Plecanatide Improves Treatment Satisfaction and Quality of Life Among Patients With Chronic Idiopathic **Constipation and Irritable Bowel Syndrome With Constipation: Analyses From Four Phase 3 Trials** D.M. Brenner, MD*, C. Chang, MD, PhD[†], E. Shah, MD[‡], K. Chong, PhD[†], S.M. Lorenzen, PhD[§], G.S. Sayuk, MD[¶]

*Northwestern University Feinberg School of Medicine, NM; *Dartmouth-Hitchcock Health, Lebanon, NH; *Salix Pharmaceuticals, Inc., Bridgewater, NJ (Former Employee); Washington University School of Medicine, St. Louis, MO



INTRODUCTION

- Chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C) are common disorders affecting 7.9%-8.6% and 4.4%-4.8% of population, respectively, in the US, Canada, and UK, where both significantly impact health-related quality of life (HRQOL).¹
- In 60% of CIC and ~50% of IBS-C patients, symptoms interfered with personal activities approximately 4 days/month and 1 day/month, respectively.^{2,3}
- CIC and IBS-C also frequently impact work and/or school attendance.^{2,3}
- 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, improve bowel function, and reduce visceral hypersensitivity.^{4,5}
- Plecanatide has demonstrated clinical efficacy with a benign safety and tolerability profile in four pivotal, phase 3 clinical trials (two in CIC and two in IBS-C) and is approved for the treatment of adults with CIC and IBS-C in the United States.⁶⁻⁸
- In the CIC trials, plecanatide treatment resulted in significant changes from baseline in Patient Assessment of Constipation-Quality of Life (PAC-QOL) total score at each assessment (Weeks 4, 8, and 12).^{6,7}
- In the IBS-C trials, significantly more plecanatide-treated patients indicated being satisfied with treatment compared with placebo-treated patients at Week 12.8
- The objective of this post hoc analysis is to assess the impact of plecanatide on treatment satisfaction and HRQOL among patients with CIC and IBS-C experiencing the lowest bowel-related QOL at baseline (i.e., patients experiencing the greatest impact of CIC/IBS-C on their QOL and therefore the most to gain from effective treatment).

METHODS

We aggregated data from four randomized, double-blinded, placebo-controlled, phase 3 clinical trials: two in CIC (NCT02122471 and NCT01982240) and two in IBS-C (NCT02387359 and NCT02493452]).

Data were pooled separately for the two CIC and two IBS-C studies.

- Patients who met Rome III criteria for CIC (modified) or IBS-C were randomized to receive plecanatide 3 mg, 6 mg, or placebo. Results are presented for the FDA-approved dose, plecanatide 3 mg.
- In the CIC trials, patients completed the PAC-QOL, a 28-item questionnaire measuring worries/ concerns, physical discomfort, psychosocial discomfort, satisfaction, and overall effects.
- Patients rated their responses using a scale of 0 (not at all) to 4 (extremely/all the time), with higher scores indicating lower HRQOL.
- A \geq 1-point reduction in PAC-QOL total score is a validated threshold for clinically meaningful response.
- In the IBS-C trials, patients completed the IBS-QOL, a 34-item questionnaire measuring dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual items, relationship, and overall effects.
- Patients rated their responses using a scale of 1 (not at all) to 5 (extremely/a great deal), with higher scores indicating lower HRQOL.
- A \geq 14-point reduction in IBS-QOL total score is a validated indicator for clinically meaningful response.
- > Both the PAC-QOL and IBS-QOL were administered on Day 1 and at Weeks 4, 8, and 12.
- Treatment satisfaction was evaluated at Weeks 4, 8, and 12 using a scale of 1 (not at all satisfied) to 5 (very satisfied).

References

- **1.** Palsson OS, Whitehead W, Törnblom H, Sperber AD, Simren M. *Gastroenterology*. 2020;158(5): 1262-1273.
- **2.** Harris LA, Horn J, Kissous-Hunt M, Magnus L, Quigley EMM. *Adv Ther*. 2017;34(12):2661-2673.
- **3.** Quigley EMM, Horn J, Kissous-Hunt M, Crozier RA, Harris LA. Adv Ther. 2018;35(7):967-980.
- **4.** Sharma A, Herekar AA, Bhagatwala J, Rao SS. *Clin Exp Gastroenterol*. 2019;12:31-36.
- 837-851.



RESULTS

Subgroup analysis included patients with the poorest QOL, defined as the quintile (20%) of patients with the highest PAC-QOL or IBS-QOL total scores at baseline.

– Due to multiple occasions of the same score, actual subgroup population was slightly smaller than 20% of total population.

Table 1. Demographics and Clinical Characteristics of CIC and IBS-C Patients in the Poorest QOL Quintile at Baseline

	CIC		IBS-C	
	Placebo n=123	Plecanatide 3 mg n=146	Placebo n=127	Plecanatide 3 mg n=144
Age, yrs, mean (SD)	45.0 (13.1)	43.8 (11.7)	43.1 (12.9)	44.0 (12.5)
Sex, n (%)				
Male	32 (26.0)	23 (15.8)	24 (18.9)	35 (24.3)
Female	91 (74.0)	123 (84.2)	103 (81.1)	109 (75.7)
Race, n (%)				
White	86 (69.9)	106 (72.6)	88 (69.3)	100 (69.4)
Black/African American	32 (26.0)	36 (24.7)	36 (28.3)	37 (25.7)
Asian	3 (2.4)	2 (1.4)	3 (2.4)	5 (3.5)
Other	2 (1.6)	2 (1.4)	0	2 (1.4)
Ethnicity, n (%)				
Hispanic/Latino	61 (49.6)	71 (48.6)	66 (52.0)	79 (54.9)
Non-Hispanic/Latino	62 (50.4)	75 (51.4)	61 (48.0)	65 (45.1)
BMI (kg/m²), mean (SD)	29.0 (5.8)	28.9 (5.2)	29.2 (5.1)	28.8 (4.6)

BMI, body mass index: CIC, chronic idiopathic constipation; IBS-C, irritable bowel syndrome with constipation; QOL, quality of life; SD, standard deviation

Of 1762 (CIC) and 1453 (IBS-C) patients treated with placebo or plecanatide 3 mg in the intention-totreat populations, 269 patients with CIC (placebo, n=123; plecanatide, n=146) and 271 patients with IBS-C (placebo, n=127; plecanatide, n=144) were included in the poorest QOL subgroup.

Demographics in the poorest QOL subgroup were similar to those in the total populations (Table 1).⁵⁻⁷

Figure 1. Percent of Patients Achieving Clinically Meaningful HRQOL Improvements at Week 12 for (A) CIC and (B) IBS-C Patients in the Poorest QOL Quintile



Syndrome–Quality of Life; PAC-QOL, Patient Assessment of Constipation–Quality of Life; QOL, quality of life. At Week 12, plecanatide-treated patients reported significantly greater total score improvements

from baseline in PAC-QOL (LS mean change: placebo, -1.4; plecanatide, -1.7; P<0.05) and IBS-QOL (LS mean change: placebo, -32.6; plecanatide, -39.8; P<0.05) compared to placebo.

A significantly greater percentage of plecanatide-treated patients reported a clinically meaningful reduction in PAC-QOL (Figure 1A) and IBS-QOL (Figure 1B) compared to placebo.

5. Shailubhai K, Comiskey S, Foss JA, et al. *Dig Dis Sci*. 2013;58(9):2580-2586. 6. DeMicco M, Barrow L, Hickey B, Shailubhai K, Griffin P. Therap Adv Gastroenterol. 2017;10(11):

7. Miner Jr PB, Koltun WD, Wiener GJ, et al. Am J Gastroenterol. 2017;112(4):613-621. 8. Brenner DM, Fogel R, Dorn SD, et al. Am J Gastroenterol. 2018;113(5):735-745.

Disclosures

D.M. Brenner is a consultant and speaker for Salix Pharmaceuticals and is supported by an unrestricted research gift from the IDP Foundation. C. Chang has participated in an advisory board for Salix Pharmaceuticals. E. Shah has nothing to disclose. K. Chong has nothing to disclose. S.M. Lorenzen is a former employee at Salix Pharmaceuticals. G.S. Sayuk is a consultant and speaker for Salix Pharmaceuticals, Allergan/Ironwood Pharmaceuticals, and Alnylam, and is a consultant for the GI Health Foundation.









*P<0.05 vs placebo. CIC, chronic idiopathic constipation; IBS-C, irritable bowel syndrome with constipation; QOL, quality of life. Significantly more plecanatide-treated patients achieved a treatment satisfaction score of 4 or 5 across 12 weeks (Figure 2), with significant differences observed by Week 4.

Figure 3. Change in QOL Domain Scores From Baseline to Week 12 for (A) CIC and (B) IBS-C Patients in the Poorest QOL Quintile





*P<0.05. **P<0.01 vs placebo. CIC. chronic idiopathic constipation: IBS-C. irritable bowel syndrome with constipation; IBS-QOL, Irritable Bowel Syndrome–Quality of Life; LS, least squares; PAC-QOL, Patient Assessment of Constipation–Quality of Life; QOL, quality of life; SE, standard error. At Week 12, PAC-QOL domain scores showed significant improvements in satisfaction and worries/

- concerns compared to placebo (Figure 3A).
- IBS-QOL domain scores showed significant improvements in dysphoria, body image, social reaction, and relationship items (Figure 3B).

Acknowledgments

Funding for this study and poster support was provided by Salix Pharmaceuticals, Inc. (Bridgewater, NJ, USA). Medica 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.

Presented at American Neurogastroenterology and Motility Society 2021 | Aug 13–15, 2021 | Boston, MA



KEY FINDINGS

97

♦ These analyses suggest that plecanatide is effective in improving patientcentric HRQOL factors in a population of individuals with CIC and IBS-C.

Across two CIC and two IBS-C phase 3 trials, plecanatide 3 mg led to statistically significant and clinically meaningful improvements in treatment satisfaction and HRQOL compared to placebo among patients with the poorest HRQOL at baseline (last quintile).

♦ Plecanatide was

associated with significant improvements in satisfaction and worries/concerns (CIC), and dysphoria, body image, social reaction, and relationship improvements (IBS-C).