what domains of QOL are most impacted in a cohort of IBS patients at a tertiary care center and if age or BMI have an influence on their QOL.

Methods: Patients diagnosed with IBS by Rome III criteria visiting a general gastroenterology clinic at a tertiary medical center were surveyed using the IBS-QOL. IBS-QOL is a psychometrically validated questionnaire which assesses overall quality of life and along eight subscales: dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual, and relationships. IBS-QOL and its subscales are both scored from 0-100. Lower scores suggest worse quality of life. Demographic data including age, gender, race, clinical data including BMI and IBS subtype (IBS-U, IBS-C, IBS-D), responses to IBS-QOL questionnaires were collected and analyzed. We compared overall IBS-QOL and its subscales by subtype as well as by age and BMI. Analysis of variance (ANOVA) or non-parametric Kruskal-Wallis tests assessed differences in continuous variables. Pearson’s chi-square tests were used for categorical factors. Post-hoc comparisons were done at a significance of 0.017 (0.05/3 comparisons). Spearman’s correlation coefficients assessed if IBS-QOL correlated to age or BMI.

Results: A total of 80 patients were analyzed [mean age 49 yrs, 85% female]. Overall IBS-QOL and all subscales except body image and health worry were found to be significantly associated with diagnosis (Table 1). IBS-D patients had significantly lower QOL than IBS-C; there was no significant difference between either of these two groups and the IBS-U group (Figures 1 & 2). There was no correlation between age or BMI and any IBS-QOL subscale (Table 2).

Conclusion: Majority of QOL domains are impacted in IBS patients. Providers should acknowledge dysphoria, interference with activity, food avoidance, social reactions and relationship issues in these patients. Further study is needed to determine possible treatment modalities to improve QOL and these domains in IBS patients. A multidisciplinary clinic with nutrition, psychology and pharmacy resources may be beneficial in management of IBS patients. IBS-D patients may require more intensive therapies.

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Analysis of Potential Predictors of Symptom Recurrence in Patients Treated with Rifaximin for Diarrhea-Predominant Irritable Bowel Syndrome (IBS-D)

2016 ACG Presidential Poster Award
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Introduction: Rifaximin, a nonselective antibiotic, is indicated for the treatment of adults with IBS-D. This post hoc analysis explored potential predictors of symptom recurrence in patients responding to open-label rifaximin during a repeat treatment trial.

Methods: Adults with IBS-D received open-label rifaximin 550 mg three times daily for 2 weeks, followed by a 4-week follow-up to assess response. Responders (ie, patients with ≥75% decrease from baseline in mean weekly IBS-related abdominal pain score) were identified and analyzed in the context of daily symptom scores. Treatment-emergent adverse events were evaluated in an 18-week observation phase or until symptom recurrence. Factors evaluated: age ( < 65; ≥65 y), sex; years since onset of IBS symptoms ( < 5; 5-10; 11-20; ≥20); mean daily stool score (≤5; >5); stool consistency (≤5; >5); bloating (≤4; >4); and IBS symptoms (≤4; >4), number of daily bowel movements (≤4; >4); days per week with bowel movement urgency (≤4; >4); and prohibited medication use (yes/no).

Results: Of the 1074 responders, 692 (64.4%) experienced symptom recurrence during the 18-week follow up. For the primary endpoint, a greater percentage of patients with symptom recurrence used prohibited medications vs patients without recurrence (21.7% vs 13.8%). This was identified as a predictor of symptom recurrence (odds ratio [OR], 0.70; 95% confidence interval [CI], 0.53-0.91; P=0.02). No other factors predicting symptom recurrence were identified. The 2 components of the endpoint were also analyzed separately. For abdominal pain responders, time predictors of recurrence were duration since onset of first IBS symptoms (OR, 1.2; 95% CI, 1.1-1.3; P=0.003) and mean daily stool consistency scores (OR, 0.8; 95% CI, 0.5-1.0; P=0.05). For stool consistency responders, only prohibited medication use was significant (OR, 0.3; 95% CI, 0.2-0.4; P=0.001).

Conclusion: No baseline demographics or disease characteristics were identified as predictors of symptom recurrence after rifaximin response, except for duration since first IBS symptoms and stool consistency score in an abdominal pain responder subgroup. Further research is needed to identify predictors of symptom recurrence in patients with IBS-D.

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Safety and Tolerability of Rifaximin in the Treatment of Irritable Bowel Syndrome (IBS): A Pooled Analysis of 4 Randomized, Placebo-Controlled Trials

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Introduction: The nonselective antibiotic rifaximin is indicated for the treatment of diarrhea-predominant IBS (IBS-D). This analysis evaluated the overall safety and tolerability profile of rifaximin in IBS.

Methods: A post hoc pooled analysis included data from a phase 2b study (rifaximin 275 mg, 550 mg, or 1100 mg or placebo [PBO] twice daily for 2 weeks), phase 3 TARGET 1 and 2 (rifaximin 550 mg or PBO 3 times daily for 2 weeks), and the double-blind retreatment phase of phase 3 TARGET 3 (2 courses of rifaximin 550 mg or PBO 3 times daily for 2 weeks, separated by a 6-week treatment-free follow-up phase). Safety was assessed for 12 (phase 2b), 18 (TARGET 1 and 2), or 22 (TARGET 3) weeks post-treatment. Population included all patients with ≥1 dose of double-blind study medication and ≥1 post-baseline safety assessment.

Results: The analysis included 2568 patients (n=1431 rifaximin, n=1137 PBO). A treatment-emergent adverse event (AE) was experienced by 50.2% and 50.7% of patients in the rifaximin and PBO groups, respectively. The majority of AEs were mild to moderate in intensity; severe AEs were reported by 4.6% in the rifaximin group and 5.8% in the PBO group. Drug-related AEs were reported in 9.8% and 8.5% of patients in the rifaximin and PBO groups, respectively. The most common AEs (≥2% of patients in rifaximin group) occurring during rifaximin versus PBO were headache (4.4% vs 5.3%), upper respiratory tract infection (4.3% vs 4.8%), nausea (4.2% vs 3.3%), urinary tract infection (3.4% vs 2.9%), abdominal pain (3.1% vs 3.6%), diarrhea (3.1% vs 2.6%), nasopharyngitis (2.5% vs 4.2%), and sinusitis (2.2% vs 2.6%). Constipation was reported in 0.9% of the rifaximin group and 1.6% of the PBO group. Serious AEs were experienced by 1.4% (rifaximin) and 1.9% (PBO) of patients, 1 event in the rifaximin group (abdominal hemorrhage) was considered related to study drug. One patient developed Clostridium difficile during the TARGET 3 treatment-free observation phase. The patient had a history of C difficile and received a 10-day course of cefdinir for a urinary tract infection; this AE was nondrug-related. AEs resulted in study discontinuation in 1.6% of patients in the rifaximin group and 1.3% of patients in the PBO group.

Conclusion: The safety and tolerability profile during and following initial and repeated, intermittent 14-day treatment courses with rifaximin was generally comparable to that of PBO in patients with IBS. Funded by Salix Pharmaceuticals.

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Efficacy of Rifaximin on Bowel Movement Urgency in Patients with Diarrhea-Predominant Irritable Bowel Syndrome (IBS-D): A Pooled Analysis of 3 Phase 3 Trials

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Introduction: Rifaximin, a nonselective antibiotic, is indicated for the treatment of adults with IBS-D. Bowel movement urgency is a common symptom in patients with IBS. The aim of this post hoc analysis
was to characterize improvements in bowel movement urgency after 2 weeks of treatment with rifaximin in patients with IBS-D.

Methods: Adults with IBS-D receiving double-blind rifaximin 550 mg three times daily for 2 weeks, followed by a 4-week treatment-free follow-up period to evaluate treatment response were included in this pooled analysis of 3 trials. Bowel movement urgency response was defined as a ≥30% improvement from baseline in the percentage of days with urgency for ≥2 of the first 4 post-treatment weeks. Daily urgency was determined by patient yes/no response to the question “Have you felt or experienced a sense of urgency today?” in Trials 1 and 2, and “Have you felt or experienced a sense of urgency in the last 24 hours with any of your bowel movements?” in Trial 3. Bowel movement urgency response was also evaluated for each week of the 4-week post-treatment period. Logistic regression was used to analyze the overall treatment effect on response, whereas a general estimating equation model was used to analyze treatment effects by week.

Results: A total of 1949 patients (rifaximin [n=952], placebo [n=942]) with IBS-D were included in the pooled analysis. Mean (standard error) age in rifaximin and placebo groups was 46.6 ± 0.5 and 45.8 ± 0.5 y, 71.8% and 70.7% were females, mean baseline daily IBS symptom scores were 3.7 ± 0.6, 3.6 ± 0.7, respectively, and mean baseline days per week with bowel movement urgency were 5.8 ± 0.8 days for both groups. A significantly greater percentage of patients receiving rifaximin vs placebo demonstrated a bowel movement urgency response vs placebo (53.6% vs 44.6%; odds ratio, 1.4; 95% confidence interval, 1.2–1.7; P < 0.001). Furthermore, the percentage of bowel movement urgency responders was significantly greater with rifaximin vs placebo during the first week of the post-treatment period (week 1, 50.7% vs 42.8%; P = 0.002; week 2, 50.7% vs 42.8%, P = 0.002; week 3, 47.1% vs 39.3%, P = 0.006; week 4, 46.2% vs 39.6%, P = 0.004).

Conclusion: This pooled analysis supports that rifaximin 550 mg twice daily for 2 weeks significantly improves bowel movement urgency vs placebo in adults with IBS-D. Funded by Salix Pharmaceuticals.

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Impact of Baseline Pain Severity on the Efficacy of Eluxadoline in Patients with Irritable Bowel Syndrome with Diarrhea

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Introduction: Eluxadoline, a mixed µ-opioid receptor (OR) and k-OR agonist and δ-OR antagonist that is locally active in the gastrointestinal tract, is approved for the treatment of irritable bowel syndrome with diarrhoea (IBS-D) in adults. In two Phase 3 studies, eluxadoline significantly improved symptoms of IBS-D based on a composite endpoint of simultaneous improvement in stool consistency and abdominal pain scores. Post hoc analyses of pooled data from these trials were conducted to further evaluate the impact of baseline abdominal pain severity on treatment outcomes.

Methods: Two double-blind, placebo-controlled, Phase 3 trials (IBS-3001 and IBS-3002) randomized patients meeting Rome III criteria for IBS-D to twice daily treatment with eluxadoline 75 or 100 mg or placebo. Patients rated IBS symptoms daily, including worst abdominal pain (WAP, 0–10 scale) and stool consistency (Bristol Stool Scale [BSS]). The primary efficacy endpoint was composite response, based on simultaneous daily improvement of ≥30% in WAP score vs baseline and BSS score ≤5 with ≥50% of days demonstrating a response, evaluated over 12 and 26 weeks. The Irritable Bowel Syndrome Quality of Life instrument was assessed at baseline, Week 4, and each subsequent visit. Pooled data were stratified by baseline abdominal pain score (< 3, 3–< 5, 5– < 8, 8–). Composite, abdominal pain, and stool consistency responders rates over Weeks 1–12 and 1–26 were calculated. Statistical inferences were not made due to this being a post hoc analysis and the small sample size of patients with baseline abdominal pain score ≥8.

Results: 2428 IBS-D patients were enrolled across both trials. Proportions of composite, abdominal pain, and stool consistency responders with eluxadoline were greater than with placebo in the overall population and in all baseline abdominal pain severity subgroups over Weeks 1–12 and 1–26 (Table). Responder rates for composite, stool consistency, and abdominal pain decreased with increasing baseline abdominal pain severity, with differences from placebo largest for the lowest category of abdominal pain.

Conclusion: Greater numbers of patients show a composite, abdominal pain, and stool consistency response with eluxadoline vs placebo across baseline abdominal pain severity categories. This work was funded by Allergan plc.

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A Prospective Study on Racial Disparities in Patients with Irritable Bowel Syndrome

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Introduction: Irritable bowel syndrome (IBS) is a highly prevalent functional bowel disorder characterized by abdominal pain and change in bowel habit. This prospective study aims to validate our previous results of disparities in a racially diverse IBS patient cohort, and interim results with emphasis on quality of life measures are presented.

Methods: At Boston Medical Center (BMC) we prospectively enrolled adult outpatients with IBS (N=80) and controls (N=166) based on Rome III criteria questionnaires. Electronic medical records were reviewed and data from a 15 year period on total and IBS-related events were analyzed using Chi-square, Fisher's exact, and Wilcoxon rank sum test. IBS-specific (IBSQOL) and general quality of life (VR-12) was assessed using validated questionnaires.

Results: The mean age of IBS patients was younger, whereas the racial breakdown and BMI for IBS and control patients was similar (Table 1). Basic demographics were similar between Whites (W), Blacks (B), and Hispanics (H) (Table 2). Significantly more GI visits and IBS-related PCP visits overall were noted in IBS patients (p < 0.0001; p=0.005). PCP and GI office visits of W-IBS with B/H-IBS patients were higher for all office visits and IBS-related GI visits (p<0.05). IBSQOL was significantly lower (p < 0.0001) in IBS patients compared with controls. General QOL in both the physical (PCS) and the mental component (MCS) were significant lower (p < 0.0001, and p=0.02, respectively) for all IBS patients. Racial disparity of IBSQOL exists (p=0.018) when all IBS patients from all racial groups were compared with lowest scores seen in H and highest in W, but mcs (p=0.2) and pcs (p=0.33) scores were not different. IBSQOL subdomains for body image (p=0.37) and food avoidance (p=0.15) did not differ in all racial groups, whereas the dysphoria (p=0.006) and sexual score (p=0.03) were significantly different. Similarly, IBSQOL health worry, social reaction, and overall score were significantly different (p=0.02, p=0.008, and p=0.04) among all racial groups with H scoring lowest in all subdomains.

Table 1.

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>Composite response</th>
<th>Abdominal pain response</th>
<th>Stool consistency response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weeks 1–12 responders, n (%)</td>
<td>Weeks 1–26 responders, n (%)</td>
<td>Weeks 1–12 responders, n (%)</td>
</tr>
<tr>
<td>Overall</td>
<td>ELX 75 mg BID (n=80)</td>
<td>232 (26.2)</td>
<td>216 (26.7)</td>
</tr>
<tr>
<td></td>
<td>ELX 100 mg BID (n=80)</td>
<td>218 (27.0)</td>
<td>250 (31.0)</td>
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<tr>
<td></td>
<td>PBO BID (n=80)</td>
<td>135 (16.7)</td>
<td>158 (19.5)</td>
</tr>
<tr>
<td>Baseline abdominal pain = ≤5</td>
<td>ELX 75 mg BID (n=100)</td>
<td>64 (33.7)</td>
<td>60 (31.6)</td>
</tr>
<tr>
<td></td>
<td>ELX 100 mg BID (n=100)</td>
<td>61 (33.0)</td>
<td>67 (36.2)</td>
</tr>
<tr>
<td></td>
<td>PBO BID (n=100)</td>
<td>27 (15.0)</td>
<td>38 (21.1)</td>
</tr>
<tr>
<td>Baseline abdominal pain &gt; ≤6</td>
<td>ELX 75 mg BID (n=50)</td>
<td>126 (24.9)</td>
<td>132 (26.1)</td>
</tr>
<tr>
<td></td>
<td>ELX 100 mg BID (n=50)</td>
<td>137 (26.2)</td>
<td>159 (30.4)</td>
</tr>
<tr>
<td></td>
<td>PBO BID (n=50)</td>
<td>98 (18.3)</td>
<td>106 (20.4)</td>
</tr>
</tbody>
</table>

Composite response based on simultaneous abdominal pain response (daily improvement of ≥30% in worst abdominal pain score vs. baseline) and stool consistency response (Bristol Stool Score ≤5) with ≥50% of days demonstrating a response, evaluated over 12 and 26 weeks.