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CORRIGENDUM

Review of the Patient Burden and Therapeutic Landscape of Irritable Bowel Syndrome with Constipation in the United States [Corrigendum]

Sendzischew Shane MA, Ruddy J, Cline M, Rosenbaum DP, Edelstein S, Moshiree B. *Clin Exp Gastroenterol*. 2024;17:227–253.

The authors have advised that they have identified errors in the reporting of the analysis of one of their previous studies, T3MPO-1, which did not adhere to the pre-specified Statistical Analysis Plan. As a result, secondary endpoints, in the "Tenapanor" section on page 246, should not be considered statistically significant due to the hierarchical testing procedure and edits are needed to Table 4 on page 242 of the published paper.

Page 242, Table 4, Table caption, the text "Table 4 Key Efficacy Results from Pivotal Trials of FDA-Approved Treatments for IBS-C" should read "Table 4 Results from Pivotal Trials for FDA-Approved Treatments for IBS-C".

Page 244, Table 4, Outcomes column, the order of the two bullet points for "6/12-wk CSBM response rate" and "6/12-wk AP response rate" should be switched to align with the protocol-prespecified sequential testing procedure; a superscript "j" has been added to *p*-values $p=0.008$, $p<0.001$, $p=0.014$, $p=0.02$ and $p<0.001$ to clarify that these p-values were not obtained from formal statistical testing and thus should be considered exploratory; a superscript "k" has been added after the text "Change from baseline or % responders at week 12" and "Change from baseline or % responders at week 26" to indicate observed data; the text "CSBM/wk: 2.2 vs 1.2" should read "CSBM/wk: 2.1 vs 1.2".

The correct Table 4 is as follows.

Table 4 Results from Pivotal Trials for FDA-Approved Treatments for IBS-C

Study	Patient Population	Treatment	Demographics	Outcomes
Lubiprostone				
Drossman et al.[91] 12-wk, phase 3, r, db, m studies 1 (N=590) and 2 (N=581)	Pts with IBS-C (Rome II criteria); aged ≥18 y; <3 SBMs/wk ≥5% of the time; ≥25% of SBMs with straining of at least moderate severity; ≥25% of SBMs hard or very hard stool consistency	Study 1 and 2 combined LUBI 8 µg bid (N=769) vs PL (N=385)	• Mean age (range), years: LUBI: 46.1 (19.0, 83.0); PL: 47.7 (18.0, 85.0) • Female, n (%): LUBI: 698 (90.8); PL: 359 (93.2) • Race, n (%) ○ White: LUBI: 595 (77.4); PL: 298 (77.4) ○ Black/AA: LUBI: 102 (13.3); PL: 50 (13.0) ○ Other: LUBI: 72 (9.4); PL:37 (9.6)	• Rigorous responder rate[a] (primary end point): 17.9% vs 10.1%; $p=0.001$ • Significant ($p\leq0.05$) mean improvements in AD/AP at months 2 and 3, and straining, constipation severity, and stool consistency at months 1, 2, and 3 • Significant mean improvements ($p\leq0.05$) in AB at month 2 and bowel movement frequency at month 1

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Table 4 (Continued).

Study	Patient Population	Treatment	Demographics	Outcomes
Linaclotide				
Chey et al.[92] 26-wk, phase 3, r, db, m (N=804)	Pts with IBS-C (Rome II criteria); aged ≥18 y; average score of ≥3 for worst daily AP, average of <3 CSBMs/wk and ≤5 SBMs/wk	LINA 290 µg qd (N=401) vs PL (N=403)	• Mean age (range), years: LINA: 44.6 (19, 82); PL: 44.0 (18, 87) • Female, n (%): LINA: 368 (91.8); PL: 352 (87.3) • Race, n (%) o White: LINA: 316 (78.8); PL: 311 (77.2) o Black: LINA: 70 (17.5); PL: 78 (19.4) o Other: LINA: 15 (3.7); PL: 14 (3.5)	4 coprimary end points • 6/12-wk FDA combined response[b] rate: 33.7% vs 13.9%; $p<0.0001$ • 9/12-wk AP response rate[c]: 38.9% vs 19.6%; $p<0.0001$ • 9/12-wk CSBM response rate[c]: 18.0% vs 5.0%; $p<0.0001$ • 9/12-wk combined response: 12.7% vs 3.0% Changes from baseline and % responders[d] at weeks 12 and 26: • Worst AP: LS mean −1.9 vs −1.1; −2.1 vs −1.2; both $p<0.0001$ • AP responders[d]: 48.9% vs 34.5%; 49.1% vs 31.3%; both $p<0.0001$ • AB: LS mean −1.9 vs −1.0; −2.2 vs −1.2; both $p<0.0001$ • AB responders[d]: 42.9% vs 23.8%; 42.4 vs 25.1%; both $p<0.0001$ • CSBM/wk: LS mean 2.2 vs 0.7; 2.2 vs 0.7; both $p<0.0001$ • CSBM responders[d]; 47.6% vs 2.6%; 43.6% vs 18.6%; both $p<0.0001$
Rao et al.[93] 16-wk,[e] phase 3, r, db, m (N=800)		LINA 290 µg qd (N=405) vs PL (N=395)	• Mean age (range), years: LINA: 43.3 (19, 81); PL: 43.7 (18, 84) • Female, n (%): LINA: 367 (90.6); PL: 357 (90.4) • Race, n (%) o White: LINA: 314 (77.5); PL: 301 (76.2) o Black: LINA: 78 (19.3); PL: 75 (19.0) o Other: LINA: 13 (3.2); PL: 19 (4.8)	4 Coprimary end points • 6/12-wk FDA combined response[b]: 33.6% vs 21.0%; $p<0.0001$ • 9/12-wk AP response rate[c]: 34.3% vs 27.1%; $p=0.027$ • 9/12-wk CSBM response rate[c]: 19.5% vs 6.3%; $p<0.0001$ • 9/12-wk combined response rate[c]: 2.1% vs 5%; $p=0.0004$ Change from baseline and % responders[d] at week 12: • Worst AP: LS mean −1.9 vs −1.1; $p<0.0001$ • AP responders[d]: 50.1% vs 37.5%; $p=0.0003$ • AB: LS mean −1.9 vs −1.1; $p<0.0001$ • AB responders[d]: 43.5% vs 29.9%; $p<0.0001$ • CSBM/wk: LS mean 2.3 vs 0.7; $p<0.0001$ • CSBM responders[d]; 48.6% vs 29.6%; $p<0.0001$
Chang et al.[94] 16-wk[e], phase 3b, r, db, m (N=614)	Pts with IBS-C (Rome III criteria); aged ≥18 y; <3 SBMs/wk for ≥12 wk; average worst AP of ≥3, ≤6 CSBMs/wk, and ≤10 SBMs in the 2 wk prerandomization	LINA 290 µg qd (N=306) vs PL (N=308) (≈22% had prior LINA or PLEC therapy)	• Mean age (range), years: LINA: 46.5 (19, 85); PL: 46.8 (18, 79) • Female, n (%):LINA: 241 (78.8); PL: 255 (82.8) • Race, n (%) o White: LINA: 189 (61.8); PL:198 (64.3) o Black: LINA: 76 (24.8); PL: 70 (22.7) o Other: LINA: 41 (13.4); PL: 40 (13.0)	Change from baseline to week 12 in: • AS (primary end point[f]): LS mean change −1.9 vs −1.2; $p<0.0001$ • AB: LS mean −1.9 vs −1.1 $p<0.0001$ • AD: LS mean −1.9 vs −1.2; $p<0.0001$ • AP: LS mean −1.9 vs −1.2; $p<0.0001$ Change from baseline and % responders at week 12: • AS: LS mean −1.89 vs −1.18; $p<0.0001$ • 6/12-wk AS responders[g]: 40.5% vs 23.4%; $p<0.0001$ • AP: LS mean: −1.89 vs −1.18; $p<0.0001$ • AP responders[d]: 45.1% vs 28.9%; $p<0.0001$ • AB: LS mean −1.89 vs −1.14; $p<0.0001$ • CSBM/wk: LS mean 2.37 vs 0.96; $p<0.0001$ • CSBM responders[d]; 51.3% vs 33.8%; $p<0.0001$

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Table 4 (Continued).

Study	Patient Population	Treatment	Demographics	Outcomes
Plecanatide				
Brenner et al.[95] 12-wk, phase 3, r, db, m studies 1 (N=1054) and 2 (N=1135)	Pts with IBS-C (Rome III criteria); aged 18–85 y	Study 1: PLEC 3 mg qd (N=351) and PLEC 6 mg qd (N=349) vs PL (N=354)	• Mean age (range), years: PLEC 3 mg qd: 43.0 (18, 81); PLEC 6 mg qd: 43.2 (18, 78); PL: 43.0 (18, 81) • Female, n (%): PLEC 3 mg qd: 267 (76.1); PLEC 6 mg qd: 266 (76.2); PL: 272 (76.8) • Race, n (%) o White: PLEC 3 mg qd: 220 (62.7); PLEC 6 mg qd: 206 (59.0); PL: 237 (66.9) o Black/AA: PLEC 3 mg qd: 95 (27.1); PLEC 6 mg qd: 118 (33.8); PL: 89 (25.1) o Other: PLEC 3 mg qd: 36 (10.2); PLEC 6 mg qd: 25 (7.2); PL: 28 (8.0)	• 6/12-wk FDA combined response[b] (primary end point): 30.2% and 29.5% vs 17.8%; both $p<0.001$ • Sustained efficacy response[h]: 28.2% and 27.5% vs 17.2%; both $p\leq0.001$ • Improvement in stool consistency at week 12: mean change 1.51 and 1.72 vs 0.98; both $p<0.001$ • Reduction in straining at week 12: mean change −2.23 and −2.44 vs −1.58; both $p<0.001$
		Study 2: PLEC 3 mg qd (N=377) and PLEC 6 mg qd (N=379) vs PL (N=379)	• Mean age (range), years: PLEC 3 mg qd: 44.0 (18, 83); PLEC 6 mg qd: 43.1 (18, 83); PL: 44.8 (18, 81) • Female, n (%): PLEC 3 mg qd: 270 (71.6); PLEC 6 mg qd: 273 (72.0); PL: 272 (71.8) • Race, n (%) o White: PLEC 3 mg qd: 309 (82.0); PLEC 6 mg qd: 312 (82.3); PL: 301 (79.4) o Black/AA: PLEC 3 mg qd: 61 (16.2); PLEC 6 mg qd: 61 (16.1); PL: 73 (19.3) o Other: PLEC 3 mg qd: 7 (1.8); PLEC 6 mg qd: 6 (1.6); PL: 5 (1.3)	• 6/12-wk FDA combined response[b] (primary endpoint): 21.5% and 24.0% vs 14.2%; both $p<0.01$ • Sustained efficacy response[h]: 20.7% and 23.7% vs 14.0%; $p<0.05$ and $p\leq0.001$, respectively • Improvement in stool consistency at week 12: mean change 1.36 and 1.27 vs 0.84; both $p<0.001$ • Reduction in straining at week 12: mean change −1.85 and −1.82 vs −1.28; both $p<0.001$
		Study 1 and 2 integrated data	NA	Change from baseline to week 12 in: • AP: LS mean −1.6 and −1.6 vs – 1.3; both $p<0.0001$ • AB: LS mean −1.5 and −1.6 vs −1.1; both $p<0.0001$ • CSBM/wk: LS mean 1.2 and 1.4 vs 0.7; both $p<0.0001$
Tenapanor				
Chey et al. (T3MPO-1)[60] 16-wke, phase 3, r, db, m (N=606)	Pts with IBS-C (Rome III criteria); aged 18-75 y; during the 2-wk screening period: average ≤5 SBMs/wk and <3 CSBMs/wk; BSFS score <3; average weekly AP score ≥3; and no liquid stools for any SBM or mushy stools for >1 SBM, as per BSFS	TENA 50 mg bid (N=307) vs PL (N=299)	• Mean age, (SD), years: TENA: 45.0 (13.4); PL: 44.9 (13.0) • Female, n (%): TENA: 244 (79.5); PL: 249 (83.3) • Race, n (%) o White: TENA: 201 (65.5); PL: 186 (62.2) o Black/AA: TENA: 88 (28.7); PL: 100 (33.4) o Other: TENA: 18 (5.8); PL: 13 (4.4)	• 6/12-wk FDA combined response[b] (primary endpoint): 27.0% vs 18.7%; $p=0.02$ • 6/12-wk CSBM response rate[b]: 33.9% vs 29.4%; $p=0.270$ • 6/12-wk AP response rate[b]: 44.0% vs 33.1%; $p=0.008$[j] • 9/12-wk combined response rate[i]: 13.7% vs 3.3%; $p<0.001$[j] Change from baseline or % responders at week 12[k]: • AB responders[d]: 37.8% vs 28.1%; $p=0.014$[j] • CSBM/wk: 2.1 vs 1.2; $p=0.001$[j]

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Table 4 (Continued).

Study	Patient Population	Treatment	Demographics	Outcomes
Chey et al. (T3MPO-2)[61] 26-wk, phase 3, r, db, m (N=593)		TENA 50 mg bid (N=293) vs PL (N=300)	• Mean age (SD), years: TENA: 46.1 (13.1); PL: 44.8 (13.8) • Female, n (%): TENA: 240 (81.9); PL: 247 (82.3) • Race, n (%): o White: TENA: 185 (63.1); PL: 192 (64.0) o Black/AA: TENA: 92 (31.4); PL: 92 (30.7) o Asian: TENA: 12 (4.1); PL: 9 (3.0)	• 6/12-wk FDA combined response[b] (primary end point): 36.5% vs 23.7%; $p<0.001$ • 6/12-wk CSBM response rate[b]: 47.4% vs 33.3%; $p<0.001$ • 6/12-wk AP response rate[b]: 49.8% vs 38.3%; $p=0.004$ • 9/12-wk combined response rate[i]: 18.4% vs 5.3%; $p<0.001$ • 13/26-wk combined response rate[i]: 35.5% vs 24.3%; $p=0.003$ Change from baseline or % responders at week 26[k]: • AB responders[d]: 44.7% vs 35.3%; $p=0.02$[j] • CSBM/wk: 3.3 vs 1.6; $p<0.001$[j]

Notes: [a]Defined as a monthly responder for ≥2 of the 3 months of the study, where monthly responders were pts who rated their IBS symptoms as being at least moderately relieved (on a 7-point scale; 1 = significantly worse to 7 = significantly relieved) for all 4 weeks of the month or significantly relieved for ≥2 weeks of the month, with no ratings of moderately or severely worse. [b]US FDA responder defined as a pt who met both of the following criteria in the same week for ≥6 of the first 12 weeks of treatment period: (1) an improvement of ≥30% from baseline in the average of the daily worst abdominal pain scores (abdominal pain response) and (2) an increase of ≥1 CSBM from baseline (CSBM response). [c]At least 30% decrease in average of daily worst AP score (AP response), ≥3 CSBMs and an increase of ≥1 CSBM (CSBM response), and both outcomes in the same week (combined response) for ≥9 of 12 weeks. [d]Pts with ≥30% decrease in AP or AB or CSBM rate increase of ≥1 per week for ≥50% of weeks. [e]Pts completing 12 weeks of the double-blind treatment period could enter a 4-week, double-blind, randomized withdrawal period in which pts initially randomized to LINA were rerandomized to LINA 290 µg or PL, and pts previously randomized to PL received LINA 290 µg qd. [f]Change from baseline in weekly AS (calculated by averaging daily ASs over a week) throughout the treatment period; AS is an end point derived from the DIBSS-C. [g]Defined as a pt who experienced ≥2-point reduction from baseline in weekly AS for ≥6 of the 12 treatment weeks. [h]Defined as an overall responder plus a weekly responder for ≥2 of the last 4 weeks of the 12-week treatment period compared with placebo. [i]At least 30% decrease in average of daily worst AP score and an increase of ≥1 CSBM in the same week (combined response) for ≥9 of 12 weeks or ≥33 of 26 weeks. [j]Not obtained from formal statistical testing and therefore exploratory in nature. [k]Observed data.
Abbreviations: AA, African American; AB, abdominal bloating; AD, abdominal discomfort; AE, adverse event; AP, abdominal pain; AS, abdominal score; bid, twice daily; BSFS, Bristol Stool Form Scale; CSBM, complete spontaneous bowel movement; db, double blind; DIBSS-C, Diary for IBS Symptoms-Constipation; FDA, Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation; IBS-QOL, IBS quality of life questionnaire; LINA, linaclotide; LS, least squares; LUBI, lubiprostone; m, multicenter; NA, not available; NS, non-significant; ol, open label; PLEC, plecanatide; PL, placebo; qd, once daily; r, randomized; pt, patient; RW, randomized withdrawal; SAE, serious adverse event; SGA, Subjects Global Assessment; TEAE, treatment-emergent adverse event; TENA, tenapanor; URTI, upper respiratory tract infection.

Page 246, Tenapanor section, second paragraph, last sentence, the text "Tenapanor significantly improved global and individual symptoms of IBS-C during the 12-week treatment period, as indicated by more patients in the tenapanor group achieving 6 of 12-week US FDA combined response rates, 6 of 12-week abdominal pain and CSBM rates, as well as 9 of 12-week and/or 13 of 26-week combined response rates (Table 4)" should read "Tenapanor improved global and individual symptoms of IBS-C during the 12-week treatment period, as indicated by higher percentages of patients in the tenapanor group achieving 6 of 12-week US FDA combined response rates, 6 of 12-week abdominal pain and CSBM rates, as well as 9 of 12-week and/or 13 of 26-week combined response rates (Table 4)".

The authors apologise for these errors and advise they do not change the primary findings or scientific conclusions of the study.