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Plecanatide Improves Severe Abdominal Pain and Severe Bloating in Individuals With Irritable Bowel Syndrome With Constipation: A Pooled Analysis of Two Phase 3 Trials

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INTRODUCTION

- Irritable bowel syndrome with constipation (IBS-C) is a disorder of gut-brain interaction characterized by abdominal pain related to defecation and hard stool consistency[1,2]
- In addition, bloating is a common bothersome symptom experienced by patients with IBS-C, often leading patients to seek medical care for their symptoms[1,3]
- Plecanatide 3 mg is indicated in the United States for the treatment of IBS-C in adults[4] and is recommended by the 2021 ACG clinical guideline on the management of IBS[5] and the 2022 American Gastroenterological Association guideline on pharmacological management of IBS-C[6]
- The efficacy and safety of plecanatide for patients with IBS-C have been demonstrated in 2 randomized, double-blind, placebo-controlled, phase 3 trials[7]
  - Plecanatide improved abdominal pain, bloating, stool consistency, and stool frequency compared with placebo[7]

OBJECTIVE

- To evaluate the efficacy of plecanatide for improving severe abdominal pain and/or severe bloating in patients with IBS-C

METHODS

- Data were pooled and analyzed post hoc for two randomized, phase 3 trials of adults with IBS-C treated with plecanatide 3 mg or placebo once daily for 12 weeks[7]
- Severity of abdominal pain and bloating were rated individually using an 11-point scale (range, 0 [“no symptom”] to 10 [“worst possible symptom”])
  - Severe abdominal pain and severe bloating were defined as having a symptom score ≥8
- Subgroup analyses were conducted for patients with severe pain, severe bloating, or both, at baseline
- “Response” was defined as a ≥30% improvement from baseline in symptom score(s) at Week 12
- A correlation analysis (Spearman and Pearson coefficients) measured the strength of associations between abdominal pain and bloating
  - A coefficient (*r*) value of >0.90-1.00 was considered to be a very strong positive correlation, whereas an *r* >0.70-0.90 was considered to be a strong positive correlation

RESULTS

- Overall, 1453 patients with IBS-C were included in the analysis (plecanatide 3 mg [n=724]; placebo [n=729]; **Table 1**)

Table 1. Demographic and Baseline Disease Characteristics

Characteristic	Plecanatide 3 mg (n=724)	Placebo (n=729)
Age, y, mean (SD)	43.5 (14.2)	43.9 (14.2)
Female, n (%)	534 (73.8)	540 (74.1)
Race, n (%)		
White	527 (72.8)	536 (73.5)
Black	155 (21.4)	160 (21.9)
Other	42 (5.8)	33 (4.5)
BMI, kg/m^2, mean (SD)	28.3 (4.8)	28.0 (4.8)
Abdominal pain score, mean (SD)*	6.26 (1.7)	6.26 (1.7)
Bloating score, mean (SD)*	6.48 (1.7)	6.47 (1.8)
SBMs/week, mean (SD)	1.5 (1.1)	1.4 (1.1)
CSBMs/week, mean (SD)	0.2 (0.5)	0.2 (0.5)

*Measured using an 11-point rating scale (0 = “no symptom”; 10 = “worst possible symptom”).
BMI = body mass index; CSBM = complete spontaneous bowel movement; SBM = spontaneous bowel movement.

- Of the 1453 patients with IBS-C:
  - 285 (19.6%) reported severe abdominal pain
  - 311 (21.4%) reported severe bloating
  - 233 (16.0%) reported both severe abdominal pain and severe bloating
- A significantly greater percentage of patients with severe baseline abdominal pain treated with plecanatide were responders compared with placebo at Week 12 (Δ=14.6%; *P*=0.01; **Figure**)
- In addition, a significantly greater percentage of patients with severe baseline bloating treated with plecanatide were responders versus placebo at Week 12 (Δ=14.9%; *P*=0.005; **Figure**)
- Furthermore, a significantly greater percentage of plecanatide-treated patients with both severe abdominal pain and severe bloating at baseline were responders versus placebo at Week 12 (Δ=12.9%; *P*=0.05; **Figure**)
- Changes from baseline to Week 12 in abdominal pain and bloating were strongly and positively correlated to each other in the overall population and in those with severe pain and severe bloating at baseline (overall population, *r*=0.85-0.88; subgroup with both severe abdominal pain and bloating, *r*=0.92-0.95; **Table 2**)

Figure. Percentage of Patients With ≥30% Improvement From Baseline in Severe Abdominal Pain, Bloating, or Both at Week 12, by Subgroup

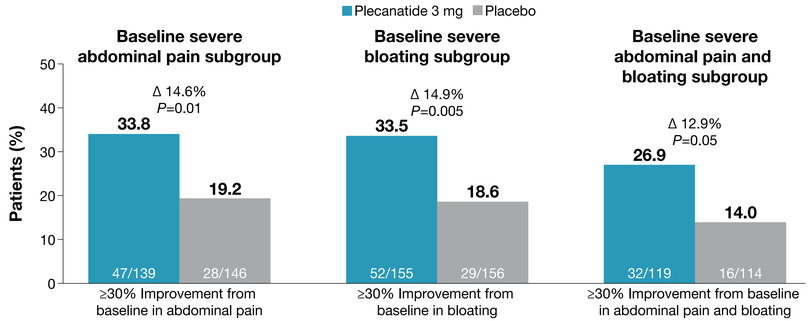

Table 2. Correlation of Change From Baseline at Week 12 in Abdominal Pain and Bloating Symptoms in Overall Population and Those With Severe Baseline Abdominal Pain and Bloating at Baseline

	Abdominal Pain and Bloating	
Population	Spearman correlation coefficient, *r*	Pearson correlation coefficient, *r*
Overall	0.85*	0.88*
Severe abdominal pain and bloating	0.92*	0.95*

*P<0.0001.

CONCLUSIONS

- **Plecanatide 3 mg once daily decreased symptom severity in patients with IBS-C and severe abdominal pain and/or severe bloating at baseline compared with placebo, with strong correlations in symptom responses**
- **The observed parallel, correlated improvement in both abdominal pain and bloating, provides indirect evidence of an associated pathogenesis of these IBS-C symptoms**

REFERENCES: **1.** Lacy BE, Mearin F, Chang L, et al. *Gastroenterology.* 2016;150:1393-1407. **2.** Johanson JF, Kralstein J. *Aliment Pharmacol Ther.* 2007;25:599-608. **3.** Ringel Y, Williams RE, Kalilani L, Cook SF. *Clin Gastroenterol Hepatol.* 2009;7:68-72; quiz 63. **4.** Trulance tablets, for oral use [package insert]. Salix Pharmaceuticals; 2021. **5.** Lacy BE, Pimentel M, Brenner DM, et al. *Am J Gastroenterol.* 2021;116(1):17-44. **6.** Chang L, Sultan S, Lembo A, et al. *Gastroenterology.* 2022;163:118-136. **7.** Brenner DM, Fogel R, Dorn SD, et al. *Am J Gastroenterol.* 2018;113:735-745.

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