Plecanatide is Effective in Severely Constipated Patients With Chronic Idiopathic Constipation and Irritable Bowel Syndrome With Constipation

B. Cash, MD*, A. Sharma, MD⁺, S.M. Lorenzen, PhD[‡], L. Chang, MD[§] *University of Texas Health Science Center, Houston, TX; *Medical College of Georgia, Augusta, GA; *Salix Pharmaceuticals, Inc., Bridgewater, NJ (Former Employee); *David Geffen School of Medicine University of California, Los Angeles, Los Angeles, CA



- Chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C) are characterized by infrequent, hard, and difficult-to-pass bowel movements as well as varying degrees of abdominal symptoms.^{1,2}
- Patients with severe constipation represent a particularly challenging population to manage, therefore understanding treatment efficacy in this subgroup is desirable.
- Plecanatide is an analog of the human GI peptide, uroguanylin, and preclinical evidence suggests that plecanatide replicates the pH-sensitive binding of uroguanylin to guanylate cyclase-C receptors, acting primarily in the small intestine to induce fluid secretion and contribute to normal bowel function.^{3,4}
- Plecanatide has demonstrated clinical efficacy with a favorable safety and tolerability profile in four pivotal phase 3 clinical trials and is approved for the treatment of adults with CIC and IBS-C in the United States.⁴⁻⁷
- The objective of this post hoc analysis is to evaluate the impact of plecanatide in severely constipated patients.

METHODS

- Data were derived from four 12-week, double-blind, placebo-controlled, phase 3 clinical trials of plecanatide for CIC and IBS-C (CIC: NCT02122471, NCT01982240; IBS-C: NCT02387359, NCT02493452).4-7
- Data were pooled separately for the two CIC and two IBS-C studies.
- Patients who met Rome III criteria for CIC or IBS-C were randomized to oral plecanatide 3 mg or placebo once daily for 12 weeks.
- Using electronic diaries, patients recorded daily straining, abdominal pain, and bloating symptoms during the pre-treatment, treatment (12 weeks), and post-treatment (2 weeks) periods.
 - Patients with CIC utilized a Likert scale of 0 (not at all) to 4 (extremely/all the time) to rate their symptom severity.
 - Patients with IBS-C utilized a numeric rating scale of 1 (not at all) to 10 (extremely/a great deal) to rate their symptom severity.
- Severe constipation was defined as having no complete spontaneous bowel movements (CSBMs) and an average straining score of ≥ 3 for CIC or ≥ 8 for **IBS-C** over the 2-week baseline period.
- Endpoints evaluated included CSBMs/week, spontaneous bowel movements (SBMs)/week, stool consistency (Bristol Stool Form Scale [BSFS]), straining, abdominal pain, and bloating.

References

- 1. Lacy BE, Pimentel M, Brenner DM, et al. Am J Gastroenterol. 2021;116(1):17-44. 2. American College of Gastroenterology Chronic Constipation Task Force. Am J
- Gastroenterol. 2005;100 Suppl 1:S1-4. 3. Sharma A, Herekar AA, Bhagatwala J, Rao SS. Clin Exp Gastroenterol. 2019;12:31-36.
- **4.** Shailubhai K, Comiskey S, Foss JA, et al. *Dig Dis Sci.* 2013;58(9):2580-2586.
- 2017;10(11):837-851.

RESULTS

Constipated Patients With CIC and IBS-C

=220) (n=168) (n=213) Age (years), mean (SD) 42.9 (13.8) 44.2 (14.4) 43.3 (14.6) 19–78 Range 18–79 18–75 **Sex,** n (%) 37 (22.0) Male 52 (24.4) 57 (25.9) Female 131 (78.0) 161 (75.6) 163 (74.1) **Race,** n (%) White/Caucasian 153 (71.8) 129 (76.8) 161 (73.2) 47 (22.1) 51 (23.2) 33 (19.6) Black or African American Other 6 (3.6) 13 (6.1) 8 (3.7) Ethnicity, n (%) 116 (54.5) 105 (62.5) 111 (50.5) Hispanic or Latino 97 (45.5) 63 (37.5) Not Hispanic or Latino 109 (49.5) **BMI** (kg/m²), mean (SD) 28.17 (4.8) 28.1 (5.0) 28.4 (4.9)

Percentages may not add up to 100% due to rounding MI. body mass index: CIC. chronic idiopathic constipation: CSBM. complete spontaneous bowel movement; IBS-C, irritable bowel ndrome with constipation; SD, standard deviation.

Of the 1762 (CIC) and 1453 (IBS-C) patients treated with placebo or plecanatide 3 mg in the intention-to-treat populations, 433 patients with CIC (plecanatide, n=220; placebo, n=213) and 356 patients with IBS-C (plecanatide, n=188; placebo, n=168) met criteria for being severely constipated and were included in the analyses (Table 1).

Demographics in the severely constipated subgroup were similar to those in the total pooled populations, with the exception of a relatively high proportion of patients who identified as Hispanic or Latino ethnicity (CIC total population: plecanatide, 39.2%; placebo, 42.5%; IBS-C total population: plecanatide, 50.4%; placebo, 51.6%).^{4,5,7}

- While it is not known why there was a higher proportion of Hispanic or Latino patients in the present cohort, it suggests there may be cultural differences in how symptoms of abdominal pain are conveyed to Healthcare Providers.

5. DeMicco M, Barrow L, Hickey B, Shailubhai K, Griffin P. Therap Adv Gastroenterol

6. Miner Jr PB, Koltun WD, Wiener GJ, et al. Am J Gastroenterol. 2017;112(4):613–621 7. Brenner DM, Fogel R, Dorn SD, et al. Am J Gastroenterol. 2018;113(5):735-745.

Disclosures

B. Cash is a consultant and speaker for Salix Pharmaceuticals. **A. Sharma** has participated in an advisory board for Ironwood Pharmaceuticals, Phathom Pharmaceuticals, and Salix Pharmaceuticals. S. Lorenzen is a former employee at Salix Pharmaceuticals. **L. Chang** has participated in an advisory board for Allergan/Ironwood Pharmaceuticals.

Plecanatide Placebo Placebo 3 mg 41 (21.8)

CIC

(no CSBM/week and

≥3 straining score)

Table 1. Demographics and Baseline Characteristics in Severely

(no CSBM/week and ≥8 straining score)

IBS-C

- Plecanatide 3 mg (n=188)
- 43.0 (12.5) 20-80
- 147 (78.2)
- 134 (71.3)
- 47 (25.0)
- 7 (3.7)
- 107 (56.9)
- 81 (43.1)
- 28.47 (4.5)

Figure 1. Average Change in Bowel-Related Symptoms and Stool **Consistency Over 12 Weeks in Severely Constipated Patients With** (A) CIC and (B) IBS-C



P<0.01, *P<0.001 vs placeb BSFS. Bristol Stool Form Scale: CIC. chronic idiopathic constipation: CSBM. complete spontaneous bowel movement; IBS-C, irritable bowel syndrome with constipation; LS, least squares; SBM, spontaneous bowel movement; SE, standard error.

- Plecanatide treatment was associated with improvements in bowel-related symptoms in both CIC and IBS-C severely constipated patients.
- Across 12 weeks, plecanatide-treated patients experienced significantly more CSBMs and SBMs per week as well as significant improvementsin stool consistency compared with patients receiving placebo (Figure 1A and 1B).

Figure 2. Average Change in Straining and Abdominal Symptoms Over 12 Weeks in Severely Constipated Patients With (A) CIC and (B) IBS-C



P<0.01, *P≤0.001 vs placeb CIC, chronic idiopathic constipation; IBS-C, irritable bowel syndrome with constipation; LS, least squares; SBM, spontaneous bowel ovement: SE. standard error

Plecanatide-treated patients also reported significant improvements in straining, abdominal pain, and bloating for both CIC (Figure 2A) and IBS-C (Figure 2B).

Acknowledgments

Funding for this study and poster support was provided by Salix Pharmaceuticals, Inc (Bridgewater, NJ, USA). Medical writing and editorial support were provided by The Medicine Group (New Hope, PA, USA), in accordance with Good Publication Practice guidelines.

This poster was funded by Salix Pharmaceuticals.

Baseline Mean

Baseline Mean

Baseline Mean

Baseline Mean



KEY FINDINGS

Overall, plecanatide was demonstrated to be an efficacious treatment for patients with CIC and IBS-C with severe constipation.

With nearly 25% of patients enrolled in the trials meeting the definition for severe constipation at baseline, this subgroup of patients may represent those having more difficult-totreat symptoms and are often underrepresented in clinical trials.

Severely constipated patients with CIC and **IBS-C** treated with plecanatide experienced significant improvements in both bowel-related and abdominal symptoms.