C0400

Early Symptom Control With Mirikizumab in Patients With Moderately to Severely Active Ulcerative Colitis in the LUCENT-1 Induction Trial

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BACKGROUND

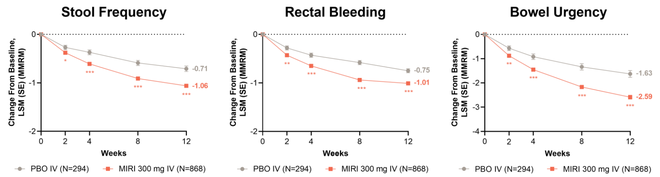
- Ulcerative colitis is a chronic inflammatory disease associated with symptoms of diarrhea, rectal bleeding, abdominal pain, and bowel urgency[1]
- Mirikizumab is a humanized immunoglobulin G4–variant monoclonal antibody that specifically binds to the p19 subunit of interleukin (IL)-23[2]
- Mirikizumab has demonstrated efficacy compared with placebo in patients with moderately to severely active ulcerative colitis in the 12-week, Phase 3, randomized, double-blind LUCENT-1 study (NCT03518086)[3]

OBJECTIVE

- To evaluate the early onset of symptomatic improvement and symptomatic control during treatment induction with mirikizumab in LUCENT-1

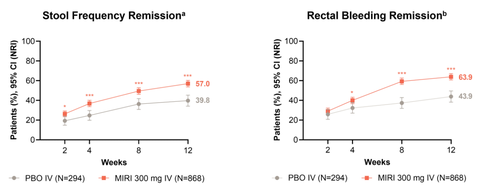
KEY RESULTS

Significant Reductions in Stool Frequency, Rectal Bleeding, and Bowel Urgency Were Observed With MIRI vs. PBO as Early as Week 2



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

Remission Rates for Stool Frequency and Rectal Bleeding Were Significantly Greater With MIRI vs. PBO as Early as Weeks 2 and 4, Respectively

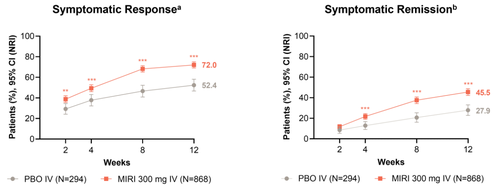


* p<0.05; ** p<0.01; ***p<0.001 vs. PBO

[a] Stool frequency subscore 0, or 1 with ≥1-point decrease from baseline

[b] Rectal bleeding subscore 0

Symptomatic Response and Remission Rates Were Significantly Greater With MIRI vs. PBO From Weeks 2 and 4, Respectively



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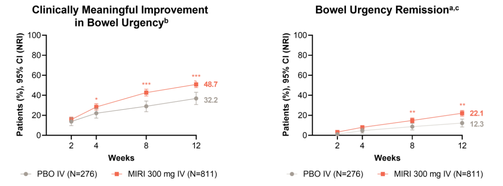
[a] ≥30% decrease from baseline in sum of stool frequency and rectal bleeding subscores

[b] Stool frequency subscore 0, or 1 with ≥1-point decrease from baseline and rectal bleeding subscore 0

Bowel Urgency Response Rate and Remission Rate Were Significantly Improved With MIRI vs. PBO From Weeks 4 and 7,[a] Respectively



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[a] Week 7 bowel urgency remission (minimal to no bowel urgency: UNRS (0,1)) not shown in the graph; PBO IV, 7.2%; MIRI 300 mg IV, 14.1% (p<0.05)

[b] UNRS ≥3-point improvement from baseline in patients with baseline UNRS ≥3

[c] UNRS (0,1) in patients with baseline UNRS

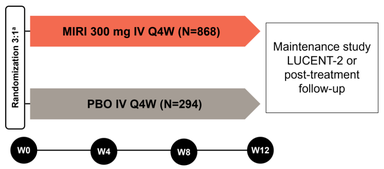
CONCLUSIONS

- As early as Week 2, significant improvements in stool frequency, rectal bleeding, bowel urgency, and fatigue were seen with mirikizumab vs. placebo, with continued separation from placebo through the Induction Period
- Increases in stool frequency remission and rectal bleeding remission with mirikizumab vs. placebo were observed as early as Week 2 and Week 4, respectively; at Week 12, ≥57% of mirikizumab-treated patients had stool frequency remission and rectal bleeding remission
- Symptomatic remission increased with mirikizumab vs. placebo from Week 4, with 46% of mirikizumab-treated patients in symptomatic remission at Week 12
- Significantly more mirikizumab-treated patients vs. placebo achieved clinically meaningful improvement in bowel urgency from Week 4 and bowel urgency remission from Week 7
- Significantly more mirikizumab-treated patients vs. placebo achieved clinically meaningful improvement in abdominal pain from Week 4
- Mirikizumab provides early and consistent control of symptoms in patients with moderately to severely active ulcerative colitis

METHODS

Study Design, LUCENT-1

Phase 3, multicenter, randomized, parallel-arm, double-blind, placebo-controlled trial of mirikizumab in patients with moderately to severely active ulcerative colitis



[a] Patients were randomized at baseline to receive treatment at Weeks 0, 4, and 8 during induction. Patients were stratified by biologic failure status, baseline corticosteroid use, baseline disease activity, and global region

Key Eligibility Criteria

- Age ≥18 and ≤80 years
- Moderately to severely active ulcerative colitis
  - Modified Mayo Score (MMS) of 4-9, with an endoscopic subscore of 2-3
- Inadequate response, loss of response, or intolerance to:
  - ≥1 corticosteroid, immunomodulator, biologic therapy, or Janus kinase inhibitor for ulcerative colitis
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies

Assessments

- Patient-reported outcomes were recorded daily in the patient eDiary then averaged by week[a]:
  - **Stool frequency Mayo subscore:** 0 (stools per day normal for the patient) to 3 (≥5 stools per day more than normal)
  - **Rectal bleeding Mayo subscore:** 0 (no blood) to 3 (blood alone passed)
  - **Bowel urgency severity (UNRS):** 0 (no urgency) to 10 (worst possible urgency)
  - **Abdominal pain NRS:** 0 (none) to 10 (worst possible pain)
  - **Fatigue NRS:** 0 (none) to 10 (worst possible fatigue)
- Change from baseline was assessed at Weeks 2, 4, 8, and 12 for stool frequency, rectal bleeding, bowel urgency, and fatigue
- Proportion of patients at Weeks 2, 4, 8, and 12 who achieved:
  - **Stool frequency remission:** Subscore 0, or 1 with ≥1-point decrease from baseline
  - **Rectal bleeding remission:** Rectal bleeding subscore 0
  - **Symptomatic response:** ≥30% decrease from baseline in sum of stool frequency and rectal bleeding subscores
  - **Symptomatic remission:** Stool frequency remission and rectal bleeding remission
  - **Bowel urgency clinically meaningful improvement:** ≥3-point UNRS improvement in patients with baseline UNRS ≥3
  - **Bowel urgency remission:** Minimal to no bowel urgency, UNRS (0,1), in patients with baseline UNRS ≥3
  - **Abdominal pain improvement:** NRS ≥30% reduction from baseline in patients with baseline abdominal pain NRS ≥3

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

Statistical Analyses

- Analyses were conducted using the modified Intent-to-Treat population (patients receiving ≥1 dose of mirikizumab or placebo)[a]
- Change from baseline was compared between treatment arms using mixed-effects model of repeated measures, including treatment, baseline value, visit, interaction of baseline value-by-visit interaction, treatment-by-visit interaction, prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity (MMS), and global region
- Response rates were compared between treatment arms using the Cochran-Mantel-Haenszel test adjusted for prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity (MMS), and global region
- Missing data were handled using non-responder imputation

RESULTS

Baseline Demographic Characteristics

	PBO IV (N=294)	MIRI 300 mg IV (N=868)
Age, years, mean (SD)	41.3 (13.8)	42.9 (13.9)
Male	165 (56.1)	530 (61.1)
Disease duration, years, mean (SD)	6.9 (7.0)	7.2 (6.7)
Disease extent		
Left-sided colitis	188 (64.2)	544 (62.7)
Pancolitis	103 (35.2)	318 (36.6)
MMS category		
Moderate [score 4-6]	138 (47.1)	404 (46.5)
Severe [score 7-9]	155 (52.9)	463 (53.3)
Endoscopic Mayo subscore, severe [score 3]	200 (68.3)	574 (66.1)
Stool frequency Mayo subscore, ≥5 per day more than normal [score 3]	162 (55.1)	471 (54.3)
Rectal bleeding Mayo subscore, blood alone passed [score 3]	13 (4.4)	55 (6.3)
Bowel urgency severity (UNRS), mean (SD)	6.2 (2.2)	6.1 (2.2)
Fatigue NRS, mean (SD)	5.8 (2.3)	5.7 (2.3)
Abdominal pain NRS, mean (SD)	5.1 (2.5)	4.9 (2.4)

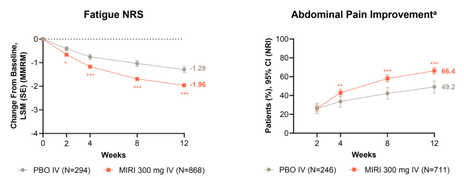
Data are presented as n (%) unless stated otherwise

Prior and Baseline Treatments

	PBO IV (N=294)	MIRI 300 mg IV (N=868)
Baseline corticosteroid use	113 (38.4)	351 (40.4)
Prior systemic corticosteroid failure	152 (51.7)	473 (54.5)
Baseline immunomodulator use	69 (23.5)	211 (24.3)
Prior systemic immunomodulator failure	104 (35.4)	279 (32.1)
Number of prior biologics or tofacitinib used		
0	171 (58.2)	492 (56.7)
1	61 (20.7)	180 (20.7)
2	57 (19.4)	164 (18.9)
>2	5 (1.7)	32 (3.7)
Prior biologic or tofacitinib failure	118 (40.1)	361 (41.6)
Prior anti-TNF failure	97 (33.0)	325 (37.4)
Prior vedolizumab failure	59 (20.1)	159 (18.3)
Prior tofacitinib failure	6 (2.0)	34 (3.9)

Data are presented as n (%) unless stated otherwise

Fatigue NRS Change From Baseline and Abdominal Pain Improvement Were Significantly Greater With MIRI vs. PBO From Weeks 2 and 4, Respectively



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[a] Abdominal pain NRS ≥30% improvement from baseline in patients with baseline abdominal pain NRS ≥3

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1. Ordás I, et al. Lancet. 2012;380:1606-1619.
2. Sandborn WJ, et al. Gastroenterology. 2020;158:537-549.
3. D'Haens G, et al. J Crohns Colitis. 2022;16:i028-i029.

ABBREVIATIONS

CI=confidence interval; IL=interleukin; IV=intravenous; LSM=least squares mean; MRI=mirikizumab; MMRM=mixed-effects model of repeated measures; MMS=Modified Mayo Score; NRI=non-responder imputation; NRS=Numeric Rating Scale; PBO=placebo; Q4W=every 4 weeks; SD=standard deviation; SE=standard error; TNF=tumor necrosis factor; UNRS=Urgency Numeric Rating Scale; W=Week

DISCLOSURES

- S. Danese has received honoraria as a consultant for: 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 Therapeutics, Takeda, TiGenix, UCB Pharma, and Vifor Pharma; and has received lecture fees from: AbbVie, Amgen, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Mylan, Pfizer, and Takeda; A. Dignass has received honoraria as a consultant for: AbbVie, Abivax, Amgen, Arena Pharmaceuticals, Celgene/Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Falk Foundation, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos NV, Gilead Sciences, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Pharmacosmos, Roche, Sandoz/Hexal, Takeda, Tillotts Pharma AG, and Vifor Pharma; has received lecture fees from: AbbVie, Amgen, Bristol Myers Squibb, Falk Foundation, Ferring Pharmaceuticals, Galapagos NV, High5MD, Janssen, Materia Prima, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, Tillotts Pharma AG, and Vifor Pharma; and has received payment for manuscript preparation from: Falk Foundation, Janssen, Takeda, and Thieme; K. Matsuoka has received grants and/or contracts from: AbbVie, EA Pharma, Eli Lilly and Company, JIMRO, Kissei Pharmaceutical, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon, and Zeria Pharmaceutical; and has received lecture fees from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon,Takeda, and Zeria Pharmaceutical; M. Ferrante has received grants and/or contracts from: AbbVie, Amgen, Biogen, Janssen Cilag, Pfizer, Takeda, and Viatris; has received honoraria as a consultant for: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Regeneron, Sandoz, Takeda, and Thermo Fisher Scientific; has received lecture fees 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 Scientific; has received support to attend meetings from: AbbVie, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Janssen, Pfizer, and Takeda; and has received 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 honoraria as a consultant for: AbbVie, Bristol Myers Squibb, Calibr, Eli Lilly and Company, Genentech, Janssen, Pfizer, Prometheus Therapeutics and Diagnostics, 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, N. Morris, X. Li, and C. Milch are employees and shareholders of: Eli Lilly and Company; M. T. Abreu has received grants and/or contracts from: Pfizer, Prometheus Therapeutics and Diagnostics, and Takeda; has received honoraria as a consultant for: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Janssen, Microba Life Sciences, Prometheus Therapeutics and Diagnostics, UCB Pharma, and WebMD; has received lecture fees from: Alimentiv, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Prime CME, and Takeda; has received 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, Prime CME, Prometheus Therapeutics and Diagnostics, Takeda, UCB Pharma, and WebMD; has received data safety monitoring fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, and Gilead Sciences; and is an advisory board member for: Janssen, Microba, Prometheus Therapeutics and Diagnostics, UCB Pharma, and WebMD
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