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Clinical Effect of Mirikizumab Treatment on Bowel Urgency in Patients With Moderately to Severely Active Ulcerative Colitis and the Clinical Relevance of Bowel Urgency Improvement For Disease Remission

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Dubinsky MC, et al. *Crohns Colitis 360.* 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Background

Bowel Urgency in Ulcerative Colitis (UC)

- The primary symptoms of UC include rectal bleeding, increased stool frequency, and bowel urgency
- Bowel urgency is the sudden or immediate need to have a bowel movement and is associated with reduced health-related quality of life
- Bowel urgency has been identified as the UC symptom patients most want to improve; it may persist even when symptoms such as increased stool frequency and rectal bleeding are considered inactive
- Despite its importance to patients, bowel urgency is often not assessed or prioritized by healthcare providers and was not previously a recommended endpoint in clinical trials
- A recent update of the US FDA Draft Guidance for UC encourages the exploration of additional UC symptoms identified by patients as important, such as bowel urgency

Development of the Urgency Numeric Rating Scale (NRS)

- Bowel urgency is not considered in most UC disease activity indices, such as the Modified Mayo Score (MMS)
- To study bowel urgency severity and the effect of mirikizumab on bowel urgency, the Urgency NRS was developed and psychometrically validated as a novel single-item assessment tool

IL=Interleukin.

Dubinsky MC, et al. *Crohns Colitis 360.* 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Aims

- Utilize the Urgency NRS to evaluate the efficacy of mirikizumab versus placebo for reduction of bowel urgency symptoms, bowel urgency clinically meaningful improvement (CMI), and bowel urgency remission in UC

- Examine associations between bowel urgency and other clinical outcomes (clinical remission, endoscopic remission, symptomatic remission, clinical response, normal C-reactive protein, and normal fecal calprotectin at Weeks 12 and 52, and corticosteroid-free remission at Week 52)

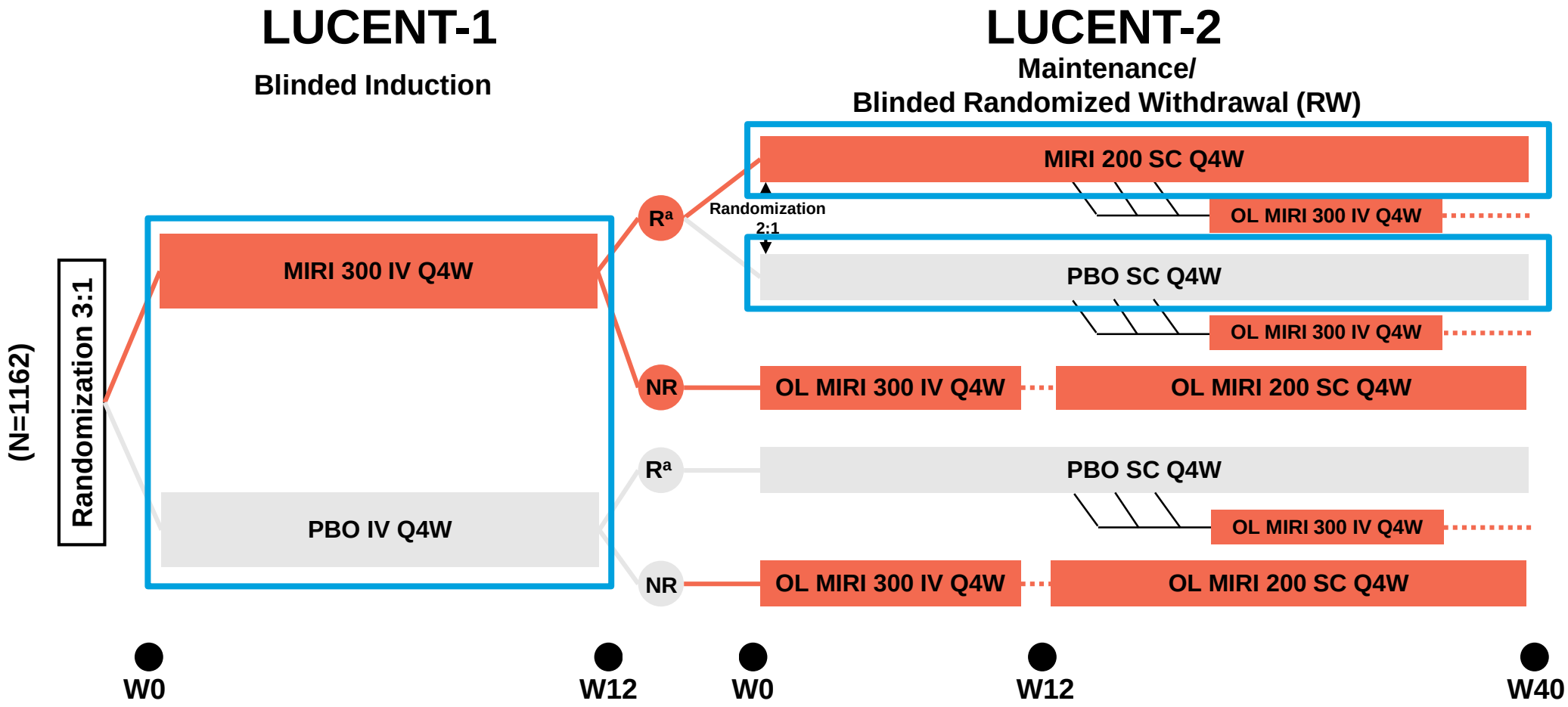
- Analyze the association of bowel urgency with improvement in Inflammatory Bowel Disease Questionnaire (IBDQ) scores at Weeks 12 and 52

UC=Ulcerative Colitis; NRS=Numeric Rating Scale.

Dubinsky MC, et al. *Crohns Colitis 360.* 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Methods – Study Design

LUCENT-1 and LUCENT-2



Note: Responders to induction MIRI at Week 12 of LUCENT-1, defined as achieving ≥2-point and ≥30% decrease in the MMS from baseline with RB = 0 or 1, or ≥1-point decrease from baseline, were randomized to receive maintenance MIRI or PBO in LUCENT-2. Non-responders to induction MIRI in LUCENT-1 received additional induction MIRI for the first 12 weeks of LUCENT-2, followed by maintenance MIRI to Week 40 in patients who achieved delayed clinical response at LUCENT-2 Week 12. NR=Nonresponder; OL=Open-Label; R=Responder. D'Haens G, et al. *N Eng J Med*. 2022 (Communicated).

Methods – Participants

Study population (LUCENT-1 and LUCENT-2)

Key Inclusion Criteria

- 18-80 years of age
- Moderately to severely active UC at screening:
  - Modified Mayo Score (MMS) of 4-9
  - Endoscopic Subscore (ES) of 2-3
  - Blinded central reading of endoscopic videos and histologic findings performed
- Inadequate response, loss of response or intolerance to:
  - 1 or more corticosteroids or immunomodulators for UC (conventional-failed)
  - Biologic therapy or JAK inhibitors for UC (biologic-failed)

Key Exclusion Criteria

- Previous exposure to anti-IL-12/23p40 or anti-IL-23p19 antibodies
- Failed three or more different biologic therapies (excluding JAK inhibitors)

- Patients were allowed use of stable doses of oral 5-ASA, oral corticosteroids[a], and immunomodulators (AZA, 6-MP, methotrexate)
- All patients who completed LUCENT-1, regardless of clinical response or treatment assignment, were eligible to participate in LUCENT-2

[a]Oral corticosteroids were maintained at a stable dose during LUCENT-1 and tapered during LUCENT-2 in induction responders. 5-ASA=5-Aminosalicylic Acid; 6-MP=6-Mercaptopurine; JAK=Janus Kinase; IL=Interleukin; MMS=Modified Mayo Score; UC=Ulcerative Colitis.

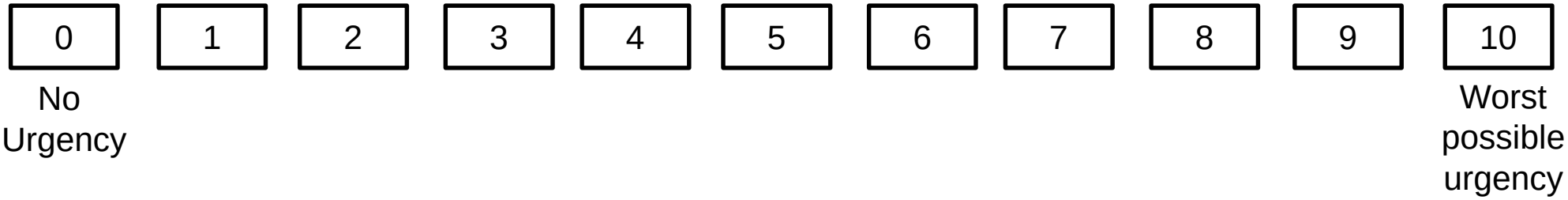
D'Haens G, et al. *N Eng J Med*. 2022 (Communicated).

Methods – Patient-Reported Outcomes

The Urgency NRS

- The Urgency NRS is a single-item measure of bowel urgency severity in the previous 24 hours
- Bowel urgency is scored on an 11-point NRS ranging from 0 (no urgency) to 10 (worst possible urgency)

How severe was your urgency (sudden or immediate need) to have a bowel movement in the past 24 hours?



- Patients completed the Urgency NRS as part of a daily electronic diary
- Weekly average scores for the Urgency NRS were subsequently calculated (to the nearest whole number) for 7-day periods
- A weekly score was considered missing if scores were available for fewer than 4 days in a given week

NRS=Numeric Rating Scale; UC=Ulcerative Colitis.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Methods – Patient-Reported Outcomes

Bowel Urgency Clinically Meaningful Improvement (CMI) and Bowel Urgency Remission

Bowel Urgency CMI[1]

- Bowel urgency CMI is defined as Urgency Numeric Rating Scale (NRS) improvement of ≥3 points in patients with baseline Urgency NRS ≥3

Bowel Urgency Remission[1]

- Bowel urgency remission is defined as an Urgency NRS score of 0 or 1 (no or minimal urgency) in patients with a baseline Urgency NRS ≥3

These thresholds were based on qualitative and psychometric findings by Dubinsky, et al[2] ,where an Urgency NRS score **improvement of ≥3 points** was considered to be **clinically meaningful** for patients with moderately to severely active UC, and that an Urgency NRS score of ≤1 point represented **resolution or near resolution of bowel urgency**

NRS=Numeric Rating Scale; UC=Ulcerative Colitis.

1. Dubinsky MC, et al. *Crohns Colitis 360.* 2022; doi:10.1093/crocol/otac044 (Ahead of print). 2. Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6(1):114.

Methods – Patient-Reported Outcomes

The Inflammatory Bowel Disease Questionnaire (IBDQ)

- **The Inflammatory Bowel Disease Questionnaire (IBDQ)** is a 32-item PRO instrument comprising four domains:
  - Bowel symptoms
  - Systemic symptoms
  - Emotional functioning
  - Social functioning
- Each item is scored on a 7-point Likert scale ranging from 1 (“a very severe problem”) to 7 (“not a problem at all”)

- The total score ranges from 32 to 224, with a higher score indicating better quality of life
- The IBDQ was completed at screening, baseline, Week 12, and Week 52
- IBDQ remission was defined as an IBDQ total score ≥170

PRO=Patient-Reported Outcome.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Methods – Disease Activity Measures

Defined Endpoints and Biomarkers For LUCENT-1 and LUCENT-2

Endpoint[a]	Definition
Bowel urgency CMI	Change from baseline in Urgency NRS ≥3 in patients with Urgency NRS≥3 at induction baseline
Bowel urgency remission	Urgency NRS=0 or 1 in patients with Urgency NRS ≥3 at induction baseline (no or minimal urgency)
Clinical remission	SF=0 or SF=1 with ≥1-point decrease in MMS from baseline; RB=0; and ES=0 or 1 (excluding friability)
Clinical response	≥2-point and ≥30% decrease in MMS from baseline; RB=0 or 1 or, ≥1-point decrease from baseline
Endoscopic remission	ES=0 or 1 (excluding friability); score ranges 0 to 4; a lower score indicates less mucosal damage
Symptomatic remission	SF=0 or SF=1 with ≥1-point decrease in MMS from baseline; RB=0
Corticosteroid-free remission	Clinical remission at W40, symptomatic remission at W28, and no corticosteroid use for ≥12 weeks prior to W40
IBDQ	Total score ranges from 32 to 224; a higher score indicates a better quality of life
Normal C-reactive protein	≤6 mg/L
Normal fecal calprotectin	≤250 µg/g
Urgency NRS	Change from baseline in Urgency NRS score; range 0 to 10; a lower score indicates less severe bowel urgency

[a]Endpoint analyses for LUCENT-1 were at W12 and for LUCENT-2 at W40 (W52 of continuous treatment). CMI=Clinically Meaningful Improvement; ES=Endoscopic Subscore; IBDQ=Inflammatory Bowel Disease Questionnaire; MMS=Modified Mayo Score (0-3 for SF, RB, and ES subscores for total 0-9 score); RB=Rectal Bleeding; SF=Stool Frequency; NRS=Numeric Rating Scale; W=Week.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Baseline Characteristics and Disease Characteristics

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2) (1 of 2)

	Induction Treatment		Maintenance Treatment MIRI Induction Responders	
	PBO N=294	**MIRI 300 mg IV N=868**	**PBO N=274**	**MIRI 200 mg SC N=365**
Age, mean years (SD)	41.3 (13.8)	42.9 (13.9)	41.2 (12.8)	43.4 (14.2)
Male, n (%)	165 (56)	530 (61)	104 (58)	214 (59)
BMI category, n (%)				
Normal (≥18.5 and <25 kg/m^2)	149 (51)	451 (52)	97 (54)	196 (54)
Overweight, obese, or extreme obese (≥25 kg/m^2)	117 (40)	362 (42)	74 (41)	143 (39)
Disease duration, mean years (SD)	6.9 (7.0)	7.2 (6.7)	6.7 (5.6)	6.9 (7.1)
Disease location, n (%)				
Left-sided colitis	188 (64)	544 (63)	119 (66)	234 (64)
Pancolitis	103 (35)	318 (37)	59 (33)	128 (35)
Modified Mayo Score, n (%)				
Moderate [4-6]	138 (47)	404 (47)	77 (43)	181 (50)
Severe [7-9]	155 (53)	463 (53)	102 (57)	184 (50)
Mayo endoscopic subscore: severe disease (3), n (%)	200 (68)	574 (66)	106 (59)	235 (64)
Bowel urgency severity (Urgency NRS)				
Median (Q1, Q3)	7.0 (5.0, 8.0)	6.0 (5.0, 8.0)	6.0 (5.0, 8.0)	6.0 (5.0, 8.0)
Urgency NRS ≥3, n (%)	276 (94)	811 (93)	172 (96)	336 (92)
Fecal calprotectin, µg/g, median (Q1, Q3)	1471.5 (626.5, 2944.5)	1559.0 (634.0, 3210.0)	1750.0 (754.0, 3519.0)	1482.0 (558.0, 3045.0)
CRP, mg/L, median (Q1, Q3)	4.2 (1.2, 9.5)	4.1 (1.5, 9.6)	3.0 (1.0, 7.7)	3.8 (1.4, 8.7)

BMI=Body Mass Index; CRP=C-reactive Protein; IV=Intravenous; MIRI=Mirikizumab; NRS=Numeric Rating Scale; PBO=Placebo; SC=Subcutaneous; SD=Standard Deviation.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Baseline Characteristics and Disease Characteristics

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2) (2 of 2)

	Induction Treatment		Maintenance Treatment MIRI Induction Responders	
	PBO N=294	**MIRI 300 mg IV N=868**	**PBO N=274**	**MIRI 200 mg SC N=365**
IBDQ total score, median (Q1, Q3)	128 (103, 150)	132 (108, 155)	132 (107, 150)	137 (109, 158)
Prior UC therapy, n (%)				
Prior biologic or tofacitinib failure	118 (40)	361 (42)	64 (36)	128 (35)
Prior anti-TNF failure	97 (33)	325 (37)	58 (32)	112 (31)
Prior vedolizumab failure	59 (20)	159 (18)	23 (13)	47 (13)
Prior tofacitinib failure	6 (2)	34 (4)	8 (4)	8 (2)
Number of failed biologics or tofacitinib				
0	176 (60)	507 (58)	115 (64)	237 (65)
1	65 (22)	180 (21)	35 (20)	77 (21)
≥2	53 (18)	181 (21)	29 (16)	51 (14)
Baseline UC therapy, n (%)				
Corticosteroids	113 (38)	351 (40)	68 (38)	135 (37)
Immunomodulators	69 (23)	211 (24)	39 (22)	78 (21)
Aminosalicylates	217 (74)	646 (74)	134 (75)	278 (76)

IBDQ=Inflammatory Bowel Disease Questionnaire; IV=Intravenous; MIRI=Mirikizumab; PBO=Placebo; UC=Ulcerative Colitis; TNF=Tumor Necrosis Factor; SC=Subcutaneous.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Bowel Urgency CMI and Remission

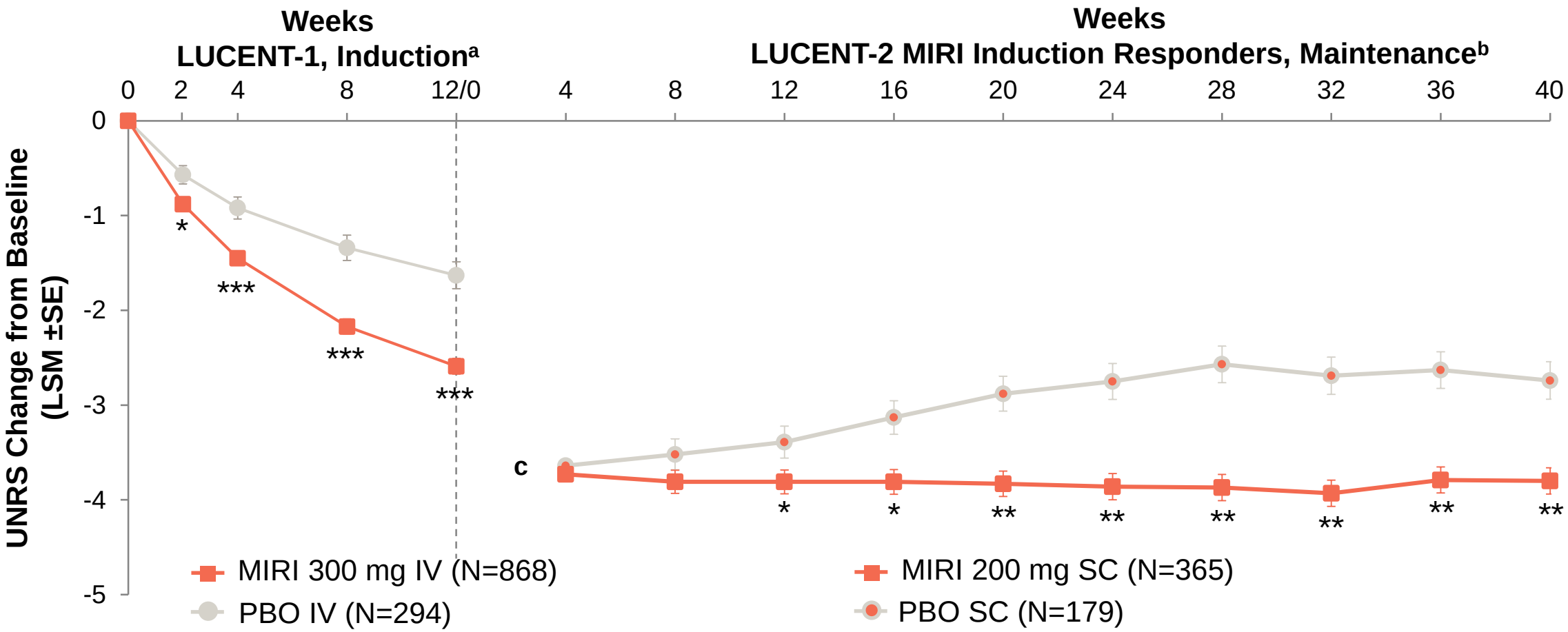
mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

Endpoint	Induction (W12 Analysis) PBO N=294	Induction (W12 Analysis) MIRI 300 mg IV N=868	Induction (W12 Analysis) p-value[a]	Maintenance (W52 Analysis) MIRI Induction Responders PBO N=179	Maintenance (W52 Analysis) MIRI Induction Responders MIRI 200 mg SC N=365	Maintenance (W52 Analysis) MIRI Induction Responders p-value[a]
Urgency NRS change from baseline (LSM±SE)						
Overall patients	-1.63±0.14	-2.59±0.08	p<0.001	-2.74±0.20	-3.80±0.14	p<0.001
Biofailed patients[b]	-0.95±0.23	-2.46±0.13	p<0.001	-2.66±0.35	-3.60±0.23	p<0.001
Bowel urgency CMI[c], n (%)						
Overall patients	89/276 (32.2)	395/811 (48.7)	p<0.001	72/172 (41.9)	219/336 (65.2)	p<0.001
Biofailed patients[b]	22/115 (19.1)	157/344 (45.6)	p<0.001	22/63 (34.9)	73/122 (59.8)	p=0.002
Bowel urgency remission[c], n (%)						
Overall patients	34/276 (12.3)	179/811 (22.1)	p<0.001	43/172 (25.0)	144/336 (42.9)	p<0.001
Biofailed patients[b]	5/115 (4.3)	67/344 (19.5)	p<0.001	12/63 (19.0)	43/122 (35.2)	p=0.027

[a]Treatment comparison for Urgency NRS change from baseline was made using MMRM; model included treatment, baseline value, treatment by visit interactions, baseline value by visit interactions, and stratification factors. Treatment comparison for bowel urgency CMI and remission was made using CMH tests adjusting for stratification factors; missing data were considered as nonresponse. [b]The biofailed patients included patients who had inadequate response to, loss of response to, or were intolerant to a biologic therapy for UC (such as anti-TNFs or anti-integrins) or to the Janus kinase inhibitor tofacitinib. [c]Bowel urgency CMI and remission were assessed in mITT patients with baseline Urgency NRS ≥3 in LUCENT-1 and mirikizumab induction responders with baseline UNRS ≥3 in LUCENT-2. CMH=Cochran-Mantel-Haenszel; CMI=Clinically Meaningful Improvement; IV=Intravenous; LSM=Least Squares Mean; MIRI=Mirikizumab; mITT=modified Intent-to-treat Population; MMRM=Mixed-effects Model for Repeated Measures; PBO=Placebo; Q4W Every 4 Weeks; SC=Subcutaneous; SE=Standard Error; TNF=Tumor Necrosis Factor; UC=Ulcerative Colitis; NRS=Numeric Rating Scale; W=Week. Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Bowel Urgency Change From Baseline by Visit Through Week 52

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

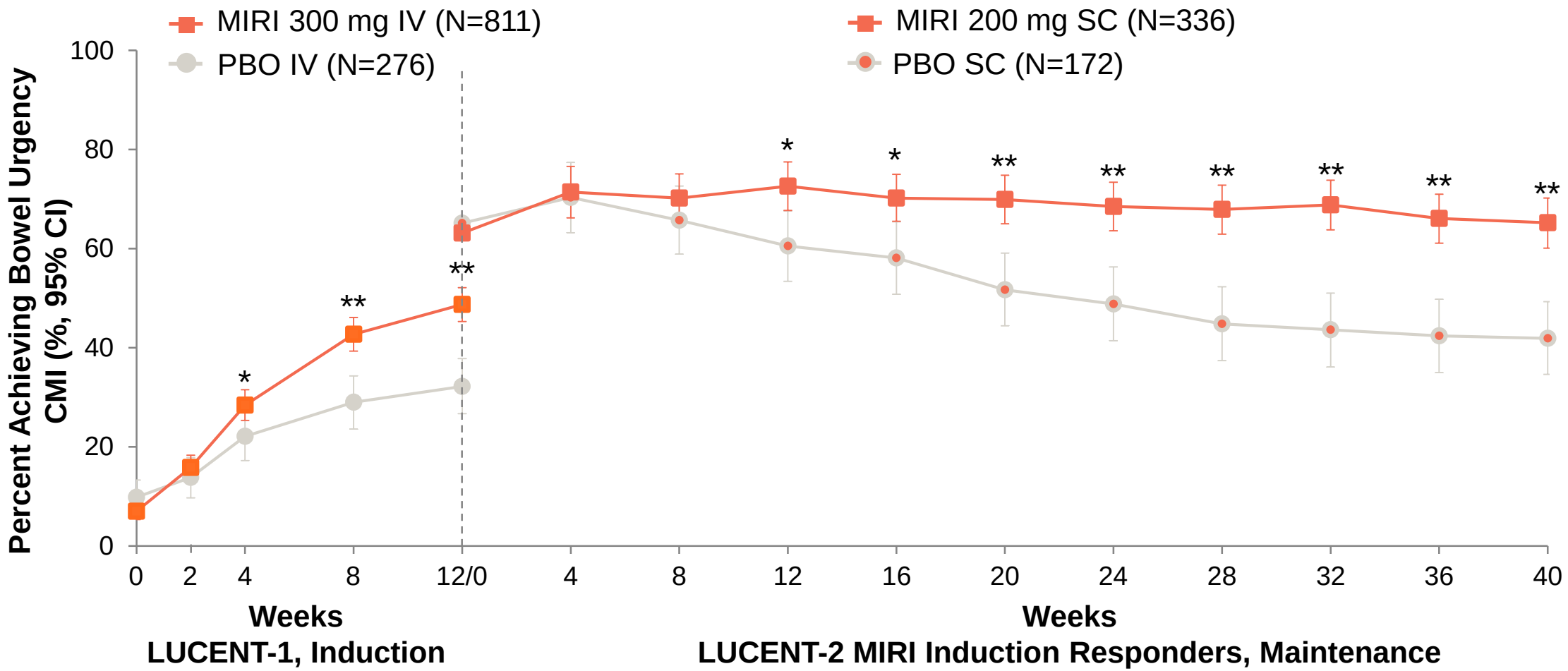


vs. PBO: *p<0.05; **p<0.001; ***p<0.0001. [a]UNRS change from baseline was assessed in the modified intent-to-treat (mITT) population; [b]UNRS change from baseline was assessed in the subpopulation of mirikizumab induction responders in LUCENT-2. [c]LSM reported for each treatment group except for Week 0 of maintenance. Note: Mixed-effects model for repeated measures was used for treatment comparison adjusting for baseline stratification factors.
CI=Confidence Interval; IV=Intravenous; LSM=Least Square Mean; MIRI=Mirikizumab; PBO=Placebo; Q4W=Every 4 Weeks; SC=Subcutaneous; SE=Standard Error; UNRS=Urgency Numeric Rating Scale.
Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Bowel Urgency CMI by Visit Through Week 52

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

Patients With UNRS ≥3 at Baseline

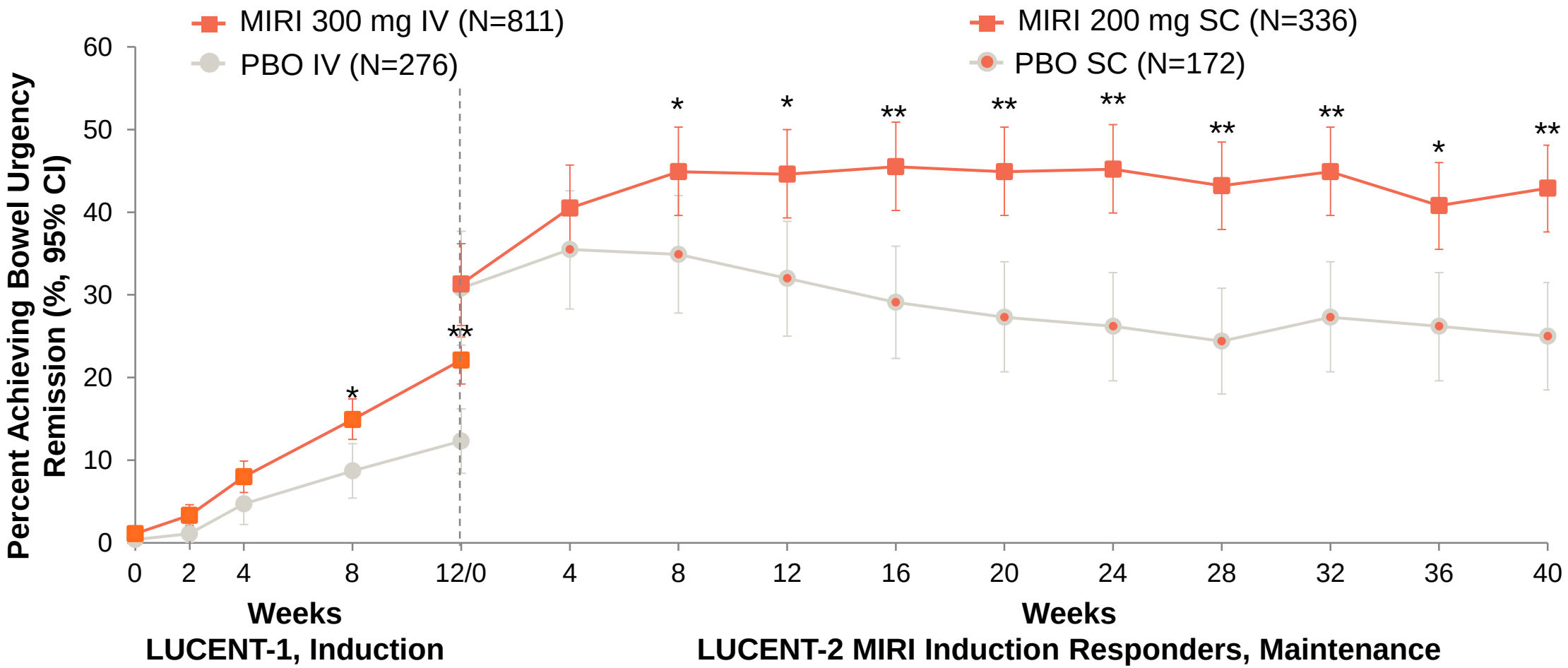


vs. PBO: *p<0.05; **p<0.001; ***p<0.0001. Note: Bowel urgency CMI was assessed in the mITT population in patients with UNRS ≥3 at induction baseline in LUCENT-1 and the subpopulation of mirikizumab induction responders in LUCENT-2. Cochran-Mantel-Haenszel (CMH) tests were used for treatment comparison adjusting for baseline stratification factors. Missing data were considered as nonresponse. CI=Confidence Interval; CMH=Cochran-Mantel-Haenszel; CMI=Clinically Meaningful Improvement; IV=Intravenous; MIRI=Mirikizumab; PBO=Placebo; Q4W=Every 4 Weeks; SC=Subcutaneous. Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Bowel Urgency Remission by Visit Through Week 52

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

Patients With UNRS ≥3 at Baseline



vs. PBO: *p<0.05; **p<0.001; ***p<0.0001. Note: Bowel urgency remission was assessed in the mITT population in patients with UNRS ≥3 at induction baseline in LUCENT-1 and the subpopulation of mirikizumab induction responders in LUCENT-2. Cochran-Mantel-Haenszel (CMH) tests were used for treatment comparison adjusting for baseline stratification factors. Missing data were considered as nonresponse. CI=Confidence Interval; CMH=Cochran-Mantel-Haenszel; IV=Intravenous; MIRI=Mirikizumab; PBO=Placebo; mITT=modified intent-to-treat; Q4W=Every 4 Weeks; SC=Subcutaneous. Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Associations Between BU CMI and Clinical Outcomes

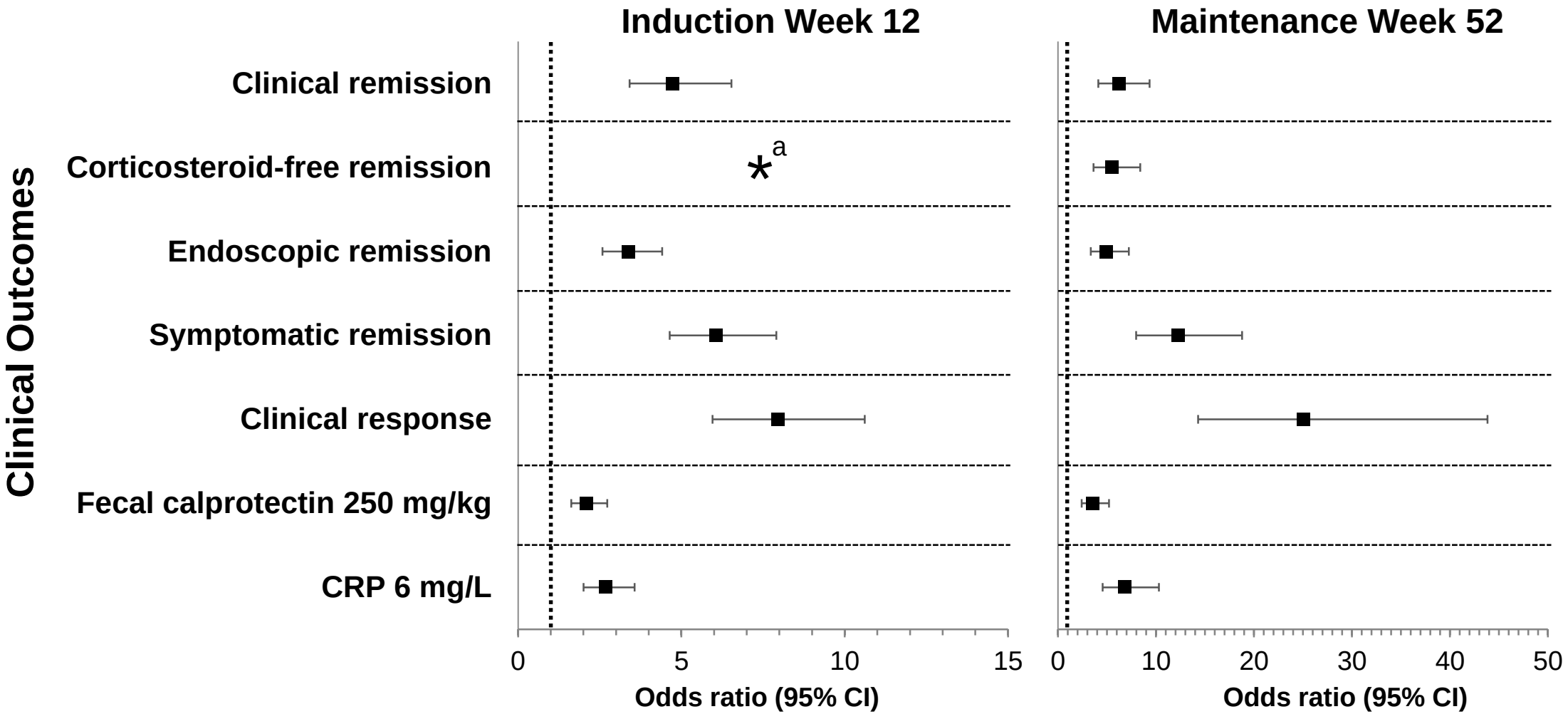
mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

	Induction (W12 Analysis)			Maintenance (W52 Analysis) MIRI Induction Responders		
Clinical outcome, n (%)	**BU CMI Yes N=484**	**BU CMI No N=603**	**p-value[a]**	**BU CMI Yes N=291**	**BU CMI No N=217**	**p-value[a]**
Clinical remission	168 (34.7)	61 (10.1)	<0.0001	174 (59.8)	42 (19.4)	<0.0001
Corticosteroid-free remission	NA[b]	NA[b]	-	157 (54.0)	38 (17.5)	<0.0001
Endoscopic remission	222 (45.9)	121 (20.1)	<0.0001	190 (65.3)	60 (27.6)	<0.0001
Symptomatic remission	310 (64.0)	137 (22.7)	<0.0001	246 (84.5)	67 (30.9)	<0.0001
Clinical response	402 (83.1)	230 (38.1)	<0.0001	274 (94.2)	85 (39.2)	<0.0001
Normal fecal calprotectin (≤250 mg/kg)	200 (41.3)	151 (25.0)	<0.0001	159 (54.6)	55 (25.3)	<0.0001
Normal C-reactive protein (≤6 mg/L)	400 (82.6)	386 (64.0)	<0.0001	242 (83.2)	91 (41.9)	<0.0001

[a]p-values were calculated from Chi-square test. [b]Patients were required to stay on stable dose of corticosteroid during LUCENT-1; therefore, corticosteroid-free remission was not defined in this study.
BU=Bowel Urgency; CMI=Clinically Meaningful Improvement; NA=Not applicable.
Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Association of Achieving Clinical Outcomes With BU CMI (Yes vs. No)

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)



[a]Corticosteroid-free remission was not defined in the induction study. BU=Bowel Urgency; CI=Confidence Interval; CMI=Clinically Meaningful Improvement; CRP=C-Reactive Protein; W=Week.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Associations Between BU Remission and Clinical Outcomes

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

	Induction (W12 Analysis)			Maintenance (W52 Analysis) MIRI Induction Responders		
Clinical outcome, n (%)[a]	**BU Remission Yes N=213**	**BU Remission No N=874**	**p-value[a]**	**BU Remission Yes N=187**	**BU Remission No N=321**	**p-value[a]**
Clinical remission	90 (42.3)	139 (15.9)	<0.0001	126 (67.4)	90 (28.0)	<0.0001
Corticosteroid-free remission	NA[b]	NA[b]	-	116 (62.0)	79 (24.6)	<0.0001
Endoscopic remission	107 (50.2)	236 (27.0)	<0.0001	131 (70.0)	119 (37.1)	<0.0001
Symptomatic remission	164 (77.0)	283 (32.4)	<0.0001	174 (93.0)	139 (43.3)	<0.0001
Clinical response	191 (89.7)	441 (50.5)	<0.0001	180 (96.3)	179 (55.8)	<0.0001
Normal fecal calprotectin (≤250 mg/kg)	100 (46.9)	251 (28.7)	<0.0001	111 (59.4)	103 (32.1)	<0.0001
Normal C-reactive protein (≤6 mg/L)	185 (86.9)	601 (68.8)	<0.0001	156 (83.4)	177 (55.1)	<0.0001

[a]p-values were calculated from Chi-square test. [b]Patients were required to stay on stable dose of corticosteroid during LUCENT-1; therefore, corticosteroid-free remission was not defined in this study.
BU=Bowel Urgency; CMI=Clinically Meaningful Improvement; NA=Not applicable.
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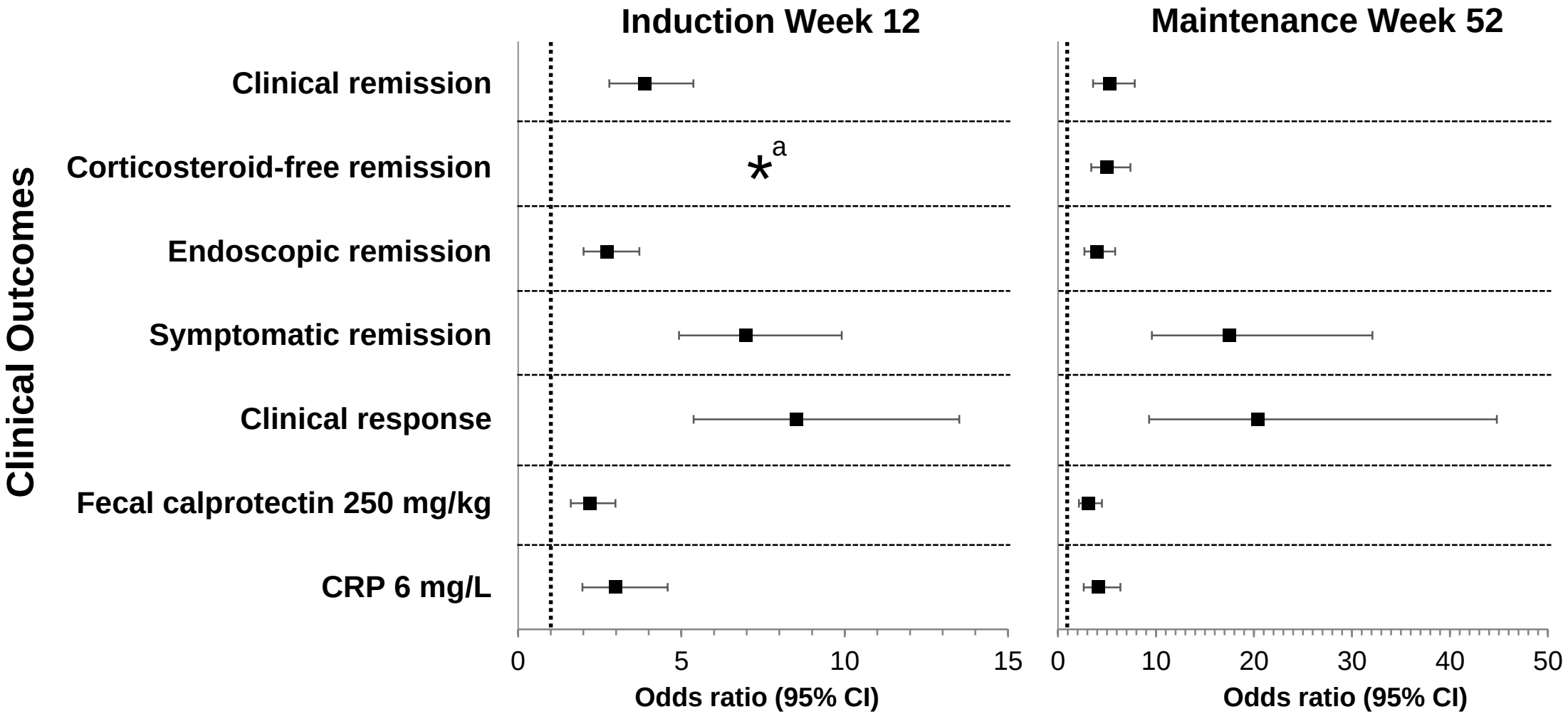
Association of Achieving Clinical Outcomes With BU Remission (Yes vs. No)

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)



[a]Corticosteroid-free remission was not defined in the induction study. BU=Bowel Urgency; CI=Confidence Interval; CRP=C-Reactive Protein; W=Week.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Association Between BU CMI and IBDQ Scores

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

Induction (W12 Analysis)

LSM Change From Baseline (SE)	BU CMI Yes N=484	BU CMI No N=533	LSM Diff (95% CI)	p-value[a]
IBDQ total score	52.4 (1.22)	25.6 (1.17)	26.8 (23.5, 30.2)	<0.0001
IBDQ bowel symptoms	19.6 (0.42)	10.2 (0.40)	9.4 (8.3, 10.6)	<0.0001
IBDQ emotional functions	15.9 (0.47)	7.3 (0.45)	8.6 (7.3, 9.9)	<0.0001
IBDQ social functions	9.1 (0.26)	4.4 (0.25)	4.7 (4.0, 5.4)	<0.0001
IBDQ systemic symptoms	7.8 (0.22)	3.8 (0.21)	4.0 (3.4, 4.6)	<0.0001

Maintenance (W52 Analysis)
MIRI Induction Responders

LSM Change From Baseline (SE)	BU CMI Yes N=291	BU CMI No N=103	LSM Diff (95% CI)	p-value[a]
IBDQ total score	62.2 (1.41)	40.4 (2.38)	21.8 (16.3, 27.2)	<0.0001
IBDQ bowel symptoms	22.6 (0.47)	15.4 (0.80)	7.2 (5.4, 9.1)	<0.0001
IBDQ emotional functions	19.5 (0.56)	12.2 (0.94)	7.3 (5.1, 9.4)	<0.0001
IBDQ social functions	10.8 (0.27)	7.4 (0.46)	3.4 (2.3, 4.5)	<0.0001
IBDQ systemic symptoms	9.2 (0.28)	5.6 (0.48)	3.6 (2.5, 4.7)	<0.0001

[a]Treatment comparisons were assessed using an analysis of covariance (ANCOVA) model, with IBDQ score change from baseline as the dependent variable and baseline IBDQ score and BU CMI as independent variables.
BU=Bowel Urgency; CI=Confidence Interval; CMI=Clinically Meaningful Improvement; IBDQ=Inflammatory Bowel Disease Questionnaire; LSM=Least Square Mean; LSM Diff=Least Square Mean Difference; SE=Standard Error.
Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Association Between BU Remission and IBDQ Scores

mITT Population (LUCENT-1) and MIRI Induction Responders (LUCENT-2)

Induction (W12 Analysis)

LSM Change From Baseline (SE)	BU Remission Yes N=213	BU Remission No N=804	LSM Diff (95% CI)	p-value[a]
IBDQ total score	61.1 (1.91)	32.4 (0.98)	28.7 (24.4, 32.9)	<0.0001
IBDQ bowel symptoms	23.1 (0.64)	12.4 (0.33)	10.6 (9.2, 12.1)	<0.0001
IBDQ emotional functions	18.3 (0.73)	9.6 (0.38)	8.7 (7.1, 10.3)	<0.0001
IBDQ social functions	10.7 (0.40)	5.6 (0.21)	5.1 (4.2, 6.0)	<0.0001
IBDQ systemic symptoms	9.2 (0.34)	4.8 (0.17)	4.4 (3.6, 5.1)	<0.0001

Maintenance (W52 Analysis)
MIRI Induction Responders

LSM Change From Baseline (SE)	BU Remission Yes N=187	BU Remission No N=207	LSM Diff (95% CI)	p-value[a]
IBDQ total score	67.8 (1.72)	46.2 (1.65)	21.5 (16.9, 26.2)	<0.0001
IBDQ bowel symptoms	24.6 (0.57)	17.2 (0.55)	7.4 (5.8, 8.9)	<0.0001
IBDQ emotional functions	21.2 (0.69)	14.3 (0.66)	6.8 (5.0, 8.7)	<0.0001
IBDQ social functions	11.8 (0.33)	8.2 (0.32)	3.7 (2.8, 4.6)	<0.0001
IBDQ systemic symptoms	10.2 (0.35)	6.6 (0.33)	3.6 (2.6, 4.5)	<0.0001

[a]Treatment comparisons were assessed using an analysis of covariance (ANCOVA) model, with IBDQ score change from baseline as the dependent variable and baseline IBDQ score and BU remission as independent variables.
BU=Bowel Urgency; CI=Confidence Interval; IBDQ=Inflammatory Bowel Disease Questionnaire; LSM=Least Square Mean; LSM Diff=Least Square Mean Difference; SE=Standard Error.
Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).

Conclusions

- The Urgency NRS assessment tool was able to quantify baseline level and change in bowel urgency after UC treatment
- Mirikizumab-treated patients with moderately to severely active UC reported greater statistically significant improvements vs. placebo in:
  - Change in Urgency NRS scores
  - Achievement of bowel urgency CMI
  - Achievement of bowel urgency remission
- This was true for both induction and maintenance treatment periods

Bowel urgency CMI or remission was associated with better outcomes during induction and maintenance:

- Clinical outcomes, including:
  - Clinical remission
  - Corticosteroid-free remission
  - Endoscopic remission
  - Symptomatic remission
  - Clinical response
- Quality of life[a], including total scores and domain scores for:
  - Bowel symptoms
  - Emotional functions
  - Social functions
  - Systemic symptoms
- Inflammatory biomarkers:
  - Fecal calprotectin
  - C-reactive protein

[a]As assessed by the IBDQ. CMI=Clinically Meaningful Improvement; IBDQ=Inflammatory Bowel Disease Questionnaire; NRS=Numeric Rating Scale; UC=Ulcerative Colitis.

Dubinsky MC, et al. *Crohns Colitis 360*. 2022; doi:10.1093/crocol/otac044 (Ahead of print).