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Mirikizumab Improves Work Productivity and Activity Impairment Questionnaire Scores in Moderately to Severely Active Ulcerative Colitis: The LUCENT-1 and LUCENT-2 Randomized, Double-Blind, Placebo-Controlled Phase 3 Induction and Maintenance Studies

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BACKGROUND

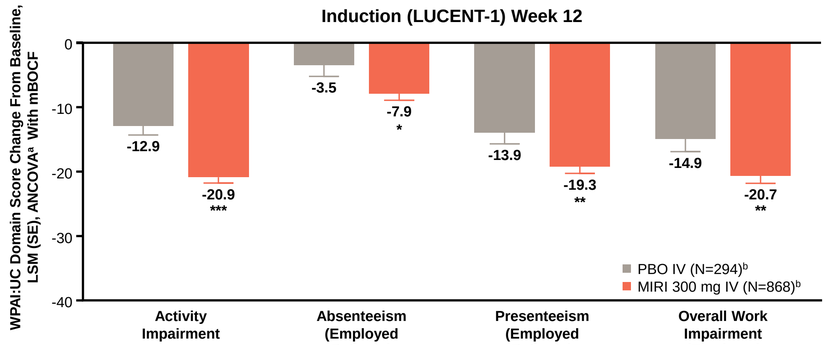
- Ulcerative colitis negatively affects patients' quality of life and ability to work[1]
- Mirikizumab, a p19-directed anti–interleukin (IL)-23 antibody, has demonstrated efficacy in Phase 3 induction (LUCENT-1; NCT03518086)[2] and maintenance (LUCENT-2; NCT03524092)[3] studies in patients with moderately to severely active ulcerative colitis
- The Work Productivity and Activity Impairment Questionnaire: Ulcerative Colitis (WPAI:UC) is used to measure the impact of an individual's health status on their work and daily activities

OBJECTIVE

- To evaluate the effect of mirikizumab vs. placebo on WPAI:UC scores over a total of 52 weeks of treatment in the LUCENT-1 and LUCENT-2 studies in patients with moderately to severely active ulcerative colitis who had failed prior conventional or biologic therapy

KEY RESULTS

Activity Impairment, Absenteeism, Presenteeism, and Work Productivity Loss Were Significantly Reduced From Baseline With MIRI vs. PBO at Induction Week 12



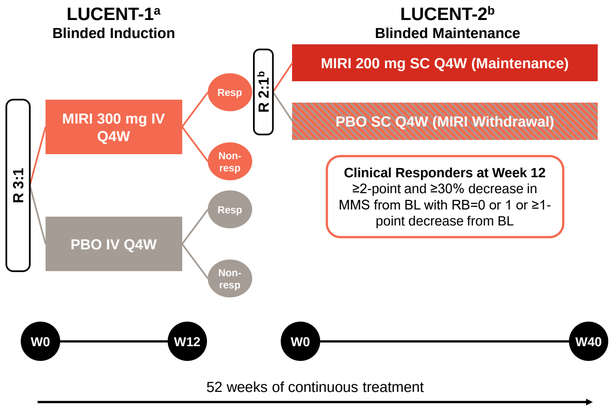
* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] Induction ANCOVA model includes treatment, baseline value, prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, MMS group at baseline, and global region
[b] Patients employed at baseline: PBO, N=173; MIRI, N=532

CONCLUSIONS

- Mirikizumab significantly improved work productivity and activity impairment vs. placebo, as measured by the WPAI:UC, in patients with moderately to severely active ulcerative colitis who had failed prior conventional or biologic therapies
- Greater improvements with mirikizumab vs. placebo were observed in all 4 WPAI:UC domains at Week 12 of induction therapy
- In mirikizumab clinical responders who received maintenance treatment, the improvements in activity impairment, presenteeism, and work productivity loss were sustained for a total treatment duration of 52 weeks

METHODS

Study Design



[a] LUCENT-1 was a Phase 3, randomized, parallel-arm, double-blind, PBO-controlled induction trial of MIRI in patients with moderately to severely active ulcerative colitis
[b] LUCENT-2 was a Phase 3, double-blind, randomized, withdrawal maintenance study in patients who responded to MIRI induction therapy in LUCENT-1. Figure is not the full LUCENT-2 program, only the patient cohort who were MIRI responders during induction and randomized to maintenance treatment is presented here. Clinical responders to induction MIRI therapy at Week 12 of LUCENT-1 were randomized to receive maintenance MIRI therapy or PBO for 40 weeks (52 weeks of treatment). Randomization in LUCENT-2 was stratified by induction remission status, biologic failure status, baseline corticosteroid use, and region

Key Eligibility Criteria: LUCENT-1

- Age ≥18 and ≤80 years
- Moderately to severely active ulcerative colitis
  - Modified Mayo Score 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 and Statistical Analyses

- The WPAI:UC is a patient-completed questionnaire over 4 domains: activity impairment (assessed in all patients) and absenteeism, presenteeism, and overall work impairment (assessed in employed patients)
  - Score range 0-100, with higher scores indicating greater impairment
- Change from baseline was assessed at Week 12 of induction treatment (LUCENT-1) and Week 40 of maintenance treatment (LUCENT-2) using analysis of covariance with treatment, stratification factors, and baseline scores as covariates
  - Missing data were imputed using modified baseline observation carried forward

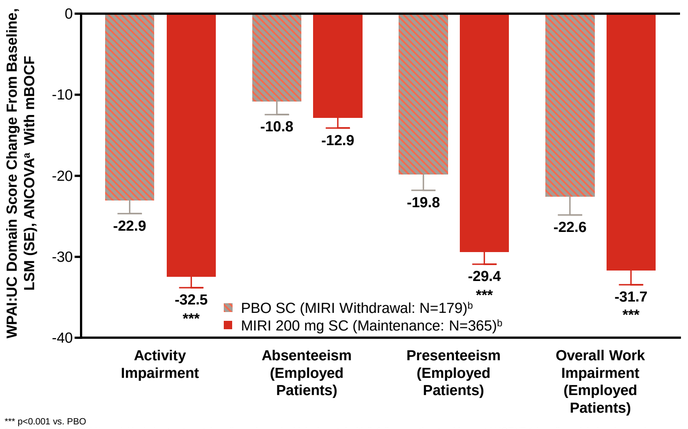
RESULTS

Demographics and Baseline Characteristics[a]

	LUCENT-1 (mITT)		LUCENT-2 (mITT MIRI Induction Responders)	
	PBO IV (N=294)	MIRI 300 mg IV (N=868)	PBO SC (MIRI Withdrawal) (N=179)	MIRI 200 mg SC (N=365)
Age, years, mean (SD)	41.3 (13.8)	42.9 (13.9)	41.2 (12.8)	43.4 (14.2)
Male	165 (56.1)	530 (61.1)	104 (58.1)	214 (58.6)
Disease duration, years, mean (SD)	6.9 (7.0)	7.2 (6.7)	6.7 (5.6)	6.9 (7.1)
Disease location				
Left-sided colitis	188 (64.2)	544 (62.7)	119 (66.5)	234 (64.1)
Pancolitis	103 (35.2)	318 (36.6)	59 (33.0)	128 (35.1)
MMS category				
Moderate [score 4-6]	138 (47.1)	404 (46.5)	77 (43.0)	181 (49.6)
Severe [score 7-9]	155 (52.9)	463 (53.3)	102 (57.0)	184 (50.4)
Endoscopic Mayo subscore, severe [score 3]	200 (68.3)	574 (66.1)	106 (59.2)	235 (64.4)
Bowel urgency severity (UNRS), mean (SD)	6.2 (2.2)	6.1 (2.2)	6.2 (1.9)	6.0 (2.2)
WPAI:UC overall work impairment score, mean (SD)	50.0 (28.1)	47.8 (25.8)	50.4 (25.6)	46.5 (26.5)
WPAI:UC employment status, yes	173 (59.7)	532 (62.1)	120 (67.4)	224 (62.0)
Baseline corticosteroid use	113 (38.4)	351 (40.4)	68 (38.0)	135 (37.0)
Baseline immunomodulator use	69 (23.5)	211 (24.3)	39 (21.8)	78 (21.4)
Prior biologic or tofacitinib failure	118 (40.1)	361 (41.6)	64 (35.8)	128 (35.1)

Data are presented as n (%) unless stated otherwise
[a] Baseline refers to Week 0 of LUCENT-1

Improvements in Activity Impairment, Presenteeism, and Work Productivity Loss Were Sustained in MIRI Induction Responders Who Received Maintenance Treatment



*** p<0.001 vs. PBO
[a] Maintenance ANCOVA model includes treatment, baseline value, prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, global region, and clinical remission status at LUCENT-1 Week 12
[b] Patients employed at baseline: PBO, N=120; MIRI, N=224

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1. Danese S, et al. *Dig Dis*. 2019;37:266-283.
2. D'Haens G, et al. *J Crohns Colitis*. 2022;16:i028-i029.
3. Dubinsky MC, et al. *Gastroenterol*. 2022;162:S1393-1394.

ABBREVIATIONS

ANCOVA=analysis of covariance; BL=baseline; IV=intravenous; LSM=least squares mean; mBOCF=modified baseline observation carried forward; MIRI=mirikizumab; mITT=modified Intent-to-Treat; MMS=Modified Mayo Score; Non-resp=non-responders; PBO=placebo; Q4W=every 4 weeks; R=randomization; RB=rectal bleeding; Resp=responders; SC=subcutaneous; SD=standard deviation; SE=standard error; UNRS=Urgency Numeric Rating Scale; W=Week; WPAI:UC=Work Productivity and Activity Impairment Questionnaire:Ulcerative Colitis

DISCLOSURES

- **B. E. Sands** has received fees or grant/research support and/or served as a consultant and/or speaker for: Abivax, Amgen, Arena Pharmaceuticals, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Eli Lilly and Company, Enthera, Evommune, Galapagos NV, Genentech, Gilead Sciences, GlaxoSmithKline, Gossamer Bio, InDex Pharmaceuticals, Innovation Therapeutics, Inotrem, Ironwood Pharmaceuticals, Janssen, Kaleido Biosciences, Kallyope, MiroBio, Morphic Therapeutic, MRM Health, Pfizer, Progenity, Prometheus Therapeutics and Diagnostics, Protagonist Therapeutics, Q32 Bio, Surrozen, Takeda, Teva, TLL Pharmaceutical, USWM Enterprises, and Viela Bio; **B. Feagan** has served as a consultant, speaker, and/or advisory board member for: AbbVie, AdMIRx, AgomAb Therapeutics, Akebia Therapeutics, Alivio Therapeutics, Allakos, Amgen, Applied Molecular Transport, Arena Pharmaceuticals, Avir Pharma, Azora Therapeutics, Boehringer Ingelheim, Boston Scientific, Celgene/Bristol Myers Squibb, Connect Biopharma, Cytoki Pharma, Disc Medicine, EcoR1 Capital, Eli Lilly and Company, Equillium, Everest Clinical Research, F. Hoffman-La Roche, Ferring Pharmaceuticals, Galapagos NV, Galen/Atlantica, Genentech/Roche, Gilead Sciences, Glenmark Pharmaceuticals, Gossamer Bio, GlaxoSmithKline, HotSpot Therapeutics, Imhotex, ImmuNext, InDex Pharmaceuticals, Intact Therapeutics, Janssen, Japan Tobacco, Kaleido Biosciences, Leadiant Biosciences, Millennium Pharmaceuticals, MiroBio, Morphic Therapeutic, Mylan, Novartis, OM Pharma, Origo Biopharma, Otsuka, Pandion Therapeutics, Pfizer, Progenity, Prometheus Therapeutics and Diagnostics, PTM Therapeutics, Q32 Bio, Rebiotix, RedHill, Redx Pharma, Sandoz, Sanofi, Seres Therapeutics, Surrozen, Takeda, Teva, Thelium Therapeutics, Theravance Biopharma, TiGenix, Tillotts Pharma AG, UCB Pharma, VHsquared, Viatris, Ysios Capital, and Zealand Pharma; and is a stock/shareholder of: Gossamer Bio; **T. Hunter Gibble**, **K. A. Traxler**, **N. Morris**, and **X. Li** are employees and shareholders of: Eli Lilly and Company; **S. Schreiber** has received personal fees and/or travel support from: AbbVie, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos NV, Gilead Sciences, I-MAB Biopharma, Janssen, Merck Sharp & Dohme, Mylan, Novartis, Pfizer, Protagonist Therapeutics, Provention Bio, Roche, Sandoz/Hexal, Shire, Takeda, and Theravance Biopharma; **V. Jairath** has served as a consultant, speaker, and/or advisory board member for: AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Flagship Pioneering, Fresenius Kabi, Galapagos NV, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen, Merck, Mylan, Pandion Therapeutics, Pendopharm, Pfizer, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Shire, Takeda, Teva, Topivert, Ventyx Biosciences, and Vividion Therapeutics; **A. Armuzzi** has received lecture fees or grant/research support and/or served as a consultant for: AbbVie, Allergan, Amgen, Arena Pharmaceuticals, Biogen, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Galapagos NV, Gilead Sciences, Janssen, Merck Sharp & Dohme, Mylan, Novartis, Pfizer, Protagonist Therapeutics, Roche, Samsung Bioepis, Sandoz, Takeda, and TiGenix
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