
| **Abdominal symptom responder endpoints  (based on an improvement ≥2.0 from baseline in the individual symptom)** |  |  |  |  |
| 6-/12-week abdominal bloating responder | 75 (24.4) | 123 (40.2) | 2.04 (1.44–2.88) | <0.0001 |
| 6-/12-week abdominal discomfort responder | 80 (26.0) | 129 (42.2) | 2.05 (1.45–2.89) | <0.0001 |
| 6-/12-week abdominal pain responder | 77 (25.0) | 129 (42.2) | 2.14 (1.51–3.02) | <0.0001 |
| 6-/12-week abdominal pain 30% responder (pain improved ≥30% from baseline) | 89 (28.9) | 138 (45.1) | 1.96 (1.40–2.74) | <0.0001 |
| 6-/12-week CSBM responder (increase ≥1/week CSBM from baseline) | 104 (33.8) | 157 (51.3) | 2.05 (1.48–2.84) | <0.0001 |
| 6-/12-week combined abdominal pain (≥30% improvement) and constipation (APC+1) responder | 52 (16.9) | 90 (29.4) | 2.02 (1.37–2.97) | 0.0003 |
| 6-/12-week adequate relief responder (yes/no) | 124 (40.3) | 192 (62.7) | 2.50 (1.80–3.46) | <0.0001 |
| SBM within 24 hours after first dose responder | 94 (30.5) | 158 (51.6) | 2.47 (1.78–3.44) | <0.0001 |
| **Overall CFB throughout treatment period, LS mean change (SE)** |  |  |  |  |
| Abdominal bloatinga | −1.141 (0.112) | −1.888 (0.114) |  | <0.0001 |
| Abdominal discomforta | −1.220 (0.111) | −1.914 (0.113) |  | <0.0001 |
| Abdominal paina | −1.184 (0.112) | −1.891 (0.114) |  | <0.0001 |
| CSBM frequency rate | 0.961 (0.195) | 2.371 (0.199) |  | <0.0001 |
| SBM frequency rate | 1.153 (0.239) | 3.002 (0.245) |  | <0.0001 |
| BSFS (stool consistency)b,c | 0.914 (0.072) | 1.706 (0.075) |  | <0.0001 |
| Strainingb,d | −0.731 (0.052) | −1.163 (0.054) |  | <0.0001 |
| Percent days with use of rescue medicine during the treatment period | −4.541 (0.940) | −2.907 (0.967) |  | 0.1632 |
| Constipation severitye,f | −0.671 (0.049) | −1.128 (0.051) |  | <0.0001 |
| IBS symptom severitye,f | −0.611 (0.045) | −0.984 (0.046) |  | <0.0001 |
| **Overall treatment satisfaction,g,h LS mean (SE)** |  |  |  |  |
| Week 1 | 2.136 (0.068) | 2.665 (0.069) |  | <0.0001 |
| Week 2 | 2.163 (0.068) | 2.806 (0.070) |  | <0.0001 |
| Week 3 | 2.203 (0.069) | 2.863 (0.070) |  | <0.0001 |
| Week 4 | 2.279 (0.071) | 2.907 (0.072) |  | <0.0001 |
| Week 5 | 2.299 (0.072) | 2.956 (0.074) |  | <0.0001 |
| Week 6 | 2.290 (0.071) | 2.933 (0.073) |  | <0.0001 |
| Week 7 | 2.353 (0.074) | 2.981 (0.075) |  | <0.0001 |
| Week 8 | 2.274 (0.073) | 3.050 (0.075) |  | <0.0001 |
| Week 9 | 2.344 (0.074) | 3.006 (0.076) |  | <0.0001 |
| Week 10 | 2.359 (0.075) | 3.003 (0.077) |  | <0.0001 |
| Week 11 | 2.340 (0.075) | 3.083 (0.077) |  | <0.0001 |
| Week 12 | 2.397 (0.075) | 3.047 (0.077) |  | <0.0001 |

LS means, SEs, LSMDs, and *P* values were obtained based on an MMRM with treatment, analysis week, geographic region, and treatment-by-week interactions as fixed effects, and baseline score as a covariate; “6-/12-week” refers to patients being responders for ≥6 of the 12 treatment weeks.  
aPlacebo, n = 306;  
bPlacebo, n = 274; linaclotide, n = 281;  
cBSFS is a 7-point ordinal scale (1=separate hard lumps like nuts; 7=watery, no solid pieces);  
dStraining measured on a 5-point ordinal scale (1=not at all; 5=an extreme amount);  
eConstipation severity and IBS symptom severity measured on a 5-point ordinal scale (1=none; 5=very severe);  
fPlacebo, n = 304; linaclotide, n = 301;  
gFor each week, n = 271–287 for placebo and 263–285 for linaclotide;  
hTreatment satisfaction measured on a 5-point ordinal scale (1=not at all satisfied; 5=very satisfied).  
BSFS, Bristol Stool Form Scale; CFB, change from baseline; CI, confidence interval; CSBM, complete spontaneous bowel movement; LS, least squares; LSMD, least squares mean difference; MMRM, mixed model with repeated measures; N, number of patients in the intention-to-treat population; n, number of patients within a specific category; OR, odds ratio; SBM, spontaneous bowel movement; SE, standard error of the LS mean.