P4

Efficacy and Safety of Mirikizumab Treatment in Adults ≥60 Years with Moderately-to-Severely Active Ulcerative Colitis

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OBJECTIVE

- To evaluate the efficacy and safety of mirikizumab vs. placebo during induction and maintenance therapy in patients aged ≥60 years with moderately to severely active ulcerative colitis (UC)

CONCLUSIONS

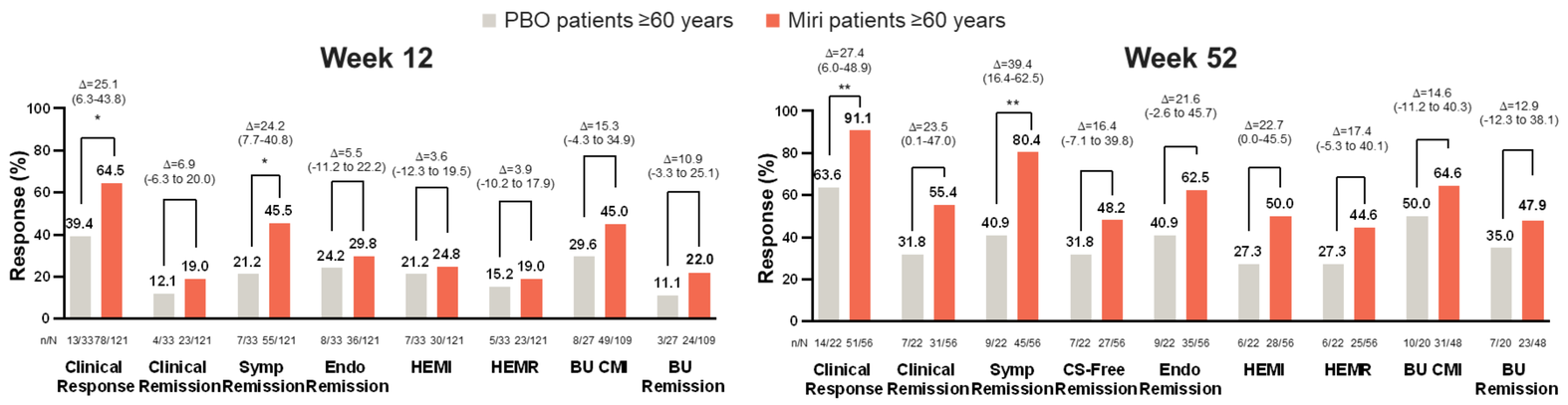
- In an older population with higher prevalence of comorbidities and longer disease duration, mirikizumab treatment induced and maintained clinical outcomes at Week 12 and Week 52, respectively
  - 64.5% of patients achieved a clinical response at Week 12 and 55.4% achieved clinical remission at Week 52
- The safety profile for mirikizumab in an older population aged ≥60 years (mean age at diagnosis: 57.2) was consistent with the overall study population (mean age at diagnosis: 35.9)[1]
  - The proportion of patients with adverse events (AEs) was similar in the mirikizumab and placebo groups
  - No deaths or discontinuations due to AEs were reported in mirikizumab-treated patients ≥60 years
- Mirikizumab is an efficacious and well-tolerated treatment option for patients ≥60 years with moderately to severely active UC

BACKGROUND

- Mirikizumab, a humanized immunoglobulin G4 monoclonal antibody that selectively binds to the p19 subunit of anti–interleukin (IL)-23, achieved the primary endpoint of clinical remission and other key secondary outcomes, including endoscopic and histologic improvement and remission, at Week 12 of the LUCENT-1 induction trial (NCT03518086), Week 40 of the LUCENT-2 maintenance trial (NCT03524092; Week 52 of continuous treatment), and Weeks 52 and 100 of the LUCENT-3 long-term extension study (NCT03519945; Weeks 104 and 152 of continuous treatment) in patients with moderately to severely active UC[1-3]
- Novel therapies for UC have not been extensively studied in adults ≥60 years of age, a particularly vulnerable subgroup of patients[4-6]

KEY RESULTS

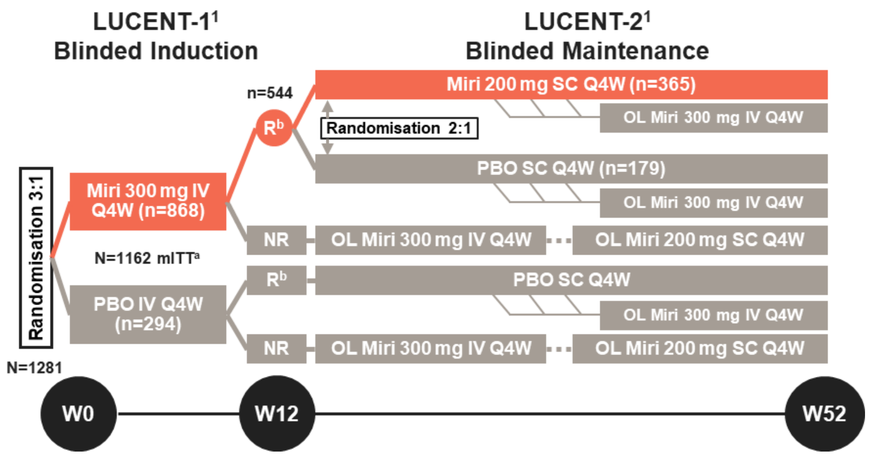
A Significantly Greater Proportion of Patients ≥60 Years Treated With Mirikizumab vs. Placebo Achieved Clinical Response and Symptomatic Remission at Week 12 and Week 52



- While the studies were not powered to detect differences between mirikizumab and placebo in this subgroup, there were numerically higher response rates for mirikizumab vs. placebo for all other outcomes

*p<0.05, **p<0.01; p-values calculated using Fisher exact test.
Note: All responses calculated using NRI. The difference (Δ) is shown with a 95% confidence interval constructed using the asymptotic method, without continuity correction.

STUDY DESIGN



Key Eligibility Criteria

LUCENT-1

- Age ≥18 and ≤80 years
- MMS of 4-9, with an ES of 2-3
- Inadequate response, loss of response, or intolerance to ≥1 corticosteroid, immunomodulator, biologic therapy, or Janus kinase inhibitor (tofacitinib) for UC
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies

LUCENT-2

- Completed LUCENT-1
- Received ≥1 dose of study drug in LUCENT-1
- Had MMS evaluations at the end of LUCENT-1

- At LUCENT-1 baseline, 13.3% of the mITT patients were ≥60 years (n=154)

[a]The mITT population consists of all randomised patients who received study treatment, regardless of whether the patients received the correct treatment or otherwise did not follow the protocol; 118 patients who were impacted by the eCOA transcription errors in Poland and Turkey during LUCENT-1 or -2 were excluded; 1 patient was randomised but not dosed; [b]Responders at W12 were defined as achieving ≥2-point and ≥30% decrease in the MMS from baseline with RB score=0 or 1, or ≥1-point decrease from baseline.

METHODS

Patient Population and Statistical Analyses

Efficacy

- Of patients ≥60 years at baseline, post hoc analyses were performed in the mITT population at Weeks 12[a] and 52[b]
  - p-Values for comparison of treatments are from the Fisher exact test
  - Missing values were imputed using non-responder imputation

Safety

- All randomised patients ≥60 years who received ≥1 dose of study treatment (mirikizumab or placebo)

[A]Treatment-by-subgroup interaction was assessed using a logistic regression analysis with prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity, and region as factors; [b]Treatment-by-subgroup interaction assessed using a logistic regression analysis with prior biologic or tofacitinib failure, baseline corticosteroid use, Week 12 remission status, and region as factors. In both cases, no statistically significant differences were observed (p-values were calculated using Firth correction).

Methods

Assessments[1]

Endpoint	Definition
Clinical response	≥2-point and ≥30% decrease in MMS from baseline; RB=0 or 1, or ≥1-point decrease from baseline
Clinical remission	SF=0, or SF=1 with a ≥1-point decrease from baseline; RB=0, and ES=0 or 1 (excluding friability)
Symptomatic remission	SF=0, or SF=1 with a ≥1-point decrease from baseline and RB=0
Endoscopic remission	Mayo ES=0 or 1 (excluding friability)
Corticosteroid-free remission[a]	Clinical remission at Week 52, symptomatic remission at Week 40, and no corticosteroid use for ≥12 weeks prior to Week 52
Histo-endoscopic mucosal improvement (HEMI)	Mayo ES=0 or 1 (excluding friability) + Geboes score ≤3.1
Histo-endoscopic mucosal remission (HEMR)	Mayo ES=0 or 1 (excluding friability) + Geboes score ≤2B.0
Bowel urgency: Clinically meaningful improvement	Decrease from baseline in UNRS ≥3 in patients with UNRS ≥3 at induction baseline
Bowel urgency: Remission	UNRS=0 (no urgency) or 1 (minimal urgency) in patients with UNRS ≥3 at induction baseline

[a]Week 52 only.

Results

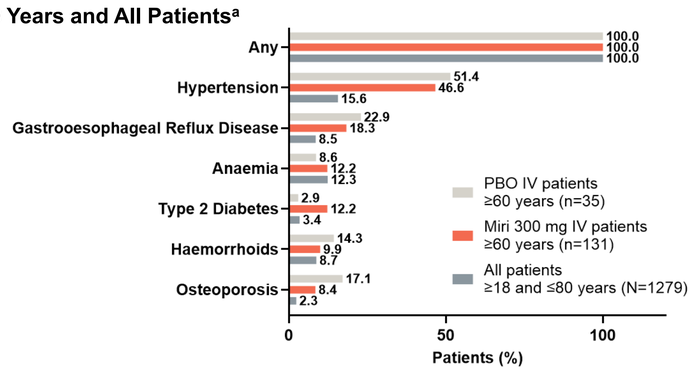
Baseline Demographics and Characteristics

Characteristics	PBO Patients ≥60 Years (n=33)	Miri Patients ≥60 Years (n=121)	All Patients[a] ≥18 and ≤80 Years (N=1162)
Age, years, median (IQR)	65.0 (62.0-66.0)	65.0 (63.0-69.0)	41.0 (31.0-53.0)
Male	17 (51.5)	73 (60.3)	695 (59.8)
Weight, kg, mean (SD)	72.3 (16.7)	74.7 (17.2)	72.1 (17.1)
Disease duration, years, mean (SD)	11.0 (11.4)	9.0 (8.5)	7.1 (6.8)
Age at diagnosis, years, mean (SD)	54.2 (11.3)	58.0 (9.6)	35.9 (13.6)
Disease location			
Left-sided colitis	18 (54.5)	86 (71.1)	732 (63.0)
Pancolitis	15 (45.5)	34 (28.1)	421 (36.3)
Proctitis	0	1 (0.8)	8 (0.7)
MMS, mean (SD)	6.3 (1.3)	6.4 (1.3)	6.5 (1.3)
MMS, severe (score 7-9)	16 (48.5)	62 (51.2)	618 (53.2)
ES, severe (score 3)	25 (75.8)	86 (71.1)	774 (66.7)
Faecal calprotectin, µg/g, median (IQR)	1417.0 (583.0-2345.0)	1433.0 (828.0-3245.0)	1524.0 (633.0-3197.0)
CRP, mg/L, median (IQR)	3.4 (1.3-7.9)	5.6 (2.2-12.2)	4.1 (1.4-9.6)
Corticosteroid use[b]	11 (33.3)	52 (43.0)	464 (39.9)
Immunomodulator use[c]	4 (12.1)	24 (19.8)	280 (24.1)
Prior biologic or tofacitinib failure[d]	14 (42.4)	47 (38.8)	479 (41.2)

[a]The mITT population consists of all patients who received study treatment, regardless of whether the patients received the correct treatment or otherwise did not follow the protocol; 118 patients who were impacted by the eCOA transcription errors in Poland and Turkey during LUCENT-1 or -2 were excluded; 1 patient was randomised but not dosed; [b]Included budesonide and beclomethasone; [c]Included methotrexate and thiopurines; [d]Failure defined as prior treatment discontinuation due to loss of response, inadequate response, or intolerance to medication.
Note: Data are n (%) unless otherwise stated.

- Apart from higher prevalence of comorbidities, longer disease duration, older age at diagnosis, and lower frequency of concomitant treatment with immunomodulators, the baseline demographics and characteristics in patients ≥60 years were similar to that in the overall patient population[1]

Baseline Comorbidities: Patients ≥60 Years and All Patients[a]



[a]The patient cohort for the baseline comorbidities is the safety population, which included all the patients who had undergone randomization and received any amount of mirikizumab or placebo, including those patients who were affected by the eCOA transcription error; all patients includes those randomised to placebo or mirikizumab.

Safety Overview of Mirikizumab vs. Placebo for Patients ≥60 Years

	Induction Population		Maintenance Population	
	PBO IV (n=35)	Miri 300 mg IV (n=131)	PBO SC (n=24)	Miri 200 mg SC (n=59)
TEAEs[a]	19 (54.3)	58 (44.3)	19 (79.2)	37 (62.7)
Mild	9 (25.7)	30 (22.9)	13 (54.2)	19 (32.2)
Moderate	8 (22.9)	27 (20.6)	4 (16.7)	12 (20.3)
Severe	2 (5.7)	1 (0.8)	2 (8.3)	6 (10.2)
SAEs	2 (5.7)[b]	4 (3.1)[c]	2 (8.3)[d]	6 (10.2)[e]
Death	0	0	0	0
Discontinuation due to AE	4 (11.4)	0	2 (8.3)	0

[a]Patients with multiple occurrences of the same event are counted under the highest severity; [b]2 UC; [c]1 vertigo, 1 viral gastroenteritis, 1 spinal compression fracture, and 1 hypertension; [d]1 UC and 1 anaphylactic reaction; [e]8 SAEs in 6 patients: 1 inguinal hernia, 1 COVID-19 pneumonia, 1 diverticulitis, 1 retinal detachment, 1 spinal compression fracture, 1 back pain, 1 migraine, and 1 retinopexy.
Note: Data are n (%) unless otherwise stated.

Abbreviations: *AE=adverse event; BU=bowel urgency; CMI=clinically meaningful improvement; COVID-19=coronavirus 2019 disease; CRP=C-reactive protein; CS=corticosteroid; eCOA=electronic clinical outcome assessment; Endo=endoscopic; ES=endoscopic subscore; HEMI=histologic-endoscopic mucosal improvement; HEMR=histologic-endoscopic mucosal remission; IL=interleukin; IQR=interquartile range; IV=intravenous; Miri=mirikizumab; mITT=modified intent-to-treat; MMS=modified Mayo Score; NR=non-responder; NRI=non-responder imputation; OL=open-label; PBO=placebo; Q4W=every 4 weeks; R=responder; RB=rectal bleeding; SAE=serious AE; SC=subcutaneous; SD=standard deviation; SF=stool frequency; Symp=symptomatic; TEAE=treatment-emergent AE; UC=ulcerative colitis; UNRS=Urgency Numeric Rating Scale; W=Week*

References: 1. D'Haens G, et al. *N Engl J Med*. 2023;388:2444-2455. 2. Sands BE, et al. *Inflamm Bowel Dis*. 2024;izae024. 3. Sands BE, et al. *Inflamm Bowel Dis*. 2024;izae253. 4. Ananthakrishnan AN, et al. *Gastroenterology*. 2021;160:445-451. 5. Sturm A, et al. *J Crohns Colitis*. 2017;11:263-273. 6. Kochar B, et al. *Inflamm Bowel Dis*. 2021;izab052.

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