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Radar plots: A novel modality for displaying disparate data on the efficacy of eluxadoline for the treatment of irritable bowel syndrome with diarrhea

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Abstract

Background: Patients with irritable bowel syndrome with diarrhea (IBS-D) experience a range of abdominal and bowel symptoms; successful management requires alleviation of this constellation of symptoms. Eluxadoline, a locally active mixed μ- and κ-opioid receptor agonist and δ-opioid receptor antagonist, is approved for the treatment of IBS-D in adults based on the results of 2 Phase 3 studies. Radar plots can facilitate comprehensive, visual evaluation of diverse but interrelated efficacy endpoints.

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 eluxadoline 75 or 100 mg or placebo. Radar plots were prepared showing pooled Weeks 1-26 response rates for the primary efficacy composite endpoint (simultaneous improvement in abdominal pain and stool consistency), stool consistency, abdominal pain, urgency-free days, and adequate relief, and change from baseline to Week 26 in IBS-D global symptom score, abdominal discomfort, abdominal pain, abdominal bloating, and daily number of bowel movements.

Key Results: The studies enrolled 2428 patients. Eluxadoline increased Weeks 1-26 responder proportions vs placebo for the composite endpoint, stool consistency, abdominal pain, urgency-free days, and adequate relief. Changes from baseline to Week 26 in IBS-D global symptom score, abdominal discomfort, abdominal pain, abdominal bloating, and number of bowel movements were greater with eluxadoline vs placebo.

Conclusions and Inferences: Data presentation in radar plot format facilitates interpretation across multiple domains, demonstrating that eluxadoline treatment led to improvements vs placebo across 13 endpoints representing the range of symptoms experienced by patients with IBS-D.

KEYWORDS
abdominal pain, diarrhea, eluxadoline, irritable bowel syndrome, radar plots

Abbreviations: BSFS, Bristol Stool Form Scale; GSS, global symptom score; IBS, irritable bowel syndrome; IBS-D, irritable bowel syndrome with diarrhea; xSD, standard deviation.

1 | INTRODUCTION

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder estimated to affect up to 20% of adults in the US population, with the diarrhea subtype (IBS-D) experienced by approximately 40% of patients with IBS.[1,2] IBS-D is characterized by recurring abdominal pain associated with loose, frequent stools in the absence of demonstrable organic disease.[3-5]

While abdominal pain and diarrhea are the cardinal symptoms of IBS-D, patients may experience a broad range of abdominal and bowel symptoms,[6-8] including abdominal bloating and distention,[7] unpredictable bowel patterns involving both form and frequency, and fecal urgency and incontinence.[6,7,9] Symptoms such as bloating and urgency are common in IBS-D and may be extremely bothersome, greatly impacting patients' daily lives. In a survey including 1001 patients with IBS-D, loss of bowel control or fecal incontinence was reported as the most bothersome symptom.[10] Symptoms of IBS-D can range from mild and intermittent to more severe and continuous, with abdominal pain and bloating being strongly related to perceived disease severity.[11,12]

Traditionally, pharmacologic management has primarily involved addressing specific symptoms, with limited evidence that many existing treatments effectively control the multiple symptoms of IBS-D.[13] In one study, more than half of patients with IBS-D reported inadequate symptom control with the currently available medication options.[14] IBS-D is associated with a substantial economic burden in terms of its impact on work productivity and healthcare resource use, and patients with inadequate symptom control use significantly more healthcare resources and incur significantly greater costs.[14,15]

Eluxadoline, a mixed μ- and κ-opioid receptor agonist and δ-opioid receptor antagonist approved for the treatment of IBS-D in adults,[16] has demonstrated efficacy for multiple IBS-D symptoms, based on 2 large Phase 3 trials. Significantly greater proportions of patients receiving eluxadoline were responders vs placebo based on a primary composite endpoint consisting of simultaneous reduction in abdominal pain and improvement in stool consistency.[17] Further analyses demonstrated sustained benefits in patients with IBS-D, as more than two-thirds of patients who were composite or adequate relief responders with eluxadoline over the first month of therapy retained their response throughout 6 months of treatment.[18] Furthermore, multiple secondary endpoints were improved across both trials.

Measurement of treatment effects in IBS is inherently multivariate, necessitating presentation formats that can accommodate multiple measures simultaneously. Radar plots are useful for visually presenting complex multivariate data across multiple domains or outcomes in a single graph and in a simple, easily interpretable manner.[19,20] These graphs have been used to analyze and present data across a variety of areas of medical research, from monitoring of chronic liver disease to brain injury rehabilitation, mapping of medication dispensing for atherosclerotic cardiovascular disease, and assessment of sleep disturbances.[21-24]

Key Points

- Data presentation in radar plot format can facilitate evaluation of the diverse array of symptoms and outcomes that are relevant to a symptom-based condition like irritable bowel syndrome with diarrhea (IBS-D).
- In 2 Phase 3 trials, eluxadoline treatment improved stool consistency and frequency, abdominal pain, bloating and discomfort, feelings of urgency, global symptom score, and adequate relief.
- Radar plots provide a visual demonstration of improvements with eluxadoline across 13 endpoints encompassing the diverse constellation of symptoms experienced by patients with IBS-D.

We report data from the 2 Phase 3 studies of eluxadoline and utilize radar plots to present the wide range of efficacy measures assessed and address the spectrum of symptoms experienced by patients with IBS-D in 2 simple graphical representations.

2 | MATERIALS AND METHODS

2.1 | Study design

Two double-blind, placebo-controlled, Phase 3 clinical trials (IBS-3001; https://clinicaltrials.gov/: NCT01553591 and IBS-3002; https://clinicaltrials.gov/: NCT01553747) randomized patients 1:1:1 to twice-daily treatment with eluxadoline 75 or 100 mg or placebo; the methodology and results of these studies have been described previously.[17] Both studies comprised an identical 26-week treatment period. IBS-3001 was followed by a 26-week safety assessment, with a 2-week follow-up period, while IBS-3002 was followed by a 4-week single-blind placebo withdrawal period.

These studies were conducted in compliance with the principles of the International Conference on Harmonisation tripartite guideline E6(R1): Good Clinical Practice and according to the Declaration of Helsinki. The institutional review board or ethics committee at each participating site approved the protocols, and all patients provided written informed consent.

2.2 | Study assessments

Participants recorded daily and weekly assessments of IBS-D symptoms and bowel function using an electronic diary with an interactive voice response system.[17] Abdominal pain in the past 24 hours was reported daily on an 11-point scale, where 0 indicates no pain and 10 indicates worst pain imaginable. Stool consistency was reported daily on the Bristol Stool Form Scale (BSFS), a 7-point scale where 1 indicates hard stool and 7 indicates watery diarrhea.[25] IBS-D global symptom score (GSS) in the past 24 hours

was reported daily on a 5-point scale, where 0 indicates no symptoms and 4 indicates very severe symptoms. Adequate relief was assessed once weekly with a dichotomous response to the following question: "Over the past week, have you had adequate relief of your IBS symptoms?" Abdominal bloating in the past 24 hours was reported daily on an 11-point scale, where 0 indicates no bloating and 10 indicates worst bloating imaginable (abdominal bloating ratings were not collected in the Spanish language version of the electronic diary). Abdominal discomfort in the past 24 hours was reported daily on an 11-point scale, where 0 indicates no discomfort and 10 indicates worst discomfort imaginable. Number of bowel movements and number of urgency episodes over the past 24 hours were recorded daily.

2.3 | Patient population

The studies enrolled patients aged 18-80 years meeting the Rome III criteria for IBS-D.[17,26] During the week prior to randomization, eligible patients were required to report an average worst abdominal pain score of >3.0, an average BSFS score of ≥5.5, and an average IBS-D GSS of ≥2.0. Key exclusion criteria were the presence of inflammatory bowel disease or celiac disease, abnormal thyroid function, history of alcohol abuse[27] or binge drinking,[28] prior pancreatitis, sphincter of Oddi dysfunction, post-cholecystectomy biliary pain, cholecystitis in the past 6 months, intestinal obstruction, or gastrointestinal infection or diverticulitis in the past 3 months.

2.4 | Efficacy endpoints

As previously reported,[17] the primary efficacy endpoint of both studies was composite response defined as daily improvement of ≥30% in worst abdominal pain score vs average baseline pain and, on the same day, a BSFS score of <5 or the absence of a bowel movement if accompanied by an improvement of ≥30% in abdominal pain score, on ≥50% of treatment days. Abdominal pain response was defined as daily improvement of ≥30%, ≥40%, or ≥50% vs average baseline pain for ≥50% of days with diary entries. Stool consistency response was defined as a BSFS score of <5 on ≥50% of treatment days, or the absence of a bowel movement if accompanied by an improvement of ≥30% in abdominal pain score. Adequate relief response was defined as a weekly "yes" response for ≥50% of treatment weeks. Urgency-free responders were calculated using criteria of ≥50% or ≥75% of days with no diary entry of urgency episodes. Response rates were evaluated over 26 weeks, requiring a minimum of 110 diary-entry days for a patient to be considered as a responder. Additionally, changes from baseline to Week 26 in IBS-D GSS, abdominal discomfort, abdominal pain, abdominal bloating, and number of bowel movements were assessed.

2.5 | Data analyses

Statistical analyses for the Phase 3 trials have been described previously.[17] In brief, efficacy data from the 2 Phase 3 studies were pooled, with analyses performed on the intent-to-treat analysis set. No imputation for missing data was performed, as diary compliance rules accounted for absent diary entries. Patients with insufficient diary data were categorized as non-responders.

2.6 | Generation of radar plots

Response rates over Weeks 1-26 were displayed in radar plot format, with the composite endpoint and adequate relief endpoint at the 12 and 6 o'clock positions to serve as anchors and the 2 components of the composite endpoint (stool consistency and pain [≥30% improvement from baseline]) flanking the composite endpoint, with other endpoints grouped by similarity. Changes from baseline to Week 26 were presented in a similar fashion, with the global symptom measure IBS-D GSS at the 12 o'clock anchor position. Since the only statistical adjustment made a priori was for the examination of 2 doses, no *P*-values are presented for this multiple endpoint presentation.

3 | RESULTS

3.1 | Baseline demographics and disease characteristics

Across both studies, 2428 patients were enrolled (1282 in IBS-3001; 1146 in IBS-3002). Patient demographics and baseline characteristics were balanced between the 2 individual studies and across treatment groups.[17] Mean age (SD) was 44.9 (13.7) in IBS-3001 and 45.9 (13.5) in IBS-3002, with a greater proportion of female patients in both studies (IBS-3001: 65.4%; IBS-3002: 67.0%). In the pooled Phase 3 population, baseline disease characteristics were similar between treatment groups (Table 1).

3.2 | Proportions of responders over Weeks 1-26 in the pooled Phase 3 trial population

Treatment with eluxadoline improved the range of efficacy measures assessed vs placebo over Weeks 1-26, with a visible separation of response between eluxadoline and placebo observed for all measures (Figure 1). Composite responder proportions have been described previously and were 26.7% (216/808) and 31.0% (250/806) with eluxadoline 75 and 100 mg, respectively, vs 19.5% (158/809) with placebo ($P < .001$ vs placebo for both comparisons).[17]

Proportions of responders to eluxadoline were greater than placebo for symptom components of the composite endpoint: 31.1% (251/808) and 36.8% (297/806) of patients were stool consistency responders with eluxadoline 75 and 100 mg, respectively, vs 23.9% (193/809) with placebo, and 46.3% (374/808) and 48.3% (389/806) were abdominal pain responders with eluxadoline 75 and 100 mg, respectively, vs 44.0% (356/809) with placebo using the criteria of ≥30% improvement from baseline. Responder proportions with eluxadoline vs placebo were also higher with criteria of ≥40% improvement or ≥50% improvement from baseline in abdominal pain, with 41.5% (335/808) and 44.2% (356/806) of patients with eluxadoline 75 and 100 mg, respectively, vs

TABLE 1 Baseline symptom scores: pooled Phase 3 population

	Placebo (n = 809)	Eluxadoline 75 mg (n = 808)	Eluxadoline 100 mg (n = 806)
Weekly stool consistency, mean (SD)	6.24 (0.41)	6.25 (0.40)	6.25 (0.42)
Weekly abdominal pain, mean (SD)	6.14 (1.53)	6.07 (1.53)	6.07 (1.51)
Weekly IBS-D GSS, mean (SD)	2.85 (0.55)	2.78 (0.54)	2.83 (0.53)
Weekly abdominal bloating, mean (SD)[a]	5.90 (2.08)	5.81 (2.02)	5.73 (2.07)
Weekly abdominal discomfort, mean (SD)	6.33 (1.50)	6.28 (1.53)	6.22 (1.51)
Daily number of bowel movements, mean (SD)	4.85 (2.52)	4.78 (2.53)	4.95 (3.60)
Daily number of urgency episodes, mean (SD)	3.55 (2.40)	3.45 (2.21)	3.50 (3.25)

GSS, global symptom score; IBS-D, irritable bowel syndrome with diarrhea; SD, standard deviation. Stool consistency score was reported on a 7-point scale, where 1 indicates hard stool and 7 indicates watery diarrhea; abdominal pain score was reported on an 11-point scale, where 0 indicates no pain and 10 indicates worst pain imaginable; IBS-D GSS was reported on a 5-point scale, where 0 indicates no symptoms and 4 indicates very severe symptoms; abdominal bloating score was reported on an 11-point scale, where 0 indicates no bloating and 10 indicates worst bloating imaginable; abdominal discomfort score was reported on an 11-point scale, where 0 indicates no discomfort and 10 indicates worst discomfort imaginable. Patients were asked to record the number of bowel movements and urgency episodes daily over the past 24 h.

[a]Patients who responded to the interactive voice response system items in Spanish were not presented with the bloating item: placebo, n = 670; eluxadoline 75 mg, n = 687; eluxadoline 100 mg, n = 691.

37.7% (305/809) with placebo meeting the ≥40% improvement response criteria, and 36.4% (294/808) and 38.7% (312/806) of patients with eluxadoline 75 and 100 mg, respectively, vs 32.5% (263/809) with placebo meeting the ≥50% improvement response criteria.

Adequate relief responder rates were greater with eluxadoline vs placebo, with 49.0% (396/808) and 51.5% (415/806) of patients responding with eluxadoline 75 and 100 mg, respectively, vs 41.8% (338/809) with placebo.

Urgency-free days responder proportions were greater with eluxadoline vs placebo for both the ≥75% urgency-free days and the ≥50% urgency-free days response criteria: 26.5% (214/808) and 27.8% (224/806) of patients were ≥75% urgency-free days responders with eluxadoline 75 and 100 mg, respectively, vs 16.6% (134/809) with placebo, and 44.6% (360/808) and 45.3% (365/806) were ≥50% urgency-free days responders with eluxadoline 75 and 100 mg, respectively, vs 33.8% (273/809) with placebo.

3.3 | Change from baseline to Week 26 in the pooled Phase 3 trial population

Patients treated with eluxadoline displayed larger changes from baseline to Week 26 vs placebo across all efficacy measures assessed, with observable visual separation between the eluxadoline and placebo treatment arms (Figure 2). Weekly mean IBS-D GSS decreased from baseline to Week 26 by 1.5 points in both eluxadoline 75 mg (n = 515) and 100 mg (n = 528) cohorts vs a decrease of 1.3 points with placebo (n = 526).

Eluxadoline treatment improved abdominal discomfort, pain, and bloating vs placebo: weekly mean abdominal discomfort scores decreased from baseline to Week 26 by 3.3 and 3.4 points with eluxadoline 75 mg (n = 515) and 100 mg (n = 528), respectively, vs 2.8 points with placebo (n = 526); weekly mean abdominal pain scores decreased by 3.3 and 3.4 points with eluxadoline 75 mg (n = 515) and 100 mg (n = 528), respectively, vs 3.0 points with placebo (n = 526), and weekly mean abdominal bloating scores decreased by 2.6 and 2.8 points with eluxadoline 75 mg (n = 416) and 100 mg (n = 438), respectively, vs 2.3 points with placebo (n = 419).

Patients receiving eluxadoline also reported improved bowel movement frequency, with a daily mean number of bowel movements decrease of 2.0 for both eluxadoline 75 mg (n = 515) and 100 mg (n = 528) vs a decrease of 1.6 with placebo (n = 526).

4 | DISCUSSION

Presentation of pooled efficacy data from 2 large Phase 3 studies in radar plots demonstrates that eluxadoline treatment offers benefits across a broad range of abdominal and bowel symptoms experienced by patients with IBS-D, including abdominal pain, bloating, diarrhea (stool consistency and frequency), and fecal urgency. Two global measures commonly used to assess treatment efficacy in IBS-D, adequate relief and GSS, were also improved,

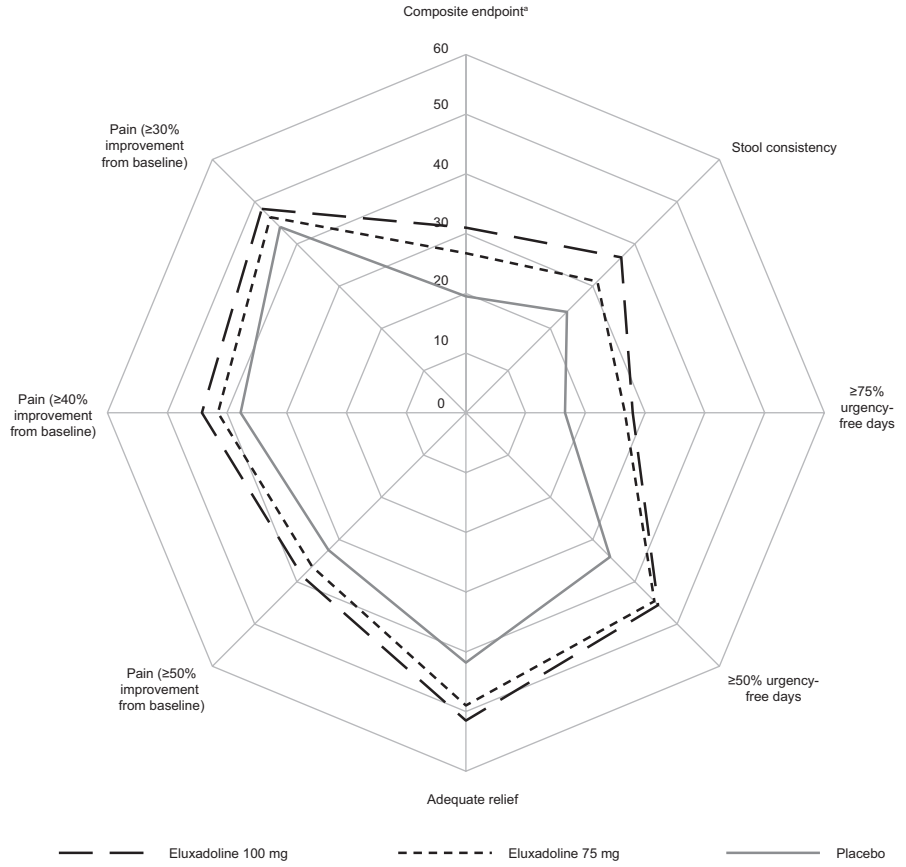

FIGURE 1 Weeks 1-26 responder rates for composite endpoint, stool consistency, urgency-free days, adequate relief, and pain with eluxadoline 75 and 100 mg vs placebo: pooled Phase 3 population. Stool consistency score was reported on a 7-point scale, where 1 indicates hard stool and 7 indicates watery diarrhea; abdominal pain score was reported on an 11-point scale, where 0 indicates no pain and 10 indicates worst pain imaginable. Patients were asked to record the number of urgency episodes daily over the past 24 hours. Composite response was defined as daily improvement of ≥30% in worst abdominal pain score vs average baseline pain and, on the same day, a Bristol Stool Form Scale score of <5 on ≥50% of treatment days.[17] Stool consistency response was defined as for the composite response. Urgency-free responders were calculated using criteria of ≥50% or ≥75% of days with no diary entry of urgency episodes. Adequate relief response was defined as a weekly "yes" response to the following question: "Over the past week, have you had adequate relief of your irritable bowel syndrome symptoms?" on ≥50% of treatment weeks. Pain response was defined as daily improvement of ≥30%, ≥40%, or ≥50% in worst abdominal pain score vs average baseline pain on ≥50% of treatment days. [a]Data reported in Lembo et al. 2016.[17]

further illustrating the broad-ranging effects of eluxadoline. These improvements are evidenced by the separation observed between the data points for eluxadoline vs placebo on each axis of the radar plots presented; although the magnitude of improvement vs placebo is less striking for measures such as abdominal pain, the plots paint a clear picture of consistency and robustness in favor of eluxadoline.

These data support and extend the previously reported benefits of eluxadoline for the treatment of patients with IBS-D. Proportions of stool consistency responders and abdominal pain responders (using a criteria of ≥30% improvement from baseline) were similar in the individual Phase 3 trials[17] and in the pooled population over Weeks 1-26, and proportions of adequate relief responders over Weeks 1-12 in the individual studies[17] were similar to those seen across Weeks 1-26 in the present analyses. Proportions of abdominal pain responders using criteria of ≥40% and ≥50% improvement from baseline in the pooled Phase 3 population were similar across Weeks 1-12[17] and Weeks 1-26. Across both Weeks 1-12[17] and Weeks 1-26, similar changes from baseline in IBS-D GSS, abdominal pain, abdominal bloating, and number of bowel movements were observed in the pooled Phase 3 population.

Effective management strategies for IBS-D, particularly in patients with moderate or more severe disease, require treatments that address not only the primary symptoms but also the range of symptoms experienced, including pain, bloating, and urgency, which may be particularly bothersome for patients. Existing treatments have been shown to be beneficial for specific symptoms or groups of symptoms for IBS-D, such as antidiarrheals for normalizing stool consistency and antispasmodics for relief of abdominal pain; however, the evidence supporting the efficacy of many pharmacological therapies in providing global relief of IBS-D symptoms is variable.[8,13,29,30] The data presented in this study, therefore, suggest that eluxadoline provides a valuable new option for the management of IBS-D.

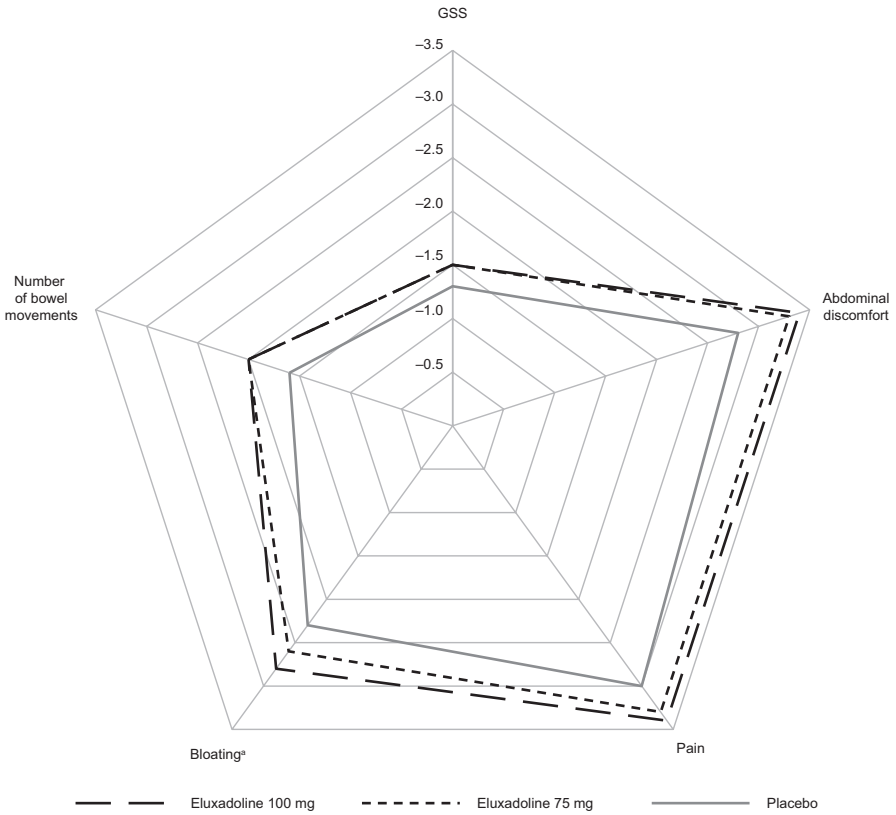

FIGURE 2 Change from baseline to Week 26 in GSS, abdominal discomfort, pain, bloating, and number of bowel movements with eluxadoline 75 and 100 mg vs placebo: pooled Phase 3 population. IBS-D GSS was reported on a 5-point scale, where 0 indicates no symptoms and 4 indicates very severe symptoms; abdominal discomfort score was reported on an 11-point scale, where 0 indicates no discomfort and 10 indicates worst discomfort imaginable; abdominal pain score was reported on an 11-point scale, where 0 indicates no pain and 10 indicates worst pain imaginable; abdominal bloating score was reported on an 11-point scale, where 0 indicates no bloating and 10 indicates worst bloating imaginable. Patients were asked to record the number of bowel movements daily over the past 24 hours. [a]Patients who responded to the interactive voice response system items in Spanish were not presented with the bloating item. GSS, global symptom score; IBS-D, irritable bowel syndrome with diarrhea

This analysis should, however, be interpreted in the light of certain limitations, as the data for the range of endpoints presented were not normalized and so do not permit quantitative comparison of the magnitude of changes observed with eluxadoline between different efficacy measures. Radar plots in this instance are, therefore, best suited to providing a visually compelling argument to support the robustness of the eluxadoline data across numerous endpoints and as an aid to interpreting previous analyses. Although the current analysis is limited to a qualitative description of the data, a consistent pattern of greater improvements with eluxadoline vs placebo is observed, which would not be present if the data supporting the efficacy of eluxadoline were less robust.

The use of radar plots to display efficacy data from 2 large Phase 3 studies facilitates simultaneous interpretation of data across multiple domains, supporting previous findings and demonstrating that treatment with eluxadoline led to consistent improvements vs placebo across 13 endpoints representing the range of abdominal and bowel symptoms experienced by patients with IBS-D. The robustness and consistency of these data suggest that eluxadoline treatment provides effective global relief of IBS-D symptoms.

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AUTHOR CONTRIBUTIONS

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors. The authors take full responsibility for the scope, direction, and content of the manuscript and have approved the submitted manuscript. DMB and WDC performed the research, analyzed and/or interpreted the data, and contributed to critically revising the manuscript for important content; LSD and PSC designed the research study, analyzed and/or interpreted the data, and contributed to critically revising the manuscript for important content; DAA and CG analyzed and/or interpreted the data and contributed to critically revising the manuscript for important content.

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REFERENCES

1. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clin Epidemiol*. 2014;6:71-80.
2. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol*. 2012;10:712-721.
3. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA*. 2015;313:949-958.
4. Drossman DA, Hasler WL. Rome IV-functional GI disorders: disorders of gut-brain interaction. *Gastroenterology*. 2016;150:1257-1261.
5. Schmulson MJ, Drossman DA. What is new in Rome IV. *J Neurogastroenterol Motil*. 2017;23:151-163.
6. Ikechi R, Fischer BD, DeSipio J, Phadtare S. Irritable bowel syndrome: clinical manifestations, dietary influences, and management. *Healthcare (Basel)*. 2017;5:21.
7. Lacy BE, Mearin F, Chang L, et al. Bowel disorders. *Gastroenterology*. 2016;150:1393-1407.
8. Lucak S, Chang L, Halpert A, Harris LA. Current and emergent pharmacologic treatments for irritable bowel syndrome with diarrhea: evidence-based treatment in practice. *Therap Adv Gastroenterol*. 2017;10:253-275.
9. Atarodi S, Rafieian S, Whorwell PJ. Faecal incontinence-the hidden scourge of irritable bowel syndrome: a cross-sectional study. *BMJ Open Gastroenterol*. 2014;1:e000002.
10. American Gastroenterological Association. IBS in America: Survey Summary Findings. http://ibsinamerica.gastro.org/files/IBS_in_America_Survey_Report_2015-12-16.pdf. Accessed October 5, 2016.
11. Drossman DA, Morris CB, Schneck S, et al. International survey of patients with IBS: symptom features and their severity, health status, treatments, and risk taking to achieve clinical benefit. *J Clin Gastroenterol*. 2009;43:541-550.
12. Spiegel B, Strickland A, Naliboff BD, Mayer EA, Chang L. Predictors of patient-assessed illness severity in irritable bowel syndrome. *Am J Gastroenterol*. 2008;103:2536-2543.
13. Ford AC, Moayyedi P, Lacy BE, et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. *Am J Gastroenterol*. 2014;109(Suppl 1):S2-S26.
14. Buono JL, Mathur K, Averitt AJ, Andrae DA. Economic burden of inadequate symptom control among US commercially insured patients with irritable bowel syndrome with diarrhea. *J Med Econ*. 2017;20:353-362.
15. Buono JL, Mathur K, Averitt A, Andrae DA. Economic burden of irritable bowel syndrome with diarrhea: retrospective analysis of a U.S. commercially insured population. *J Manag Care Spec Pharm*. 2017;23:453-460.
16. US Food and Drug Administration. Viberzi. Highlights of prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206940s002lbl.pdf. Accessed June 19, 2017.
17. Lembo AJ, Lacy BE, Zuckerman MJ, et al. Eluxadoline for irritable bowel syndrome with diarrhea. *N Engl J Med*. 2016;374:242-253.
18. Chey WD, Dove LS, Andrae DA, Covington PS. Early response predicts a sustained response to eluxadoline in patients with irritable bowel syndrome with diarrhoea in two Phase 3 studies. *Aliment Pharmacol Ther*. 2017;45:1319-1328.
19. Saary MJ. Radar plots: a useful way for presenting multivariate health care data. *J Clin Epidemiol*. 2008;61:311-317.
20. Strand V, Loftis JE. Response to M. Boers' concerns about spydergrams. *J Clin Epidemiol*. 2013;66:247-252.
21. De Vincentis A, Pennazza G, Santonico M, et al. Breath-print analysis by e-nose for classifying and monitoring chronic liver disease: a proof-of-concept study. *Sci Rep*. 2016;6:25337.
22. Exeter DJ, Zhao J, Hanham G, Grey C, Wells S, Kerr A. Construction and use of mapping techniques to describe the geographical distribution of medication dispensing for the secondary prevention of atherosclerotic CVD in New Zealand: VIEW-2. *N Z Med J*. 2014;127:70-80.
23. Ford CE, Malley D, Bateman A, Clare IC, Wagner AP, Gracey F. Selection and visualisation of outcome measures for complex post-acute acquired brain injury rehabilitation interventions. *NeuroRehabilitation*. 2016;39:65-79.
24. Yamaguchi N, Matsubara S, Momonoi F, Morikawa K, Takeyama M, Maeda Y. An attempt of radar chart expression of a self-rating scale for sleep disturbance. *Psychiatry Clin Neurosci*. 1998;52:165-167.
25. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol*. 1997;32:920-924.
26. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology*. 2006;130:1480-1491.
27. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, 5th edn. Washington, DC: American Psychiatric Press Ltd; 2013.
28. US Department of Health and Human Services. NIAAA Newsletter. Winter 2004, Number 3. http://www.niaaa.nih.gov/sites/default/files/newsletters/Newsletter_Number3.pdf. Accessed June 19, 2017.
29. Chang L, Lembo A, Sultan S. American Gastroenterological Association Institute technical review on the pharmacological management of irritable bowel syndrome. *Gastroenterology*. 2014;147:1149-1172.
30. Trinkley KE, Nahata MC. Medication management of irritable bowel syndrome. *Digestion*. 2014;89:253-267.

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