Plecanatide Provided Clinically Meaningful Improvements in Health-Related Quality of Life in Patients With Chronic Idiopathic Constipation and Irritable Bowel Syndrome With Constipation: A Post Hoc Analysis

P0398

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INTRODUCTION

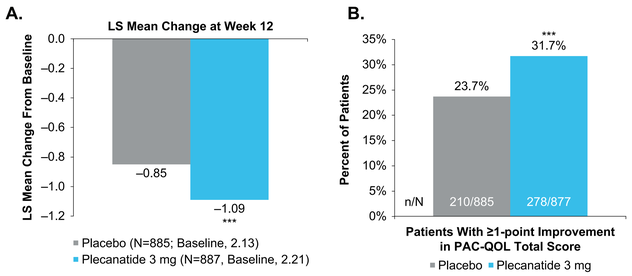
- Chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C) significantly impact health-related quality of life (HRQOL).[1]
  - Impacts in HRQOL include lower work/school productivity and attendance.[2-4]
- Most patients who were prescribed a pharmacologic intervention for CIC or IBS-C by their healthcare provider are generally unsatisfied with the available treatment options, mostly due to because of lack of efficacy.[5,6]
- Plecanatide is a pH-sensitive analog of human uroguanylin that is U.S. Food and Drug Administration approved for the treatment of CIC and IBS-C.[7]
  - Plecanatide functions as a guanylate cyclase-C receptor agonist to produce cyclic guanosine monophosphate (cGMP).[7]
  - The production of cGMP activates cystic fibrosis transmembrane regulator receptors, resulting in increased fluid secretion and intestinal peristalsis.[7]
  - Plecanatide exhibits anti-nociceptive activity and has been shown to reduce visceral hypersensitivity, thus alleviating abdominal symptoms.[7,8]
- This post hoc analysis evaluated the impact of plecanatide on HRQOL in patients with CIC and IBS-C.[9-11]

METHODS

- Data from four multicenter, double-blind, placebo-controlled phase 3 trials in CIC (NCT01982240, NCT02122471) and IBS-C (NCT02387359, NCT02493452)[9-11] were pooled (separately for each indication).
  - In the original studies, patients with CIC or IBS-C were randomized to once-daily plecanatide 3 mg or 6 mg (data not shown), or placebo.
  - 1762 patients with CIC (placebo, N=885; plecanatide, N=877) and 1453 with IBS-C (placebo, N=729; plecanatide, N=724) received placebo or plecanatide 3 mg in the intention-to-treat populations.
- Patients with CIC completed the Patient Assessment of Constipation Quality of Life (PAC-QOL) questionnaire, which is composed of 28 items rated from 0 (not at all) to 4 (extremely/all the time) that contribute to 4 domains (worries and concerns, physical discomfort, psychosocial discomfort, and satisfaction).
- Patients with IBS-C completed the IBS-QOL questionnaire, which comprises 34 items rated from 1 (not at all) to 5 (extremely/a great deal) contributing to 8 domains (dysphoria, activity interference, body image, health worry, food avoidance, social reaction, sexual, and relationship).
- The PAC-QOL and IBS-QOL were administered on Day 1 and at Weeks 4, 8, and 12; higher scores indicate poorer HRQOL for both measures.
- Clinically meaningful QOL responses have been previously validated for both surveys and characterized by a ≥1-point improvement in PAC-QOL or a ≥14-point improvement in IBS-QOL total scores from baseline.[11,12]

RESULTS

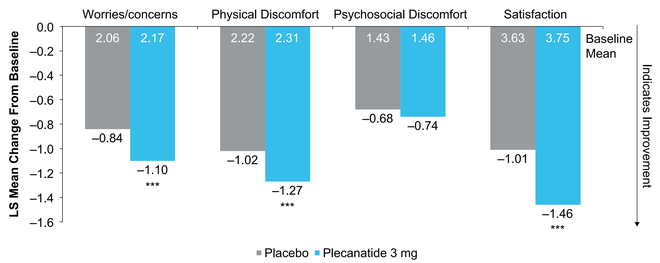
Figure 1. PAC-QOL Total Score at Week 12 in Patients With CIC: (A) Mean Change From Baseline and (B) Patients With Clinically Meaningful Improvement



***P<0.001 vs placebo. CIC, chronic idiopathic constipation; LS, least squares; PAC-QOL, Patient Assessment of Constipation Quality of Life.

- Improvements in PAC-QOL total score from baseline to Week 12 were significantly greater with plecanatide than with placebo (Figure 1A).
- Significantly more patients administered plecanatide reported a clinically relevant ≥1-point reduction in PAC-QOL total score compared with placebo (Figure 1B).
- The change in PAC-QOL total score at Week 12 was weakly correlated with Week 12 changes in complete spontaneous bowel movements (Pearson r = –0.355; P<0.0001), spontaneous bowel movements (Pearson r = –0.305; P<0.0001), and abdominal pain (Pearson r = –0.399; P<0.0001).

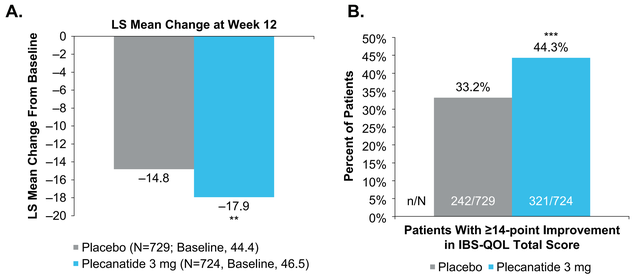
Figure 2. PAC-QOL Domain Scores in Patients With CIC: Mean Change From Baseline to Week 12



***P<0.001 vs placebo. IBS-C, irritable bowel syndrome with constipation; IBS-QOL, Irritable Bowel Syndrome Quality of Life; LS, least squares.

- PAC-QOL domain scores at Week 12 showed significant improvements in satisfaction, worries/concerns, and physical discomfort compared to placebo (Figure 2).

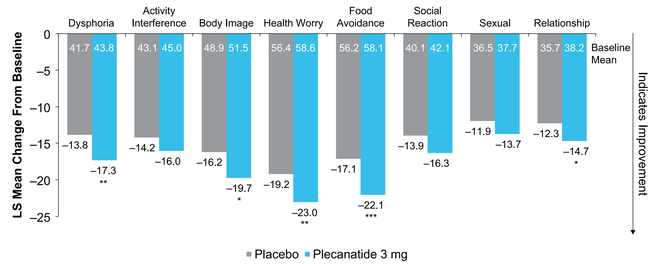
Figure 3. IBS-QOL Total Score at Week 12 in Patients With IBS-C: (A) Mean Change From Baseline and (B) Patients With Clinically Meaningful Improvement



**P<0.01, ***P<0.001 vs placebo. IBS-C, irritable bowel syndrome with constipation; IBS-QOL, Irritable Bowel Syndrome Quality of Life; LS, least squares.

- Improvement from baseline in IBS-QOL total score from baseline to Week 12 was significantly greater with plecanatide than with placebo (Figure 3A).
- Significantly more plecanatide-treated patients reported a ≥14-point reduction in IBS-QOL total score compared with placebo (Figure 3B).
- The change in IBS-QOL total score at Week 12 was weakly correlated with Week 12 changes in complete spontaneous bowel movements (Pearson r = –0.187; P<0.0001), spontaneous bowel movements (Pearson r = –0.174; P<0.0001), and abdominal pain (Pearson r = 0.280; P<0.0001).

Figure 4. IBS-QOL Domain Scores in Patients With IBS-C: Mean Change From Baseline to Week 12



*P≤0.05, **P<0.01, ***P<0.001 vs placebo. IBS-C, irritable bowel syndrome with constipation; IBS-QOL, Irritable Bowel Syndrome Quality of Life; LS, least squares.

- Plecanatide showed significant improvements versus placebo in the IBS-QOL domains of dysphoria, body image, health worry, food avoidance, and relationship (Figure 4).

KEY FINDINGS

- Compared to placebo, patients with CIC and IBS-C who were treated with plecanatide 3 mg experienced significantly greater improvements in HRQOL (per PAC-QOL and IBS-QOL total scores). A significantly greater percentage of patients receiving plecanatide in both cohorts also experienced clinically meaningful improvements in HRQOL.
- Changes in PAC-QOL domain scores showed significant improvements in worries/concerns, physical discomfort, and satisfaction in patients with CIC treated with plecanatide compared with placebo.
- In patients with IBS-C, plecanatide significantly improved the IBS-QOL domain scores of dysphoria, body image, health worry, food avoidance, and relationship compared with placebo.
- Correlations in clinical outcomes (both bowel and abdominal symptoms) and HRQOL scores suggest a complex multi-symptom relationship of symptom improvement and HRQOL; this observation underscores the importance of global symptom management in optimizing HRQOL for the CIC/IBS-C patient.

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Disclosures

Darren M. Brenner is a consultant and speaker for Salix Pharmaceuticals. His research is sponsored by an unrestricted grant from the Irene D. Pritzker Foundation. Eric Shah is a consultant for Salix Pharmaceuticals. Christopher Charng and Kelly Chong have nothing to disclose. Sarah M. Lorenzen was an employee at Salix Pharmaceuticals at the time of analysis. Gregory S. Sayuk is a consultant and speaker for Salix Pharmaceuticals, Allergan/Ironwood Pharmaceuticals, and Alnylam, and is a consultant for the GI Health Foundation.

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.

Presented at American College of Gastroenterology 2021 | Oct 22–27, 2021 | Las Vegas, NV