Impact of Plecanatide on Symptoms and Quality of Life for Patients With Chronic Idiopathic Constipation: Analysis of PAC-SYM and PAC-QOL From Two Phase III Clinical Trials

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INTRODUCTION: Plecanatide, a 16-amino acid analog of human uroguanylin, activates guanylate cyclase-C receptors in the small intestine in a pH-sensitive manner to induce fluid secretion and peristalsis. This analysis looks at whether plecanatide improved global symptoms and health-related quality of life (HRQOL) in patients with chronic idiopathic constipation (CIC) from 2 large-scale, randomized, double-blind, placebo-controlled, phase 3 studies.

METHODS: Patients (N = 2883) who met modified Rome III criteria were randomized to placebo, plecanatide 3 mg, or 6 mg QD for 12 weeks and included in the phase 3 intention-to-treat populations. Baseline characteristics were comparable between groups and across studies. CIC symptoms and HRQOL were evaluated using the Patient Assessment of Constipation–Symptoms (PAC-SYM) and Patient Assessment of Constipation–Quality of Life (PAC-QOL) scales, respectively. The PAC-SYM measured patients’ constipation symptom experience and severity over time, including abdominal, rectal, and stool symptoms of constipation. The PAC-QOL evaluated patients’ HRQOL perceptions with constipation and rated patients’ worries and concerns, physical discomfort, psychosocial discomfort, satisfaction, and overall effects on HRQOL. Scales were rated from 0 to 4 with reductions in scores indicating improvement. Efficacy analyses evaluated each plecanatide dose vs placebo.

RESULTS: Statistically and clinically significant improvements in PAC-SYM (~0.75-point changes, Table 1) and PAC-QOL (~1–0-point change, Table 2) were observed at Weeks 4, 8, and 12 for both plecanatide 3 mg and 6 mg vs placebo across both studies. Plecanatide-treated patients reported significant improvements vs placebo in all PAC-SYM domain scores, except in Study 2 for abdominal symptoms. Significant improvements in plecanatide arms vs placebo were seen in 3 of 4 PAC-QOL domain scores (worries, physical discomfort, satisfaction). The most common adverse event (AE) was diarrhea (3 mg, 4.8%; 6 mg, 5.1%; placebo, 1.3%). Discontinuation rates due to AEs were 4.1% (3 mg), 4.5% (6 mg), and 2.2% (placebo), with low discontinuation due to AEs of 0.6% (3 mg), 1.0% (6 mg), and 0.4% (placebo).

CONCLUSION: Patients who received plecanatide 3 mg and 6 mg had statistically and clinically significant improvements in global symptoms and health-related quality of life (HRQOL) at all measured time points. Plecanatide treatment was associated with a low incidence of AEs and was well tolerated.

474 Activated Duodenal Eosinophils Are Associated With Early Satiation-Predominant Functional Dyspepsia Results From a U.S. Veteran Cohort

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INTRODUCTION: Functional Dyspepsia (FD) is an unexplained epigastric discomfort, early satiety or postprandial distress for three months. FD affects 50% of care-seeking Veterans in the United States. Diagnosis of FD is based on Rome consensus symptom criteria as no objective markers exist. There is interest in duodenal eosinophilia as a driver of FD symptoms, however heterogeneity among recent studies has produced divergent results. A "normal" range of duodenal eosinophil counts should be established. The influences of a personal history of atopy, medication use and seasonal variation effects on duodenal eosinophil counts and their relation to FD symptoms are poorly studied.

METHODS: This is a cross-sectional study from the Michael E. DeBakey VA Medical Center in Houston, Texas utilizing a well described cohort. Exclusion criteria included malignancy, H. pylori, celiac disease, parasite infection, eosinophil gastroenteritis and others. FD was defined by survey-derived Rome II symptom criteria. Medication use was obtained through chart review. Histopathology was independently reviewed by two blinded observers.

RESULTS: 461 patients were included in the present study. There was good observer agreement on duodenal eosinophil counts. Duodenal eosinophilia was defined as ≥8.6 per 5 HPF. Patient characteristics grouped by presence or absence of duodenal eosinophilia are found in Table 1. Mean eosinophil counts were significantly higher in the eosinophil group compared to the non-eosinophil group. Patient characteristics grouped by presence or absence of duodenal eosinophilia are found in Table 1. Mean eosinophil counts were significantly higher in the eosinophil group compared to the non-eosinophil group.

CONCLUSION: Duodenal eosinophilia may be a marker for FD driven by eosinophilic inflammation. Further studies are needed to determine the prevalence and significance of duodenal eosinophilia in FD patients.