B0366

Effect of Mirikizumab on Bowel Urgency Clinically Meaningful Improvement and Remission: Results From the Phase 3 LUCENT Induction and Maintenance Studies

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BACKGROUND

- Bowel urgency, a sudden or immediate need to have a bowel movement, is a common and burdensome symptom for patients with ulcerative colitis (UC)[1,2]
- Mirikizumab is a humanized immunoglobulin G4–variant monoclonal antibody that specifically binds the p19 subunit of interleukin (IL)-23[3]
- Mirikizumab was evaluated in patients with moderately to severely active UC in the Phase 3 LUCENT-1[a] and LUCENT-2[b] studies
  - Bowel urgency was assessed using the validated Urgency Numeric Rating Scale (UNRS)

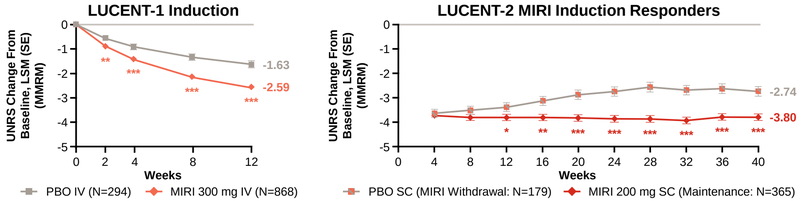
OBJECTIVE

- To evaluate the proportion of patients achieving a clinically meaningful improvement (≥3-point change in UNRS[4]) or remission (minimal to no bowel urgency: UNRS [0,1][4]) in the LUCENT-1 and LUCENT-2 studies

[a] LUCENT-1 (NCT03518086); [b] LUCENT-2 (NCT03524092)

KEY RESULTS

Bowel Urgency Severity Was Significantly Improved With MIRI vs. PBO Through Induction and Maintenance



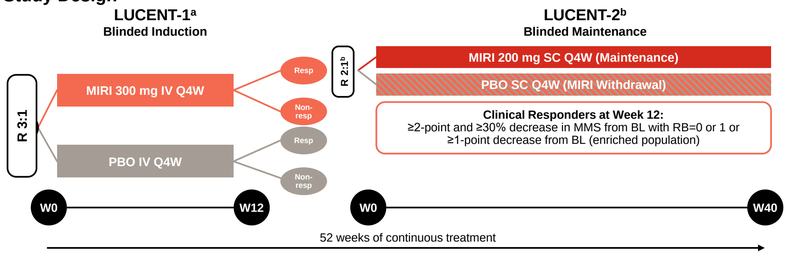
* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
MMRM includes treatment, baseline value, visit, interaction of baseline value-by-visit, interaction of treatment-by-visit, prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity (MMS), and region

CONCLUSIONS

- Mirikizumab had a highly significant and clinically meaningful benefit on reducing bowel urgency, one of the most disruptive symptoms of UC
- In LUCENT-1, patients treated with mirikizumab saw a significantly greater reduction in bowel urgency severity as early as Week 2 compared with placebo
- In LUCENT-2, patients who achieved clinical response on mirikizumab at Week 12 in LUCENT-1 and were re-randomized to placebo saw a significantly lower improvement in bowel urgency by Week 12 of LUCENT-2 (24 weeks of continuous treatment) compared with patients continuing on mirikizumab
- With 52 weeks of mirikizumab treatment, >65% of mirikizumab responders achieved clinically meaningful improvement in bowel urgency and >40% achieved bowel urgency remission
- The UNRS usefully quantified change in bowel urgency after treatment across a range of severity levels

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

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 of the following for UC:
  - Corticosteroid or immunomodulator (conventional failed), or
  - Biologic therapy or Janus kinase inhibitor (biologic failed)
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies

Statistical Analyses

- Change from baseline in UNRS was analyzed using a mixed-effects model of repeated measures (MMRM)
  - The MMRM included treatment, baseline UNRS value, visit, baseline value-by-visit interactions, treatment-by-visit interactions, and stratification factors
- Cochran-Mantel-Haenszel tests, adjusted for stratification factors, were used to compare bowel urgency clinically meaningful improvement and remission rates between treatments
  - Non-responder imputation was used to impute missing values

Assessments

Assessments

- UNRS is a patient-reported measure of bowel urgency in the past 24 hours using an 11-point scale, from 0 (no urgency) to 10 (worst possible urgency)[2]
  - UNRS score recorded daily by patients in an eDiary
  - Mean weekly UNRS scores from diary data if ≥4 days of data were available
  - Change in UNRS from baseline through 52 weeks of treatment
  - Percentage of patients achieving clinically meaningful improvement in UNRS (≥3-point change) or remission (minimal to no bowel urgency: UNRS [0,1]) were assessed at Week 12 (induction) and Week 40 (maintenance) in patients with baseline UNRS ≥3

Analysis Population

- Induction data (LUCENT-1) were analyzed for the mITT population (patients receiving ≥1 dose of MIRI or PBO)[a]
- Maintenance data (LUCENT-2) were analyzed for patients in the mITT population who were clinical responders to MIRI therapy at Week 12 of LUCENT-1

[a] Excludes patients impacted by the electronic clinical outcome assessment transcription error in Poland and Turkey

RESULTS

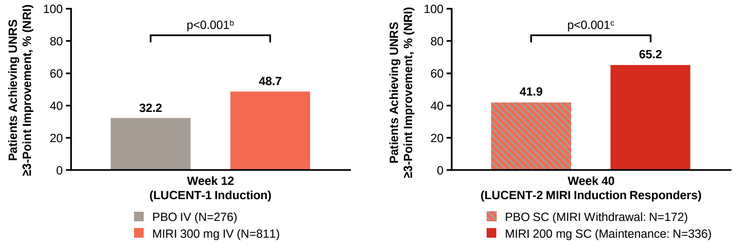
Demographics and Baseline Characteristics[a]

	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)
Modified Mayo Score 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)
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

Higher Proportions of Patients Achieved Clinically Meaningful Improvement in Bowel Urgency With MIRI vs. PBO During Induction and Maintenance

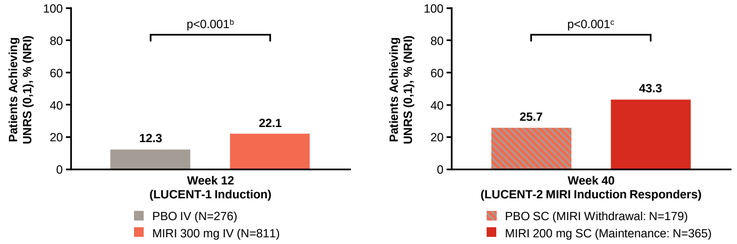
Clinically Meaningful Improvement in UNRS From LUCENT-1 Baseline[a]



[a] In patients with UNRS ≥3 at LUCENT-1 baseline; [b] p-Value vs. PBO, CMH test adjusted by prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity (MMS), and region; [c] p-Value vs. PBO, CMH test adjusted by prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, region, and clinical remission status at LUCENT-1 Week 12

Higher Proportions of Patients Achieved Bowel Urgency Remission With MIRI vs. PBO During Induction and Maintenance

Bowel Urgency Remission (Minimal to No Bowel Urgency: UNRS [0,1])[a]



[a] In patients with UNRS ≥3 at LUCENT-1 baseline; [b] p-Value vs. PBO, CMH test adjusted by prior biologic or tofacitinib failure, baseline corticosteroid use, baseline disease activity (MMS), and region; [c] p-Value vs. PBO, CMH test adjusted by prior biologic or tofacitinib failure, corticosteroid use at LUCENT-1 baseline, region, and clinical remission status at LUCENT-1 Week 12

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ABBREVIATIONS

BL=baseline; CMH=Cochran-Mantel-Haenszel; IV=intravenous; LSM=least squares mean; MIRI=mirikizumab; mITT=modified intent-to-Treat; MMRM=mixed-effects model of repeated measures; 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; UC=ulcerative colitis; UNRS=Urgency Numeric Rating Scale; W=Week

DISCLOSURES

- **S. Travis** has received grants from: AbbVie, BUHLMANN Diagnostics, ECCO, Eli Lilly and Company, Ferring Pharmaceuticals, International Organization for the Study of Inflammatory Bowel Disease, Janssen, Merck Sharp & Dohme, Normal Collision Foundation, Pfizer, Procter & Gamble, Schering-Plough, Takeda, UCB Pharma, Vifor Pharma, and Warner Chilcott; and reports other disclosures from: Abacus Pharma, AbbVie, Actial Farmaceutica, ai4gi, Alcimed, Allergan, Amgen, Aptel, Arena Pharmaceuticals, Asahi Kasei Pharma, Aspen, Astellas, AstraZeneca, Atlantic Pharmaceuticals, Barco, Biocare Medical, Biogen, BL Pharma, Boehringer Ingelheim, Bristol Myers Squibb, BUHLMANN Diagnostics, Calcico Therapeutics, Celgene, Cellerix, Cerimon Pharmaceuticals, ChemoCentryx, Chiesi, Cisbio, Comcast, Coronado Biosciences, Cosmo Pharmaceuticals, Ducentis BioTherapeutics, Dynavax Technologies, Elan, Eli Lilly and Company, Enterome, Equillium, Dr. Falk Pharma, Ferring Pharmaceuticals, FPRT Bio, Galapagos NV, Genentech/Roche, Genzyme, Gilead Sciences, Glenmark Pharmaceuticals, GlaxoSmithKline, Grünenthal, GW Pharmaceuticals, Immunocore, Immunometabolism, Indigo Biosciences, Janssen, Lexicon Pharmaceuticals, Medarex, MedTrix, Merck, Merrimack Pharmaceuticals, Mestag Therapeutics, Millennium Pharmaceuticals, Neovacs, Novartis, Novo Nordisk, NPS Pharmaceuticals/Nycomed, Ocera Therapeutics, OPTIMA Pharma, Origin Pharma, Otsuka, Procter & Gamble, Palau Pharma, Pentax Medical, Pfizer, PharmaVentures, Phesi, Phillips Pharma Group, Pronota, Proximagen, Resolute, Robarts Clinical Trials, Sandoz, Santarus, Satisfai Health, Sensyne Health, Shire, Sigmoid Pharma, Sorriso Pharmaceuticals, Souffinez, SynDermix, Synthon, Takeda, Theravance Biopharma, TiGenix, Tillotts Pharma AG, Topivert, Trino Therapeutics with Wellcome Trust, TxCell, UCB Pharma, Vertex Pharma, VHsquared, Vifor Pharma, Warner Chilcott, and Zeria Pharmaceutical; **T. Hibi** has received lecture fees from: AbbVie, Aspen Japan K.K., Ferring Pharmaceuticals, Gilead Sciences, Janssen, JIMRO, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; has received honoraria as an advisory board member or consultant for: AbbVie, Apo Plus Station, Bristol Myers Squibb, Celltrion, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen, Kyorin, Mitsubishi Tanabe Pharma, Nichi-Iko Pharmaceutical, Pfizer, Takeda, and Zeria Pharmaceutical; has received pharmaceutical and research grants from: AbbVie, Activaid, Alfresa Pharma, Bristol Myers Squibb, Eli Lilly Japan K.K., Ferring Pharmaceuticals, Gilead Sciences, Janssen Pharmaceutical K.K., JMDC, Nippon Kayaku, Mochida Pharmaceutical, Pfizer Japan, and Takeda; has received scholarship contributions from: Mitsubishi Tanabe Pharma, Nippon Kayaku, and Zeria Pharmaceutical; and has belonged to study groups sponsored by: AbbVie, Alfresa Pharma, EA Pharma, JIMRO, Kyorin, MIYARISAN Pharmaceutical, Mochida Pharmaceutical, Otsuka, and Zeria Pharmaceutical; **T. Hisamatsu** has received lecture fees from: AbbVie, EA Pharma, Gilead Sciences, Janssen Pharmaceutical K.K., JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Pfizer, and Takeda; has received honoraria as an advisory board member or consultant for: AbbVie, EA Pharma, Eli Lilly and Company, Gilead Sciences, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Pfizer, and Takeda; and has received pharmaceutical/research grants from: AbbVie, Alfresa Pharma, Daiichi Sankyo, EA Pharma, JIMRO, Kyorin, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nichi-Iko Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical; **D. Fisher**, **M. Shan**, and **T. Hunter Gibble** are employees and shareholders of Eli Lilly and Company; **D. T. Rubin** has received grants or contracts from: Takeda; has received honoraria as a consultant for: AbbVie, Allergan, AltruBio, American College of Gastroenterology, Arena Pharmaceuticals, Athos Therapeutics, Bellatrix Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene/Syneos Health, Cornerstones Health (non-profit), Eli Lilly and Company, Galen/Atlantica, Genentech/Roche, Gilead Sciences, GoDuRn, InDex Pharmaceuticals, Ironwood Pharmaceuticals, Iterative Scopes, Janssen, Materia Prima, Pfizer, Prometheus Therapeutics and Diagnostics, Reistone Biopharma, Takeda, and TechLab
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