Mirikizumab Improves Mental and Physical Health Outcomes 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

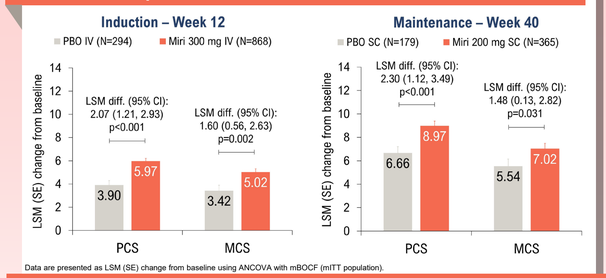
- Ulcerative colitis (UC) is a relapsing-remitting, chronic disease classically characterized by mucosal inflammation of the rectum and colon; symptoms include diarrhea, rectal bleeding, bowel urgency, and tenesmus.[1,2]
- Patients with UC experience a substantial disease burden on their functioning and well-being, and across QoL domains.[3]
- Mirikizumab, an anti-IL-23p19 monoclonal antibody, demonstrated efficacy vs 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.[4,5]
- We evaluated the effect of mirikizumab vs placebo on SF-36 (version 2) scores in LUCENT-1 and LUCENT-2 studies.

KEY RESULTS

Patient demographics and baseline disease characteristics were generally balanced between the two treatment groups across induction and maintenance studies

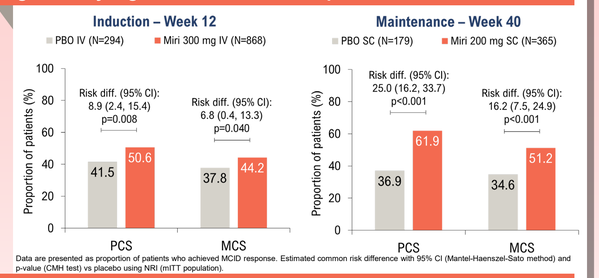
		Induction		Maintenance	
		PBO IV (N=294)	Miri 300 mg IV (N=868)	PBO SC (N=179)	Miri 200 mg SC (N=365)
Age (years), mean (SD)		41.3 (13.81)	42.9 (13.94)	41.2 (12.80)	43.4 (14.22)
Male, n (%)		165 (56.1)	530 (61.1)	104 (58.1)	214 (58.6)
BMI (kg/m^2), mean (SD)		24.5 (5.05)	25.0 (5.39)	24.8 (5.18)	24.8 (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)
MMS 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)
SF-36, mean (SD)	MCS	43.5 (10.07)	44.0 (10.23)	43.3 (10.14)	44.7 (9.88)
	PCS	41.2 (8.28)	42.4 (7.88)	42.7 (8.05)	42.4 (7.76)

Mirikizumab showed significant improvement in SF-36 PCS and MCS scores vs placebo at Weeks 12 and 40



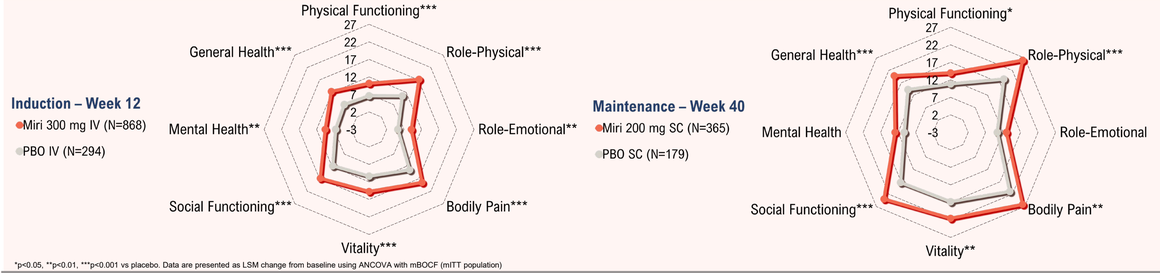
Data are presented as LSM (SE) change from baseline using ANCOVA with mBOCF (mITT population).

PCS and MCS MCID (≥5-point improvement) response rates were significantly higher in mirikizumab vs placebo at Weeks 12 and 40



Data are presented as proportion of patients who achieved MCID response. Estimated common risk difference with 95% CI (Mantel-Haenszel-Sato method) and p-value (CMH test) vs placebo using NRI (mITT population).

Mirikizumab showed significant improvement in SF-36 domain scores vs placebo at Weeks 12 and 40



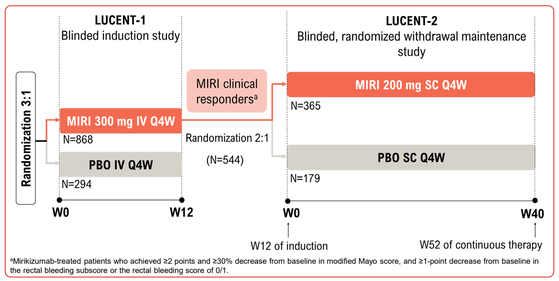
*p<0.05, **p<0.01, ***p<0.001 vs placebo. Data are presented as LSM change from baseline using ANCOVA with mBOCF (mITT population)

CONCLUSION

Mirikizumab demonstrated statistically significant and clinically important improvement in SF-36 Mental and Physical Component Summary scores in patients with moderately-to-severely active UC during LUCENT-1 induction and LUCENT-2 maintenance studies.

Study design

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



[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 rectal bleeding subscore or the rectal bleeding score of 0/1.

Study population

Inclusion criteria

- Age 18–80 years with moderately-to-severely active UC[a] at screening.
- Inadequate response, loss of response, or intolerance to conventional therapy (corticosteroid or immunomodulator), or 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.

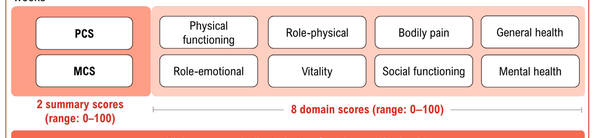
[a]Modified Mayo score of 4–9 with an endoscopic subscore ≥2

Study outcome and assessments

Endpoints assessed at Week 12 (induction) and Week 40 (maintenance) were:

- Change from baseline in SF-36 PCS, MCS, and 8 domain scores
- MCID response (≥5-point improvement from baseline[6]) rates for PCS and MCS.

SF-36 Version 2, a 36-item questionnaire, measures the following scores over a recall period of the past 4 weeks[7,8]



Statistical analyses

- 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.

[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.

	SF-36 PCS, MCS, and domain scores	PCS and MCS MCID response rates
Treatment group comparison	ANCOVA model[a]; LSM were reported for each treatment group	CMH test[a]; estimated common risk differences with 95% CI (Mantel-Haenszel-Sato method[9]) and p-value (CMH) were reported
Missing data imputation	mBOCF	NRI

[a]Adjusted for baseline stratification factors

References

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Abbreviations: ANCOVA, analysis of covariance; BMI, body mass index; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; diff, difference; IL, interleukin; IV, intravenous; LSM, least squares mean; mBOCF, modified baseline observation carried forward; MCS, Mental Component Summary; MCID, minimal clinically important difference; miri, mirikizumab; mITT, modified intent-to-treat; NRI, non-responder imputation; PBO, placebo; PCS, Physical Component Summary; Q4W, every 4 weeks; QoL, quality of life; SC, subcutaneous; SD, standard deviation; SE, standard error; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey; vs, versus; W, week.

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