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Mirikizumab Improves Quality of Life in Moderately to Severely Active Ulcerative Colitis: Improvement in Inflammatory Bowel Disease Scores in Participants of the LUCENT-1 and LUCENT-2 Randomized, Double-Blind, Placebo-Controlled Phase 3 Induction and Maintenance Trials

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BACKGROUND

- Mirikizumab, a p19-directed anti–interleukin (IL)-23 antibody, has demonstrated efficacy in Phase 3 induction (LUCENT-1, NCT03518086)[1] and maintenance (LUCENT-2, NCT03524092)[2] studies in patients with moderately to severely active ulcerative colitis (UC)
- Mirikizumab has also demonstrated improvement in Inflammatory Bowel Disease Questionnaire (IBDQ) scores in a Phase 2 study (NCT02589665) in patients with moderately to severely active UC[3]
  - The IBDQ is a widely used validated measure of health-related quality of life in patients with UC[4]

OBJECTIVE

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

KEY RESULTS

Improvement in IBDQ Total Score Was Greater With MIRI vs. PBO at Induction Week 12 and Responder Maintenance Week 40

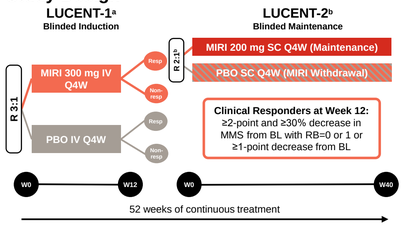
*** p<0.001 vs. PBO
[a] Induction ANCOVA model includes treatment, baseline value, prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, MMS group at baseline, and global region; [b] Maintenance ANCOVA model includes treatment, baseline value, prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, global region, and clinical remission status at LUCENT-1 Week 12

CONCLUSIONS

- Patients with moderately to severely active UC reported significantly greater improvements in IBDQ scores with mirikizumab vs. placebo at 12 weeks of induction therapy
- Among patients who were clinical responders to mirikizumab induction at Week 12, the improvement in IBDQ scores was sustained over 40 weeks of maintenance therapy (52 weeks of total treatment) vs. placebo
- A greater proportion of mirikizumab-treated patients achieved IBDQ clinically meaningful improvement and IBDQ remission at Week 12 of induction and Week 40 of maintenance compared with placebo-treated patients

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 UC. [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

Assessments and Statistical Analyses

- The IBDQ is a patient-completed questionnaire including 32 items across 4 domains of bowel symptoms, systemic symptoms, emotional function, and social function[5,6]
  - Each of the 32 questions is scored from 1 (significant impairment) to 7 (no impairment)
  - Total IBDQ score range: 32-224, with higher scores indicating greater quality of life
- Analyses were conducted at Week 12 of induction (LUCENT-1) and Week 40 of maintenance (LUCENT-2)
  - IBDQ change from baseline using analysis of covariance models and modified baseline observation carried forward with adjustment for covariates
  - Percentage of patients achieving IBDQ clinically meaningful improvement, defined as an IBDQ total score improvement ≥16 points[5]
  - Percentage of patients achieving IBDQ remission, defined as a IBDQ total score ≥170 points[5]
  - Response rates used non-responder imputation

Key Eligibility Criteria: LUCENT-1

- Age ≥18 and ≤80 years
- Moderately to severely active UC
  - 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 UC
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies

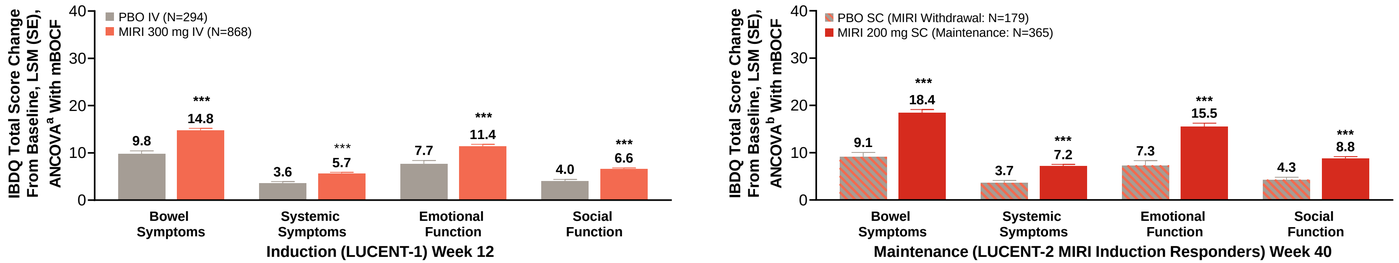
RESULTS

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)
IBDQ total score, mean (SD)	127.9 (35.3)	131.4 (33.0)	129.4 (31.9)	133.9 (33.2)
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

Improvement in IBDQ Domain Scores Was Greater With MIRI vs. PBO at Induction Week 12 and Responder Maintenance Week 40



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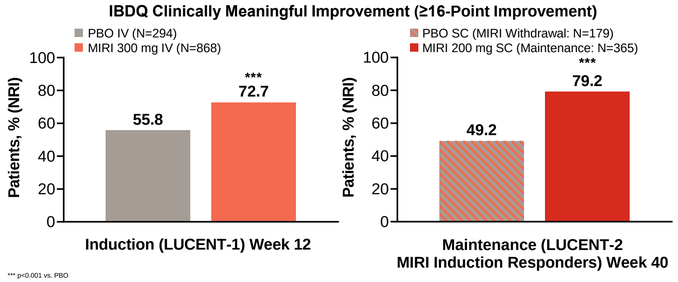
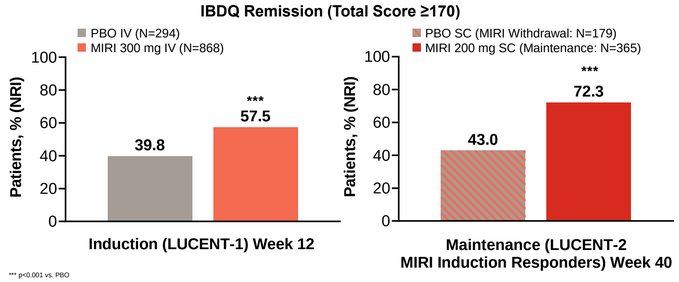
More Patients Achieved IBDQ Clinically Meaningful Improvement With MIRI vs. PBO at Induction Week 12 and Responder Maintenance Week 40



*** p<0.001 vs. PBO

More Patients Achieved IBDQ Remission With MIRI vs. PBO at Induction Week 12 and Responder Maintenance Week 40



*** p<0.001 vs. PBO

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ABBREVIATIONS

ANCOVA=analysis of covariance; BL=baseline; IBDQ=inflammatory Bowel Disease Questionnaire; 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; NRI=non-responder imputation; 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

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 Pharmaceuticals, 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, AbMetrix, 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. Hoffmann-La Roche, Ferring Pharmaceuticals, Galapagos NV, GalenAtlantica, Genentech/Roche, Gilead Sciences, GlaxoSmithKline, Glenmark Pharmaceuticals, Gossamer Bio, HotSpot Therapeutics, Imhotex, ImmuNext, InDex Pharmaceuticals, Intact Therapeutics, Janssen, Japan Tobacco, Kaleido Biosciences, Leadiant Biosciences, Millennium Pharmaceuticals, MiroBio, Morphic Therapeutics, Mylan, Novartis, OM Pharma, Origo Biopharma, Otsuka, Pandion Therapeutics, Pfizer, Progenity, Prometheus Therapeutics and Diagnostics, PTM Therapeutics, Q32 Bio, Rebiotix, RedHill, Biopharma, Reistone Biopharma, Roche, Sandoz, Sanofi, Seres Therapeutics, Surrozen, Takeda, Teva, Theliium Therapeutics, Theravance Biopharma, TiGenix, Tillotts Pharma AG, UCB Pharma, VHsquared, Viatris, Ysios Capital, and Zealand Pharma; and is a stock or 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 and/or 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
- Medical writing assistance was provided by Linda Donnini, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company
- This study was previously presented at the United European Gastroenterology Week (UEGW) 2022

Study was sponsored by Eli Lilly and Company