MP242

Sustained Symptom Control With Mirikizumab in Patients With Moderately to Severely Active Ulcerative Colitis in the LUCENT-2 Maintenance Trial

Axel Dignass,[1] Silvio Danese,[2] Katsuyoshi Matsuoka,[3] Marc Ferrante,[4] Millie Long,[5] Isabel Redondo,[6] Theresa Hunter Gibble,[6] Richard Moses,[6] Xingyuan Li,[6] Nathan Morris,[6] Catherine Milch,[6] Maria T. Abreu[7]

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BACKGROUND

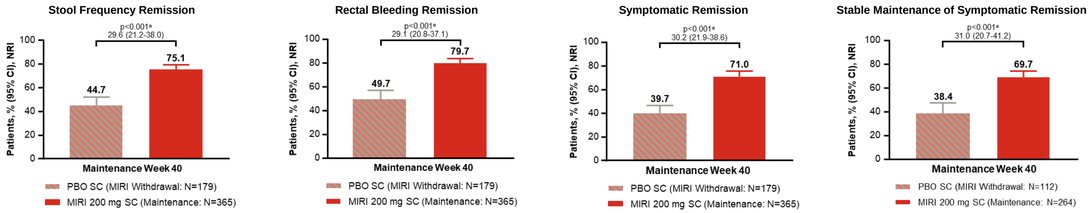
- Ulcerative colitis is a chronic inflammatory bowel disease associated with a relapsing-remitting disease course and symptoms of diarrhea, rectal bleeding, abdominal pain, and bowel urgency[1]
- Mirikizumab is a humanized IgG4–variant monoclonal antibody that specifically binds the p19 subunit of interleukin (IL)-23[2]
- In patients with moderately to severely active ulcerative colitis, treatment with mirikizumab was effective in induction of clinical remission at Week 12 (LUCENT-1; NCT03518086)[3] and in maintenance of clinical remission at Week 40, corresponding to 52 weeks of continuous treatment (LUCENT-2; NCT03524092)[4]

OBJECTIVE

- To assess sustained symptom control with mirikizumab during 40 weeks of maintenance treatment (52 weeks of continuous therapy; LUCENT-2) among patients who had a clinical response to mirikizumab during the induction study (LUCENT-1)

KEY RESULTS

Significantly Greater Rates of Stool Frequency Remission, Rectal Bleeding Remission, and Symptomatic Remission Were Observed With MIRI vs. PBO at 40 Weeks of Continuous Treatment



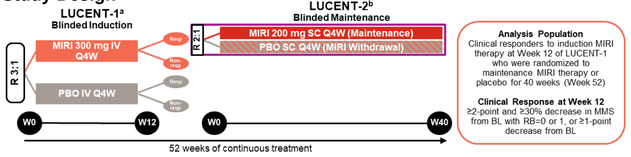
[a] Common risk difference for MIRI vs. PBO (95% CI)

CONCLUSIONS

- A greater proportion of mirikizumab-treated patients who were induction responders achieved stable maintenance of symptomatic remission compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment)
- Improvement in bowel urgency continued for patients who received mirikizumab treatment for 40 weeks, with patients accruing an additional 13.6-percentage point increase in bowel urgency remission during the first 8 weeks of maintenance therapy
- Sustained maintenance of remission of ulcerative colitis symptoms, including rectal bleeding, stool frequency, bowel urgency, and abdominal pain, was observed in mirikizumab-treated patients compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment)

METHODS

Study Design



Analysis Population
Clinical responders to induction MIRI therapy at Week 12 of LUCENT-1 who were randomized to maintenance MIRI therapy or placebo for 40 weeks (Week 52)

Clinical Response at Week 12
≥2-point and ≥30% decrease in MMS from BL with RB=0 or 1, or ≥1-point decrease from BL

[a] LUCENT-1 was a Phase 3, randomized, parallel-arm, double-blind, PBO-controlled induction trial of MIRI in patients with moderately to severely active ulcerative colitis; [b] LUCENT-2 was a Phase 3, double-blind, randomized, withdrawal maintenance study in patients who responded to MIRI induction therapy in LUCENT-1. Figure is not the full LUCENT-2 program; only the patient cohort who were MIRI responders during induction and randomized to maintenance treatment is presented here. Clinical responders to induction MIRI therapy at Week 12 of LUCENT-1 were randomized to receive maintenance MIRI therapy or PBO for 40 weeks (52 weeks of treatment). Randomization in LUCENT-2 was stratified by induction remission status, biologic failure status, baseline corticosteroid use, and region

Key Eligibility Criteria: LUCENT-1

- Age ≥18 and ≤80 years
- Moderately to severely active ulcerative colitis
  - Modified Mayo Score of 4-9, with an endoscopic subscore of 2-3
- Inadequate response, loss of response, or intolerance to:
  - Corticosteroids, immunomodulators, biologic therapy, or Janus kinase inhibitors for ulcerative colitis
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies for ulcerative colitis, regardless of mechanism of action

Assessments

- Patient-reported outcomes were recorded daily in the patient eDiary and then averaged by week[a]:
  - Stool frequency Mayo subscore, from 0 (stools/day normal for the patient) to 3 (≥5 stools/day more than normal)
  - Rectal bleeding Mayo subscore, from 0 (no blood) to 3 (blood alone passed)
  - Bowel urgency severity (UNRS), from 0 (no urgency) to 10 (worst possible urgency)
  - Abdominal pain NRS, from 0 (none) to 10 (worst possible pain)
- Proportion of patients achieving:
  - Stool frequency remission: Stool frequency subscore 0, or 1 with ≥1-point decrease from induction BL
  - Rectal bleeding remission: Rectal bleeding subscore 0
  - Symptomatic remission: Stool frequency and rectal bleeding remission
  - Stable maintenance of symptomatic remission: Patients in symptomatic remission for ≥7 of 9 visits from Weeks 4-36 and at Week 40 among patients in symptomatic remission and with clinical response at the end of LUCENT-1
  - Abdominal pain improvement: NRS ≥30% reduction from BL in patients with abdominal pain NRS ≥3 at induction BL
  - Bowel urgency remission: Minimal to no bowel urgency (UNRS [0,1]) in patients with bowel urgency severity UNRS ≥3 at induction BL
- Change in bowel urgency severity (UNRS) from induction BL

[a] For stool frequency and rectal bleeding, weekly assessments were calculated by averaging the 3 most recent available eDiary days in a 7-day period; for bowel urgency and abdominal pain, all available eDiary days in a 7-day period were averaged

Statistical Analysis

- Analyses were conducted using the modified Intent-to-Treat population (patients receiving ≥1 dose of mirikizumab or placebo)
  - Excludes patients impacted by an electronic clinical outcome assessment transcription error in Poland and Turkey
- Changes from baseline were compared between treatment arms using mixed-effects model of repeated measures, including treatment, baseline value, visit, interaction of baseline value-by-visit, interaction of treatment-by-visit, prior biologic or tofacitinib failure, corticosteroid use at baseline (LUCENT-1), global region, and clinical remission status at Week 12 (LUCENT-1)
- Response rates between treatment arms were compared using Cochran-Mantel-Haenszel test adjusted for prior biologic or tofacitinib failure, corticosteroid use at baseline (LUCENT-1), global region, and clinical remission status at Week 12 (LUCENT-1)
  - Common risk difference was the difference in proportions adjusted for stratification factors, with confidence intervals calculated using the Mantel-Haenszel-Sato method
  - Missing data were handled using non-responder imputation

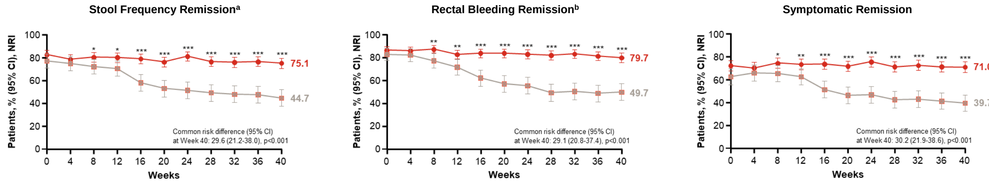
RESULTS

Baseline[a] Demographics and Disease Characteristics

	MIRI Induction Responders	
	PBO SC (N=179)	MIRI 200 mg SC (N=365)
Age, years, mean (SD)	41.2 (12.8)	43.4 (14.2)
Male	104 (58.1)	214 (58.6)
Disease duration, years, mean (SD)	6.7 (5.6)	6.9 (7.1)
Disease location		
Left-sided colitis	119 (66.5)	234 (64.1)
Pancolitis	59 (33.0)	128 (35.1)
Modified Mayo Score, mean (SD)	6.6 (1.2)	6.5 (1.3)
Endoscopic Mayo subscore, moderate [score 2]	73 (40.8)	130 (35.6)
Endoscopic Mayo subscore, severe [score 3]	106 (59.2)	235 (64.4)
Bowel urgency severity, median (Q1, Q3)	6.0 (5.0, 8.0)	6.0 (5.0, 8.0)
Abdominal pain NRS, mean (SD)	5.3 (2.2)	4.9 (2.4)
Baseline corticosteroid use	68 (38.0)	135 (37.0)
Immunomodulator use	39 (21.8)	78 (21.4)
Prior biologic (or tofacitinib) failure	64 (35.8)	128 (35.1)
Prior anti-TNF failure	58 (32.4)	112 (30.7)
Prior vedolizumab failure	23 (12.8)	47 (12.9)
Prior tofacitinib failure	8 (4.5)	8 (2.2)
Number of failed biologics (or tofacitinib)		
0	115 (64.2)	237 (64.9)
1	35 (19.6)	77 (21.1)
≥2	29 (16.2)	51 (14.0)

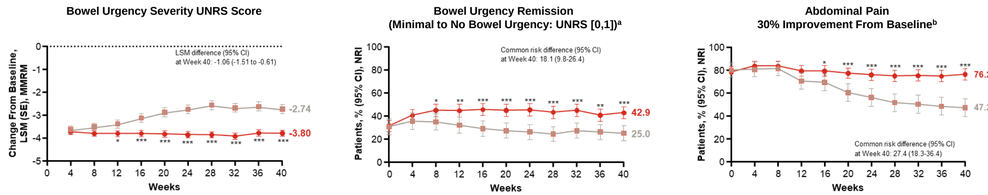
Data are presented as n (%) unless stated otherwise
[a] Refers to induction BL (Week 0 of LUCENT-1)

Remission Rates Were Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO



* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] Mean (SD) stool frequency Mayo subscore at Week 0: 0.87 (0.77) for PBO SC, 0.81 (0.73) for MIRI 200 mg SC; [b] Mean (SD) rectal bleeding Mayo subscore at Week 0: 0.17 (0.38) for PBO SC, 0.13 (0.34) for MIRI 200 mg SC

Improvement in Bowel Urgency and Abdominal Pain Was Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO



* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] In patients with Bowel Urgency NRS ≥3 at BL (LUCENT-1); [b] In patients with Abdominal Pain NRS ≥3 at BL (LUCENT-1)

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1. Ordás I, et al. *Lancet*. 2012;380:1606-1619.
2. Sands BE, et al. *Gastroenterology*. 2022;162:495-508.
3. D'Haens G, et al. *J Crohns Colitis*. 2022;16:1028-1029.
4. Dubinsky MC, et al. *Gastroenterology*. 2022;162:S1393-S1394.

ABBREVIATIONS

BL=baseline; CI=confidence interval; IV=intravenous; LSM=least squares mean; MIRI=mirikizumab; MMRM=mixed-effects model of repeated measures; MMS=Modified Mayo Score; Non-resp=non-responders; NRI=non-responder imputation; NRS=numeric rating scale; PBO=placebo; Q=quartile; Q4W=every 4 weeks; R=randomization; RB=rectal bleeding; Resp=responders; SC=subcutaneous; SD=standard deviation; SE=standard error; TNF=tumor necrosis factor; UNRS=Urgency Numeric Rating Scale; W=Week

DISCLOSURES

* **A. Dignass** has received consulting fees from: AbbVie, Abivax, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb (Celgene), Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Gilead Sciences, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Pharmacosmos, Roche, SandozHexal, Takeda, Tillotts Pharma AG, and Vifor Pharma; has received lecture fees or honoraria from: AbbVie, Amgen, Bristol Myers Squibb, Dr. Falk Pharma, Ferring Pharmaceuticals, Galapagos, HighSMd, & Dohme, Mundipharma, Mylan, Pfizer, Roche, Sandoz Sublimity, Takeda, TiGenix, UCB Pharma, and Vifor Pharma; and lecture fees from: AbbVie, Amgen, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Mylan, Pfizer, and Takeda; **K. Matsuoka** has received fees for grants and/or contracts from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, Takeda, and Zeria Pharmaceutical Nippon; and lecture fees from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, Takeda, and Zeria Pharmaceutical Nippon; and manuscript preparation fees from: Eli Lilly and Company; **M. Ferrante** has received fees for grants and/or contracts from: AbbVie, Amgen, Biogen, Janssen Cilag, Pfizer, Takeda, and Vialris; consulting fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Regeneron, Sandoz, Takeda, and Thermo Fisher Scientific; lecture fees or honoraria from: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Lanepro, Medtronic, Merck Sharp & Dohme, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda, and Thermo Fisher Scientific; support to attend meetings from: AbbVie, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Janssen, Pfizer, and Takeda; and data safety monitoring fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen, Medtronic, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, and Thermo Fisher Scientific; **M. Long** has received consulting fees from: AbbVie, Bristol Myers Squibb, Calibr, Eli Lilly and Company, Genentech, Janssen, Pfizer, Prometheus Biosciences, Roche, Takeda, TARGET PharmaSolutions, and Theravance Biopharma; and is on the Board of Trustees of: American College of Gastroenterology; **I. Redondo, T. Hunter Gibble, R. Moses, X. Li**, and **N. Morris** are employees and shareholders of: Eli Lilly and Company; **C. Milch** is a former employee of: Eli Lilly and Company; **M. T. Abreu** has received fees for grants and/or contracts from: Pfizer, Prometheus Biosciences, and Takeda; consulting fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD; lecture fees from: Alimentiv, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Prime CME, and Takeda; support to attend meetings from: AbbVie, Alimentiv, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Microba Life Sciences, Prime CME, Prometheus Biosciences, Takeda, UCB Pharma, and WebMD; data safety monitoring fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, and Gilead Sciences; and is on the advisory board of: Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD

* Medical writing assistance was provided by Serina Stretton PhD, CMPP, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

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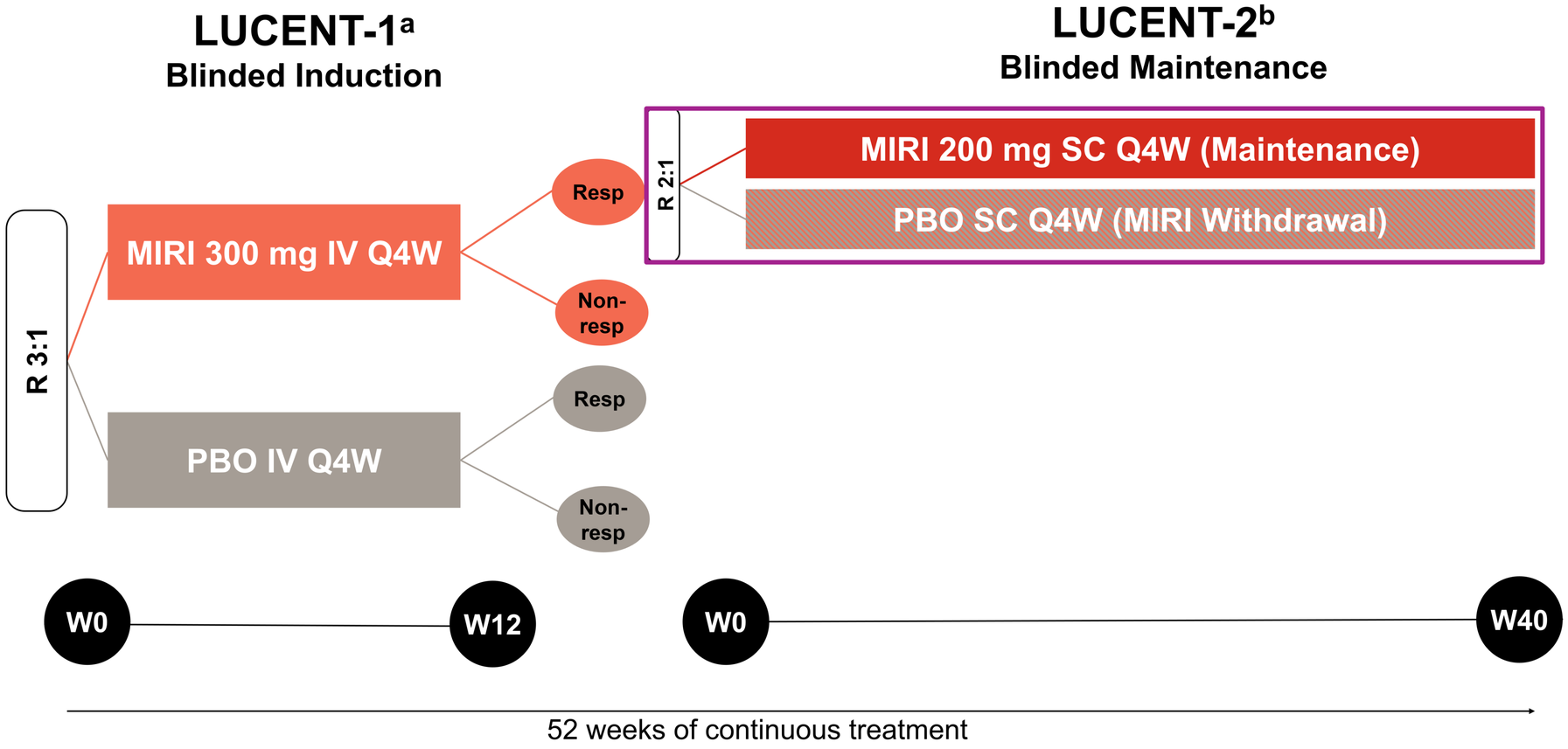

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RESULTS
Baseline[a] Demographics and Disease Characteristics (2/2)

	MIRI Induction Responders	
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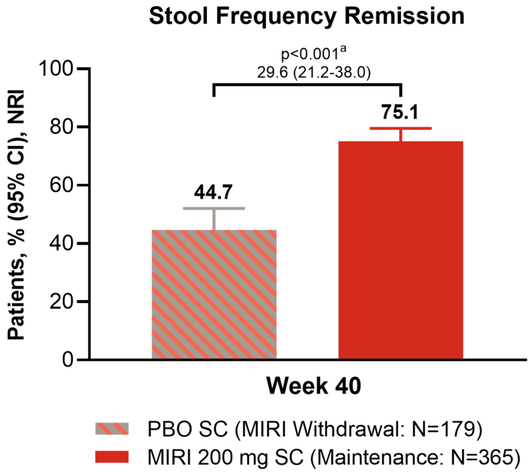

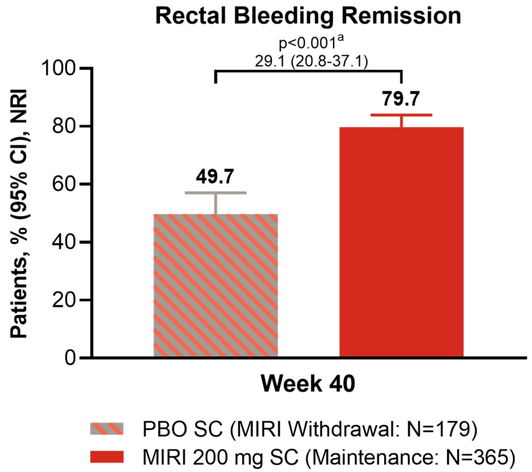

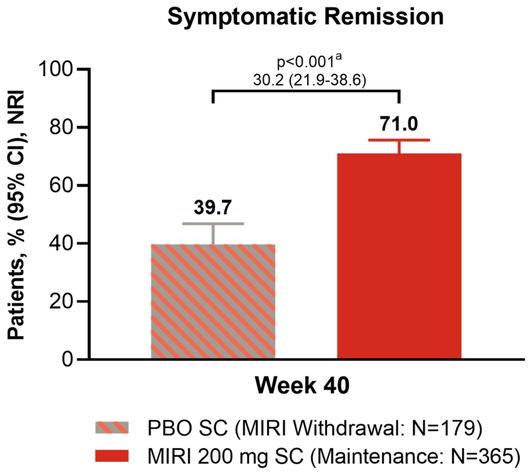

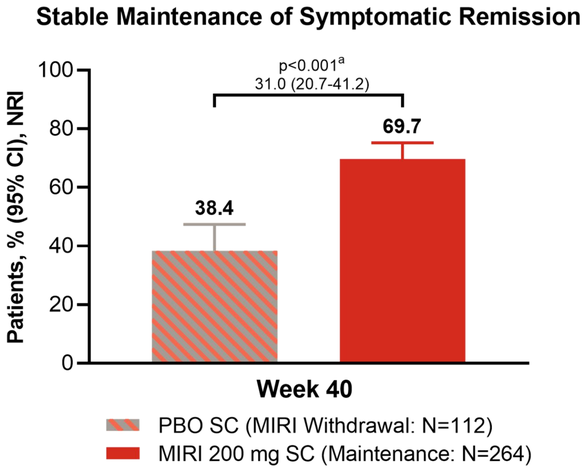

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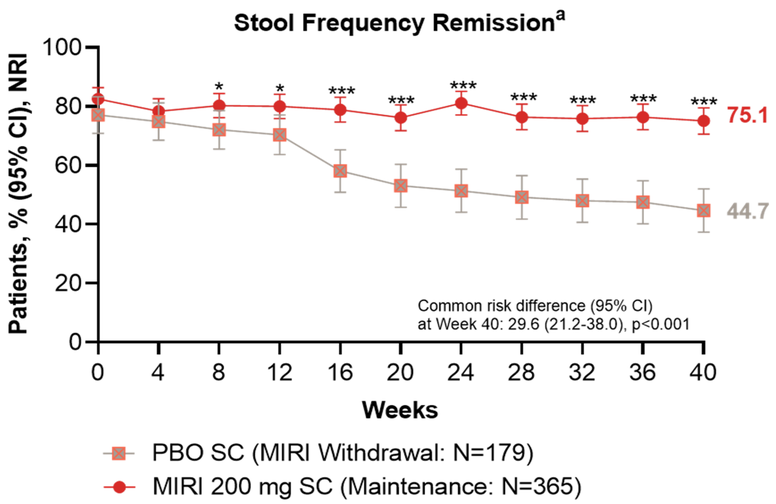
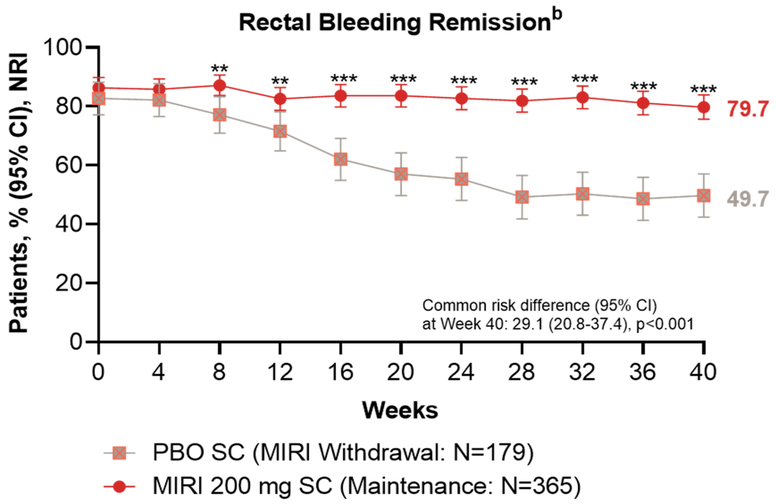
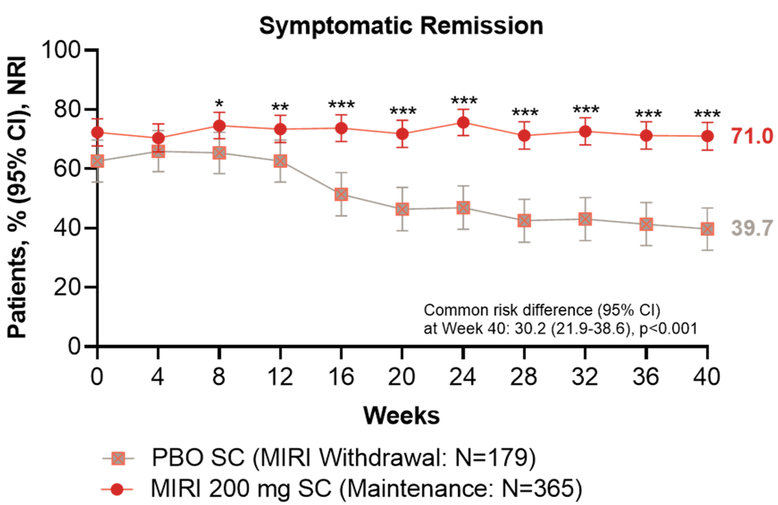
Remission Rates Were Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO[a]







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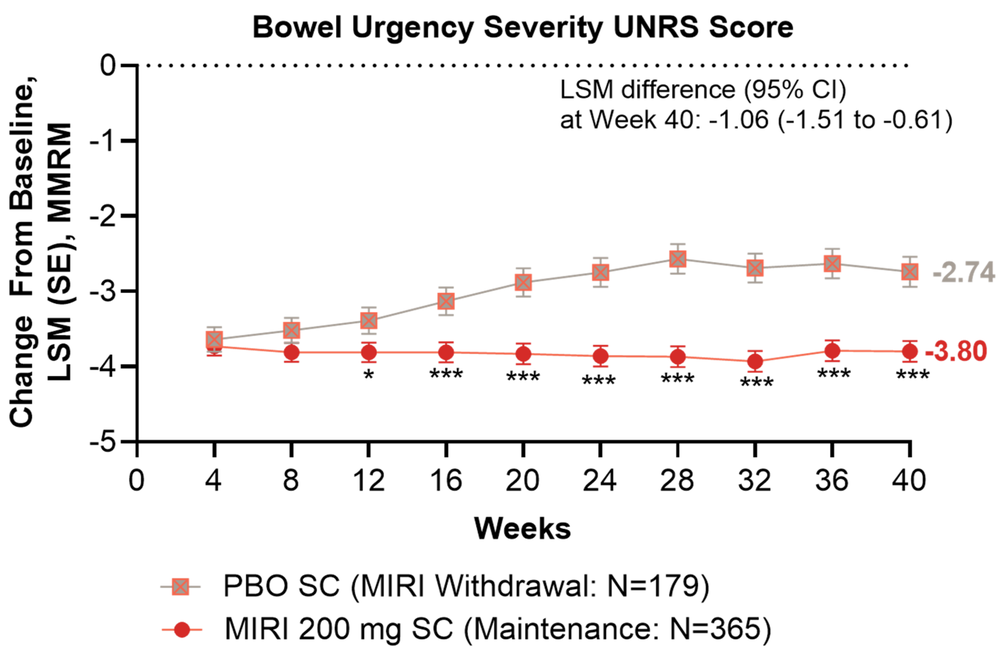
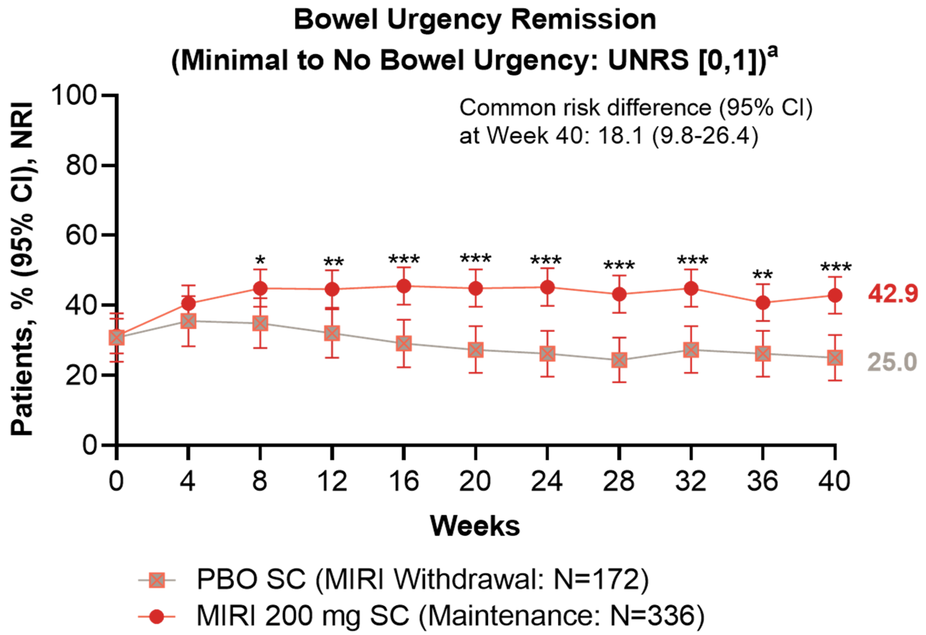
[b] Mean (SD) rectal bleeding Mayo subscore at Week 0: 0.17 (0.38) for PBO SC, 0.13 (0.34) for MIRI 200 mg SC

CI=confidence interval; MIRI=mirikizumab; NRI=non-responder imputation; PBO=placebo; SC=subcutaneous

Improvement in Bowel Urgency Was Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO



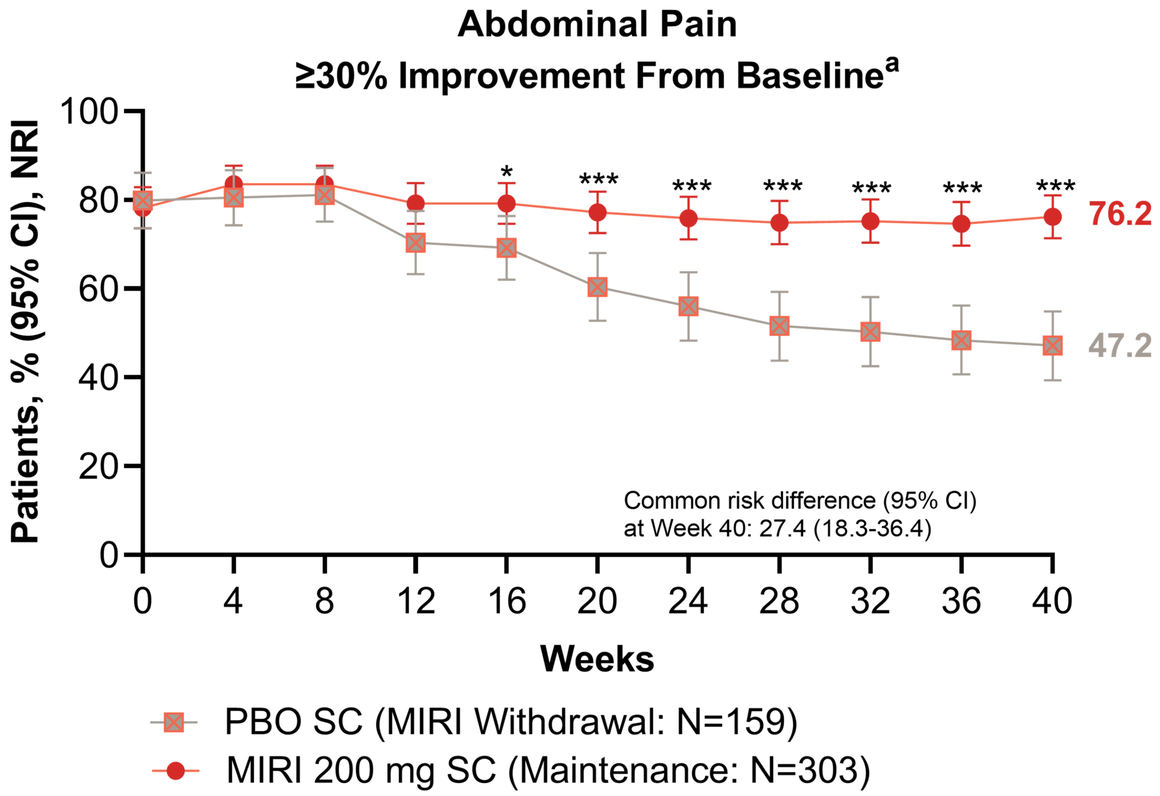


* p<0.05; ** p<0.01; *** p<0.001 vs. PBO

[a] In patients with Bowel Urgency NRS ≥3 at BL (LUCENT-1)

BL=baseline; CI=confidence interval; LSM=least squares mean; MIRI=mirikizumab; MMRM=mixed-effect model of repeated measures; NRI=non-responder imputation; PBO=placebo; SC=subcutaneous; SE=standard error; UNRS=Urgency Numeric Rating Scale

Improvement in Abdominal Pain Was Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO



* p<0.05; ** p<0.01; *** p<0.001 vs. PBO

[a] In patients with Abdominal Pain NRS ≥3 at BL (LUCENT-1)

BL=baseline; CI=confidence interval; MIRI=mirikizumab; NRI=non-responder imputation; NRS=numeric rating scale; PBO=placebo; SC=subcutaneous

CONCLUSIONS

- A greater proportion of mirikizumab-treated patients who were induction responders achieved stable maintenance of symptomatic remission compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment
- Improvement in bowel urgency continued for patients who received mirikizumab treatment for 40 weeks, with patients accruing an additional 13.6-percentage point increase in bowel urgency remission during the first 8 weeks of maintenance therapy
- Sustained maintenance of remission of ulcerative colitis symptoms, including rectal bleeding, stool frequency, bowel urgency, and abdominal pain, was observed in mirikizumab-treated patients compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment)

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ABBREVIATIONS

BL=baseline; CI=confidence interval; IV=intravenous; LSM=least squares mean; MIRI=mirikizumab; MMRM=mixed-effects model of repeated measures; *MMS=Modified Mayo Score; Non-resp=non-responders; NRI=non-responder imputation; NRS=numeric rating scale; PBO=placebo; Q=quartile; Q4W=every 4 weeks; R=randomization; Resp=responders; SC=subcutaneous; SD=standard deviation; SE=standard error; TNF=tumor necrosis factor; UNRS=Urgency Numeric Rating Scale; W=Week*

DISCLOSURES

- **A. Dignass** has received consulting fees from: AbbVie, Abivax, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb (Celgene), Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Gilead Sciences, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Pharmacosmos, Roche, Sandoz/Hexal, Takeda, Tillotts Pharma AG, and Vifor Pharma; has received lecture fees or honoraria from: AbbVie, Amgen, Bristol Myers Squibb, Dr. Falk Pharma, Ferring Pharmaceuticals, Galapagos, High5Md, Janssen, Materia, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, Tillotts Pharma AG, and Vifor Pharma; and manuscript preparation fees from: Dr. Falk Pharma, Janssen, Takeda, and Thieme; **S. Danese** has received consulting fees from: AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Enthera, Ferring Pharmaceuticals, Gilead Sciences, Hospira, Inotrem, Janssen, Johnson & Johnson, Merck Sharp & Dohme, Mundipharma, Mylan, Pfizer, Roche, Sandoz Sublimity, Takeda, TiGenix, UCB Pharma, and Vifor Pharma; and lecture fees from: AbbVie, Amgen, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Mylan, Pfizer, and Takeda; **K. Matsuoka** has received fees for grants and/or contracts from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, and Zeria Pharmaceutical Nippon; lecture fees from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, Takeda, and Zeria Pharmaceutical Nippon; and manuscript preparation fees from: Eli Lilly and Company; **M. Ferrante** has received fees for grants and/or contracts from: AbbVie, Amgen, Biogen, Janssen Cilag, Pfizer, Takeda, and Viatris; consulting fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Regeneron, Sandoz, Takeda, and Thermo Fisher Scientific; lecture fees or honoraria from: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Janssen, Lamepro, Medtronic, Merck Sharp & Dohme, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda, and Thermo Fisher; support to attend meetings from: AbbVie, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Janssen, Pfizer, and Takeda; and data safety monitoring fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen, Medtronic, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, and Thermo Fisher Scientific; **M. Long** has received consulting fees from: AbbVie, Bristol Myers Squibb, Calibr, Eli Lilly and Company, Genentech, Janssen, Pfizer, Prometheus Biosciences, Roche, Takeda, TARGET PharmaSolutions, and Theravance Biopharma; and is on the Board of Trustees of: American College of Gastroenterology; **I. Redondo**, **T. Hunter Gibble**, **R. Moses**, **X. Li**, and **N. Morris** are employees and shareholders of: Eli Lilly and Company; **C. Milch** is a former employee of: Eli Lilly and Company; **M. T. Abreu** has received fees for grants and/or contracts from: Pfizer, Prometheus Biosciences, and Takeda; consulting fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD; lectures fees from: Alimentiv, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Prime CME, and Takeda; support to attend meetings from: AbbVie, Alimentiv, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Microba Life Sciences, Prime CME, Prometheus Biosciences, Takeda, UCB Pharma, and WebMD; data safety monitoring fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, and Gilead Sciences; and is on the advisory board of: Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD
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