Mirikizumab Demonstrates Sustained Improvement in Fatigue in Patients with Moderately-to-Severely Active Ulcerative Colitis: Results from the Phase 3 LUCENT-1 Induction and LUCENT-2 Maintenance Studies

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BACKGROUND AND OBJECTIVE

- Fatigue, a debilitating, under-recognized, symptom, is a significant concern for patients with ulcerative colitis (UC).[1,2]
- More than 50% of patients with active UC report experiencing fatigue.[3] Moreover, 30%–48% of patients with UC in remission still suffer from fatigue.[4,5]
- Mirikizumab, an anti-IL-23p19 monoclonal antibody, demonstrated efficacy versus placebo in adult patients with moderately-to-severely active UC in the 12-week induction (LUCENT-1/NCT03518086) and 40-week maintenance (LUCENT-2/NCT03524092) studies.[6,7]
- Here, we report the effect of mirikizumab versus placebo on fatigue in the LUCENT-1 and LUCENT-2 studies.

KEY RESULTS

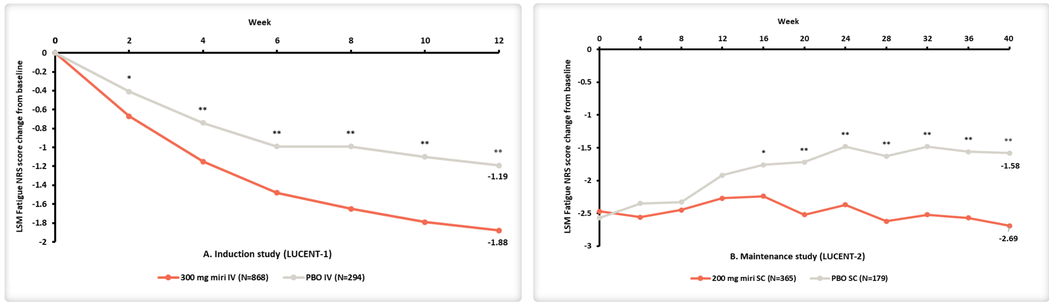
Table 1. Patient Demographics and Baseline Disease Characteristics

		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)
Fatigue NRS, mean (SD)		5.8 (2.26)	5.7 (2.25)	5.8 (2.06)	5.8 (2.33)

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. Change from Baseline in Fatigue NRS During A. Induction and B. Maintenance Studies



*p<0.05, **p<0.001 versus PBO
Data are presented as LSM change from baseline using ANCOVA with mBOCF (mITT).
ANCOVA, analysis of covariance; CI, confidence interval; IV, intravenous; LSM, least squares mean; mBOCF, modified baseline observation carried forward; miri, mirikizumab; mITT, modified intent-to-treat; N, number of patients in each group; NRS, Numeric Rating Scale; PBO, placebo; SC, subcutaneous.

Mirikizumab showed a statistically significant reduction in Fatigue NRS score versus placebo as early as Week 2 (LSM difference [95% CI]: −0.25 [−0.45, −0.05], p=0.013) of the induction study. The LSM difference from baseline at Week 12 was −0.69 (−0.98, −0.40; p<0.001; **Figure 2A**).

In the maintenance study, a statistically significant reduction in Fatigue NRS score was observed with mirikizumab compared to placebo from Week 16 (−0.48 [−0.89, −0.07]; p=0.021) and sustained through Week 40 (−1.10 [−1.53, −0.67]; p<0.001; **Figure 2B**).

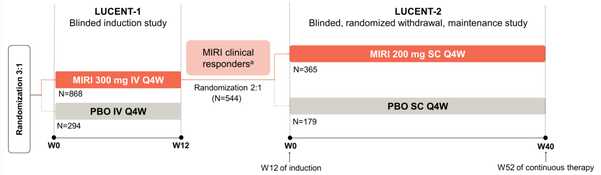
CONCLUSIONS

- **Mirikizumab-treated patients with moderately-to-severely active UC showed statistically significant improvements in fatigue compared to placebo as early as Week 2 of the induction study.**
- **Among mirikizumab induction responders who continued the maintenance therapy, the improvements were sustained through Week 40 of the maintenance study compared to placebo.**
- **Further study is needed to determine the putative role of mirikizumab in improving fatigue.**

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.

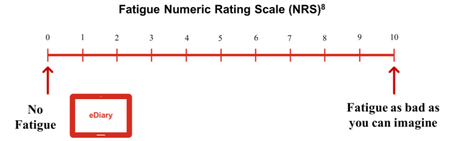
- LUCENT-1 and LUCENT-2 are phase 3, multicenter, randomized, double-blind, parallel-arm, placebo-controlled studies.

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, Numeric Rating Scale.

- Endpoints assessed included change from baseline in Fatigue NRS during induction and maintenance studies.
- Patients reported “worst fatigue (weariness, tiredness) in the past 24 hours” using an 11-point Fatigue NRS on an eDiary.
- Weekly measures were calculated by averaging data from all available daily eDiary entries of Fatigue NRS scores for a 7-day period in LUCENT-1.
- Fatigue NRS score was collected as a single measurement at each visit from Week 4 to Week 36 in LUCENT-2.

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.
- Treatment difference in Fatigue NRS was assessed using the analysis of covariance (ANCOVA) model adjusting for the stratification factors. Least squares mean (LSM) change from baseline (Week 0 of therapy) was reported. Modified baseline observation carried forward was used to impute missing data.

[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.

REFERENCES

1. Huppertz-Hauss G, et al. *Scand J Gastroenterol*. 2017;52:351-8. 2. D'Silva A, et al. *Clin Gastroenterol Hepatol*. 2022;20:995-1009.e7. 3. Jonefjäll B, et al. *United European Gastroenterol J*. 2018;6(1):148-158. 4. Graff LA, et al. *Inflamm Bowel Dis*. 2011;17(9):1882-9. 5. Lönnfors S, et al. *J Crohn's Colitis*. 2014;8(10):1281-6. 6. D'Haens G, et al. J Crohn's Colitis. 2022;16(1):i028-i029. 7. Dubinsky MC, et al. *Gastroenterology*. 2022;162(7):S1393-S1394. 8. Minnock P, et al. *Rheumatology*. 2009;48(12):1533-6.

DISCLOSURES

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