Table 2. Week 12 Treatment Satisfaction for Patients With or Without AE of Diarrhea During the 12-Week Treatment Period

	Not at all satisfied % (n=453)	A little satisfied % (n=258)	Moderately satisfied % (n=277)	Quite satisfied % (n=329)	Very satisfied % (n=260)
Patients With Diarrhea					
Placebo (n=21)	28.6% (n=6)	23.8% (n=5)	4.8% (n=1)	28.6% (n=6)	14.3% (n=3)
Linaclotide (n=150)	16.0% (n=24)	20.0% (n=30)	19.3% (n=29)	22.0% (n=33)	22.7% (n=34)
Patients Without Diarrhea					
Placebo (n=762)	42.3% (n=322)	16.7% (n=127)	17.9% (n=136)	14.2% (n=108)	9.1% (n=69)
Linaclotide (n=644)	15.7% (n=101)	14.9% (n=96)	17.2% (n=111)	28.3% (n=182)	23.9% (n=154)

Note: ITT Population 12-Week Treatment Satisfaction Scores (LOCF), patients with missing Treatment Satisfaction scores were not included in this analysis.

Tu1402

Impact of Linaclotide Treatment on Work Productivity and Activity Impairment in Adults With Irritable Bowel Syndrome With Constipation

Jessica L. Buono, Stavros Tourkodimitris, Phil W. Sarocco, Mollie J. Baird, Jeffrey M. Johnston, Robyn Carson

Background: Irritable bowel syndrome with constipation (IBS-C) is a chronic functional gastrointestinal disorder characterized by abdominal pain or discomfort with bowel symptoms of constipation. IBS-C has been shown to decrease work productivity and increase activity impairment, resulting in a substantial economic burden for patients and employers. Linaclotide is an investigational minimally absorbed guanylate cyclase-C receptor agonist shown to significantly improve abdominal and bowel symptoms in 2 Phase 3 IBS-C trials. **Aim:** To evaluate the impact of linaclotide treatment on work productivity and activity impairment in IBS-C patients. **Methods:** Adult patients meeting modified Rome II criteria for IBS-C were randomized to oral once-daily 290-μg linaclotide or placebo for 12 weeks in 2 Phase 3 trials. The Work Productivity and Activity Impairment questionnaire for IBS-C (WPAI:IBS-C), a self-administered questionnaire consisting of 6 items, was used to measure absenteeism (work hours missed due to IBS-C), presenteeism (degree IBS-C symptoms affected productivity while at work), overall work productivity loss (absenteeism + presenteeism due to IBS-C), and daily activity impairment (degree IBS-C symptoms affected regular daily activities, including housework, shopping, childcare, exercising, studying) over the previous 7 days. Based on pooled Phase 3 trial data, changes from baseline to weeks 4, 8, and 12 for all 4 WPAI scores were assessed using an analysis of covariance (ANCOVA) model. Scores are represented as percentages, with higher percentages indicating greater work productivity loss and activity impairment. **Results:** A total of 1602 patients were randomized in the 2 Phase 3 trials. Patients included in this analysis had both baseline and at least 1 postbaseline WPAI:IBS-C assessment. Daily activity impairment was computed for all patients. Summary measures for absenteeism, presenteeism, and overall work productivity included employed patients only. Compared to placebo, linaclotide significantly reduced presenteeism, overall work productivity loss, and daily activity impairment at weeks 4, 8, and 12. A greater decrease in absenteesim was also observed for linaclotide compared to placebo at weeks 4, 8, and 12. Differences versus placebo in change from baseline to week 12 were 5.6% ($p<0.0001$) for presenteeism, 4.6% ($p<0.0001$) for overall work productivity, and 4.7% ($p<0.001$) for daily activity impairment (Table). Assuming a 40-hour work week, linaclotide reduced overall work productivity loss by 1.8 hours/week. **Conclusions:** Compared to placebo, once-daily linaclotide significantly reduced overall work productivity loss and daily activity impairment among IBS-C patients, with significant improvements seen at Week 4 and maintained through Week 12.

Table. Mean WPAI Scores and Change from Baseline to Week 12

WPAI Outcome	Mean Baseline Score	Mean Week 12 Score	LS Mean Change from Baseline to Week 12	Treatment Effect*	P-Value**
Overall work productivity loss					
Linaclotide	33.5	16.1	-17.3	-4.6	<0.0001
Placebo	33.2	20.6	-12.7		
Presenteeism					
Linaclotide	35.3	16.8	-18.3	-5.6	<0.0001
Placebo	34.6	22.1	-12.7		
Absenteeism					
Linaclotide	3.1	1.8	-1.2	-0.37	0.432
Placebo	2.7	2.0	-0.8		
Daily activity impairment					
Linaclotide	40.1	20.2	-19.8	-4.7	<0.0001
Placebo	40.0	24.9	-15.2		

*Treatment effect=LS means difference between linaclotide and placebo based on ANCOVA analysis. **Based on ANCOVA with baseline score as covariate and treatment group and geographic region as fixed effects.

Tu1403

Safety and Tolerability Profile of Rifaximin for Treatment of IBS Without Constipation: Results of a Pooled Analysis of Double-Blind, Placebo-Controlled Randomized Controlled Trials

Lin Chang, William D. Chey, Douglas A. Drossman, Anthony Lembo, Mark Pimentel, Philip S. Schoenfeld, Jing Yu, Kunal Merchant, Craig Paterson, Enoch Bortey, William P. Forbes

Introduction: Rifaximin has demonstrated superiority to placebo for global IBS symptoms and bloating among irritable bowel syndrome without constipation (non-C IBS) patients in two Phase III and one Phase IIB double-blind, placebo-controlled, randomized controlled trials (RCTs). Since rifaximin is minimally absorbed systemically (<0.4%), the short-term tolerability and safety of rifaximin may be similar to placebo. **Aim:** To quantify the frequency of adverse events among rifaximin-treated patients and placebo-treated patients in two Phase III and one Phase IIB double-blind, placebo-controlled RCTs. **Methods:** In the Phase III RCTs, non-C IBS patients (n = 1258) were randomly assigned (1:1) to rifaximin 550 mg tid (n = 624) or placebo (n = 634) for 14 days and were followed for 12 weeks from initiation of study drug. In the Phase IIB trial (n = 674), non-C IBS patients were randomized (2:2:1:1:1) to placebo X 28 days (n = 195) or rifaximin at dosages of 550 mg bid X 14 days (n = 190), 275 mg bid X 14 days (n = 95), 550 mg bid X 28 days (n = 96), or 1100 mg bid X 14 days (n = 98). In the Phase IIB trial, patients were assessed for 16 weeks from initiation of study drug. Treatment-emergent adverse events (TEAEs) are events that occurred while patient was using study medication or during study follow-up. Patients were queried about adverse events during scheduled study visits and hematologic, blood chemistries and urinalysis were also obtained during study visits. For the Phase III RCTs, scheduled study visits occurred on days 1,7, 14, 28, and 84. For the Phase IIB RCT, scheduled study visits occurred on the same days plus days 42, 56, and 112. **Results:** In these RCTs, 1103 unique patients were treated with rifaximin and 829 unique patients were treated with placebo. Treatment-emergent adverse event profiles were similar for rifaximin-treated patients and placebo-treated patients, respectively, for any TEAEs (52.5% vs 52.6%), serious TEAEs (1.5% vs 2.2%), TEAEs resulting in study discontinuation (2.0% vs 1.7%), total GI system TEAEs (18.2% vs 19.5%), total infection-related TEAEs (21.8% vs 23.3%), nausea (4.4% vs 3.7%), abdominal pain (3.7% vs 4.7%), diarrhea (3.4% vs 3.1%), vomiting (2.0% vs 1.4%), and headache (5.3% vs 6.2%). Treatment-emergent AEs involving hypersensitivity (eg, pruritus or rash) were infrequent (≤ 1% of subjects) and similar in both groups. Mean changes in hematology parameters, blood chemistry parameters, and urinalysis parameters were minimal and similar in both groups. No cases of *C. difficile* colitis were reported in study patients during treatment or during follow-up. **Conclusions:** The safety and tolerability profile for rifaximin-treated non-C IBS patients is similar to placebo-treated non-C IBS patients in pooled analysis of RCTs and no cases of *C. difficile* colitis were reported.

Tu1404

Improvement of Abdominal Pain and Bloating is Independently Influenced by Male-Gender and a Combination Therapy With Pinaverium Bromide+Simethicone. a Report From the Mexican IBS Working Group

Max J. Schmulson, Jose Maria Remes Troche, Aurelio Lopez-Colombo, Arturo Jimenez, Jazmin Chiu-Ugalde, Jose L. Tamayo-de la Cuesta, Jose-Antonio Vargas, Juan C. Lopez-Alvarenga

Background: We have recently shown in a 12-week treatment trial in IBS patients that 100mg of Pinaverium Bromide + 300mg Simethicone (PB+S), decreases the severity of abdominal pain and bloating,1,2 but the effect of gender and IBS subtypes is unknown. Aims: To analyze the effect of gender, treatment and IBS subtypes on the improvement of abdominal pain and bloating. Methods: Patients with active Rome III-IBS (N=300) participated in a placebo-controlled clinical trial with PB+S vs. placebo. Active IBS was defined as the presence of abdominal pain/discomfort at least twice during the previous week. They all fulfilled 10 cm visual analogue scale for abdominal pain and bloating severity during weeks 1, 11 and 12 of the treatment trial. For maximization of the contrast we analyzed the IBS-C (N=132) and IBS-D (N=67). We ran a 2k factor analysis with 3 fixed factors: gender (Male, Female), IBS subtype (IBS-C, IBS-D) and treatment (PB+S, Placebo). In addition, two models were tested, one based on main factors and the other one based on an interaction model. The latter was not significant. Results: Patients were 36.5 (SD: 9.1) years old, gender: 79% F, and BMI: 26.5 (SD 4.4). The IBS-C were younger than the IBS-D (35.4±0.81 vs. 38.5±1.03, $p<0.023$) but there were no differences in age, sex and BMI according to the treatment groups (BP+S vs. placebo). During the first week of treatment the improvement in abdominal pain was influenced mainly by Male (effect 1.38) > BP+S (1.05) > IBS-D (0.95); but at the end of the treatment, abdominal pain improvement was mainly influenced by BP+S (0.62) > Male (0.512) > IBS-C (0.10). Bloating improvement during the first week was influenced by IBS-D (0.92) > BP+S (0.81) > Male (0.74); and at the end of treatment, mainly by BP+S (0.81) > Male (0.43) > IBS-D (0.18). Both abdominal pain and bloating improved constantly during treatment with PB+S vs. placebo ($p<0.05$). In contrast the effect of gender was constant for abdominal pain improvement ($p<0.05$) but not for bloating (NS), while the effect of IBS-D subtype was constant for bloating ($p<0.05$) but not for abdominal pain (NS). Conclusions: Treatment with PB+S is the most important determinant of improvement for both, abdominal pain and bloating at the end of the trial. Men have a higher improvement with PB+S compared to women, contrary to the findings with other treatments. This study was supported by Nycomed: A Takeda Company, Mexico. References: 1. Remes-Troche JM et al. Gastroenterology 2011;140(Suppl.1):M1332. 2. Schmulson M et al. Gastroenterology 2011;140(Suppl.1):M1327.