Mirikizumab Significantly Improves Abdominal Pain in Patients with Moderately-to-Severely Active Ulcerative Colitis: Results from the Phase 3 LUCENT-1 Induction and LUCENT-2 Maintenance Studies

B0377

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BACKGROUND AND OBJECTIVE

- Ulcerative colitis (UC) is a relapsing-remitting chronic disease characterized by mucosal inflammation of the rectum and colon.[1] Classic symptoms include bloody diarrhea, bowel urgency, tenesmus, and abdominal pain.[2]
- Abdominal pain is a burdensome symptom affecting >50% of patients with UC.[3,4]
- Mirikizumab, an anti-IL-23p19 monoclonal antibody, demonstrated efficacy versus placebo in adult patients with moderately-to-severely active UC in 12-week induction LUCENT-1 (NCT03518086) and 40-week maintenance LUCENT-2 (NCT03524092) studies.[5,6]
- Here, we evaluated the effect of mirikizumab versus placebo on abdominal pain in the LUCENT-1 and LUCENT-2 studies.

KEY RESULTS

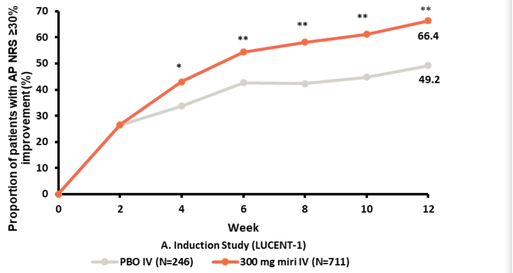
Table 1. Patient Demographics and Baseline Disease Characteristics

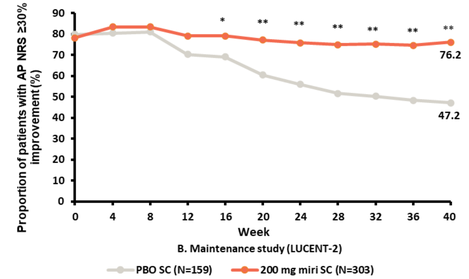
		Induction		Maintenance	
		PBO IV (N=294)	MIRI 300 mg IV (N=868)	PBO SC (N=179)	MIRI 200 mg SC (N=365)
Age (years), mean (SD)		41.3 (13.81)	42.9 (13.94)	41.2 (12.80)	43.4 (14.22)
Male, n (%)		165 (56.1)	530 (61.1)	104 (58.1)	214 (58.6)
BMI (kg/m^2), mean (SD)		24.5 (5.05)	25.0 (5.39)	24.8 (5.18)	24.8 (5.39)
Duration of UC (years), mean (SD)		6.9 (6.95)	7.2 (6.75)	6.7 (5.61)	6.9 (7.10)
Baseline disease location, n (%)	Left-sided colitis	188 (64.2)	544 (62.7)	119 (66.5)	234 (64.1)
Modified Mayo score category, n (%)	Moderate (4–6)	138 (47.1)	404 (46.5)	77 (43.0)	181 (49.6)
	Severe (7–9)	155 (52.9)	463 (53.3)	102 (57.0)	184 (50.4)
Total Mayo score category, n (%)	Moderate (6–9)	186 (66.0)	519 (62.9)	108 (63.2)	224 (64.4)
	Severe (10–12)	93 (33.0)	297 (36.0)	61 (35.7)	119 (34.2)
Prior biologic or tofacitinib failure, n (%)		118 (40.1)	361 (41.6)	64 (35.8)	128 (35.1)
Baseline UC therapy, n (%)	Corticosteroid	113 (38.4)	351 (40.4)	68 (38.0)	135 (37.0)
	Immunomodulator	69 (23.5)	211 (24.3)	39 (21.8)	78 (21.4)
Abdominal Pain NRS, mean (SD)		5.1 (2.54)	4.9 (2.41)	5.3 (2.15)	4.9 (2.44)

BMI, body mass index; IV, intravenous; MIRI, mirikizumab; n, number of patients; N, number of patients in each group; NRS, Numeric Rating Scale; PBO, placebo; SC, subcutaneous; SD, standard deviation; UC, ulcerative colitis.

Patient demographics and baseline disease characteristics were generally balanced between the two treatment groups across induction and maintenance studies (**Table 1**).

Figure 2. The Proportion of Patients who Achieved and Sustained ≥30% Improvement in Abdominal Pain NRS Score During A. Induction and B. Maintenance Studies





*p<0.05, **p<0.001 versus PBO
AP NRS, Abdominal Pain Numeric Rating Scale; CI, confidence interval; IV, intravenous; miri, mirikizumab; PBO, placebo; SC, subcutaneous.

A significant reduction of at least 30% in Abdominal Pain NRS score from baseline was observed in the mirikizumab-treated patients versus placebo from Week 4 (mirikizumab 43.0% vs placebo 33.7%; risk difference [95% CI]: 9.7 [2.8–16.6], p=0.007) through Week 12 (66.4% vs 49.2%; risk difference [95% CI] 17.4 [10.3–24.6], p<0.001) of the induction study (**Figure 2A**).

In the maintenance study, a greater percentage of mirikizumab-treated patients maintained Abdominal Pain NRS improvement compared to placebo. The separation started at Week 16 (79.2% vs 69.2%; risk difference [95% CI] 9.0 [0.5–17.5], p=0.034) and sustained through Week 40 (76.2% vs 47.2%; risk difference [95% CI] 27.4 [18.3–36.4], p<0.001; **Figure 2B**).

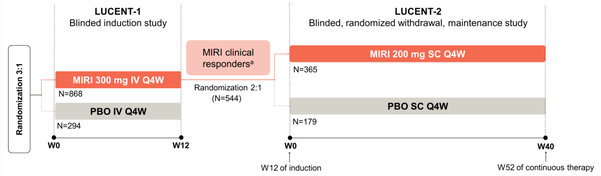
CONCLUSIONS

- Mirikizumab demonstrated significant improvement in abdominal pain compared with placebo, for patients with moderately-to-severely active UC, as early as Week 4 of the induction study.
- Among mirikizumab induction responders who continued to the maintenance therapy, improvements were sustained through Week 40 of the maintenance study compared to placebo.

METHODS

STUDY DESIGN

Figure 1. Study Design



[a]Mirikizumab-treated patients who achieved ≥2 points and ≥30% decrease from baseline in modified Mayo score and ≥1 point decrease from baseline in the RB subscore or an RB score of 0/1.
IV, intravenous; MIRI, mirikizumab; PBO, placebo; Q4W, every 4 weeks; RB, rectal bleeding; SC, subcutaneous; W, week.

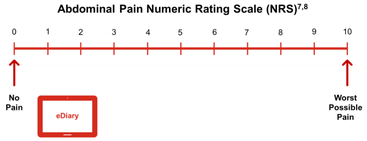
- LUCENT-1 and LUCENT-2 are phase 3, multicenter, randomized, double-blind, parallel-arm, placebo-controlled studies.

STUDY POPULATION

- **Inclusion criteria:**
  - Age 18–80 years with moderately-to-severely active UC at screening.[a]
  - Inadequate response, loss of response, or intolerance to conventional therapy (corticosteroid or immunomodulators), prior biologic, or tofacitinib therapy.
- **Exclusion criteria:**
  - Patients receiving anti-IL12p40 or anti-IL-23p19 antibodies for any indication.
  - Failed ≥3 biologic therapies for UC.

[b]Modified Mayo score of 4–9 with an endoscopic subscore ≥2.

ASSESSMENT



eDiary, electronic diary; NRS, Abdominal Pain Numeric Rating Scale.

- Endpoint was the proportion of patients, with an Abdominal Pain NRS score ≥3 at baseline, who achieved and maintained ≥30% improvement in Abdominal Pain NRS score during induction and maintenance studies.
- Patients reported “worst abdominal pain” in the past 24 hours each day using an 11-point Abdominal Pain NRS on an eDiary.
- Weekly measures were the average of daily eDiary entries of Abdominal Pain NRS for a 7-day period.[a]

[a]Excluding days preparing for, day of, and 2 days after colonoscopy.

STATISTICAL ANALYSIS

- Analyses were carried out in the modified intent-to-treat population: All randomized patients who received study treatment.[a]
- Baseline for induction and maintenance studies: Last nonmissing assessment recorded on or prior to the date of the first study drug administration at Week 0 of induction treatment.
- Response rates with Abdominal Pain NRS ≥30% improvement from baseline in the two treatment groups were compared using Cochran-Mantel-Haenszel (CMH) test adjusting for stratification factors. Estimated common risk differences with 95% confidence interval (CI)[b]; and p-value[c] were reported. Missing data were imputed using the nonresponder imputation.

[a]Excluding patients impacted by the electronic clinical outcome assessment transcription error in the wording used for assessment of rectal bleeding (Poland) and stool frequency (Turkey) Mayo subscores.
[b]Calculated using Mantel-Haenszel-Sato method.[9]
[c]Calculated using CMH test.

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DISCLOSURES

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