B0365

Impact of Mirikizumab Treatment on Health-Related Quality of Life in Patients With Crohn's Disease: A Phase 2 Study Analysis Using the SF-36

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BACKGROUND

- Mirikizumab, a p19-directed interleukin-23 inhibitor, showed efficacy in studies of moderately to severely active ulcerative colitis[1-3] and Crohn's disease (CD)[4]
- The 36-Item Short Form Health Survey (SF-36) is a patient-completed questionnaire measuring 8 domains (physical functioning, social functioning, mental health, general health, role-physical, role-emotional, bodily pain, and vitality) and Physical and Mental Component Summary scores (PCS and MCS, respectively)
- Findings from a Phase 2 study showed that patients with ulcerative colitis who were treated with mirikizumab for 52 weeks had improved health-related quality of life (HRQoL) assessed by SF-36[5]

OBJECTIVE

- To evaluate the effect of mirikizumab on SF-36 in the Phase 2 randomized, double-blind, parallel-group, placebo-controlled study in patients with moderately to severely active CD (NCT02891226)

KEY RESULTS

Numerical Improvements in SF-36 Domain Scores Were Observed During the Induction and Maintenance Periods With MIRI

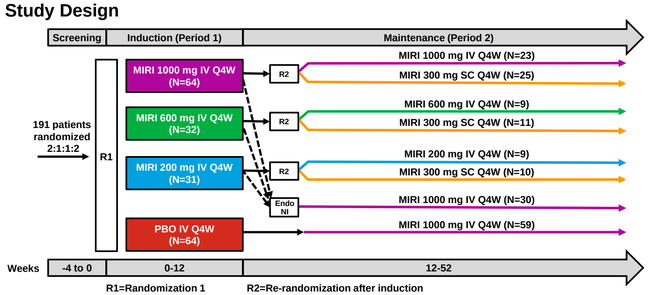
	LSM (SE) Change From Induction Baseline at Week 12				Observed Mean (SD) Change From Maintenance Baseline at Week 52			
	PBO IV (N=64)	MIRI 200 mg IV (N=31)	MIRI 600 mg IV (N=32)	MIRI 1000 mg IV (N=64)	PBO-MIRI 1000 mg IV (N=59)	NI MIRI 1000 mg IV (N=30)	All MIRI IV-IV (N=41)	All MIRI IV-SC (N=46)
PCS	3.11 (0.77)	4.70 (1.10)	8.01 (1.11)	6.70 (0.79)	9.93 (7.18)	7.11 (8.22)	10.47 (8.72)	10.70 (7.88)
MCS	2.34 (1.13)	7.47 (1.60)	6.52 (1.59)	6.05 (1.15)	7.05 (10.59)	7.28 (9.81)	8.49 (11.30)	11.45 (11.42)
Domain scores								
Physical functioning	5.30 (2.04)	12.24 (2.89)	13.17 (2.88)	12.68 (2.06)	17.56 (16.88)	9.81 (20.61)	17.29 (18.48)	22.93 (22.30)
Role-physical	8.30 (2.56)	14.33 (3.63)	22.67 (3.63)	18.76 (2.59)	27.18 (23.89)	23.32 (26.55)	30.89 (24.95)	32.01 (28.24)
Role-emotional	2.22 (2.65)	14.76 (3.77)	11.39 (3.72)	9.39 (2.70)	14.34 (23.59)	17.31 (21.33)	13.10 (25.59)	22.36 (21.36)
Bodily pain	9.31 (2.63)	18.08 (3.71)	26.04 (3.70)	19.86 (2.66)	30.02 (26.66)	26.12 (27.06)	27.20 (29.04)	34.61 (25.30)
Vitality	6.93 (2.47)	19.56 (3.47)	19.50 (3.47)	17.98 (2.49)	22.82 (22.98)	20.19 (24.26)	28.04 (27.39)	30.79 (26.16)
Social functioning	11.40 (2.99)	13.95 (4.25)	23.73 (4.19)	20.40 (3.03)	23.55 (23.97)	19.71 (27.88)	29.29 (29.85)	31.10 (24.71)
Mental health	4.43 (2.10)	13.05 (2.97)	12.17 (2.97)	12.17 (2.13)	13.49 (19.10)	10.96 (20.30)	15.57 (20.39)	21.83 (23.63)
General health	5.78 (1.87)	9.43 (2.63)	12.86 (2.73)	14.57 (1.89)	19.14 (17.06)	14.04 (18.77)	23.91 (20.38)	21.02 (18.31)

CONCLUSIONS

- Patients with moderately to severely active CD who received treatment with mirikizumab for 52 weeks had improved HRQoL, as assessed by the SF-36
- Induction treatment effects on HRQoL were observed at Week 12 for most mirikizumab doses
- Maintenance treatment effects on HRQoL were numerically consistent or increased compared with the effects during induction treatment, even among more refractory patients
- These findings will be validated in the ongoing mirikizumab Phase 3 CD study (NCT03926130)
- Pro-inflammatory signals can induce anxiety and depressive symptoms,[5] but additional mechanistic studies are required to better understand how the effects of anti-inflammatory treatment on the gut-brain axis may improve mental and physical subjective well-being

METHODS

Study Design



R1=Randomization 1
- Patients were stratified based on previous exposure to biologic therapy for the treatment of CD

R2=Re-randomization after induction
- Patients who received MIRI during induction and had endoscopic improvement were re-randomized in a 1:1 ratio at Week 12 to continue their induction regimen or receive MIRI 300 mg SC Q4W with stratification based on endoscopic response. All patients who received PBO in Period 1 received MIRI 1000 mg IV Q4W

Note: Endoscopic improvement defined as ≥1-point improvement in SES-CD. Endoscopic response defined as ≥50% reduction in SES-CD vs. baseline

Key Eligibility Criteria

Inclusion Criteria
- Duration of active CD ≥3 months since diagnosis
- Moderately to severely active disease:
  - Stool frequency ≥4 per day (loose and watery stools defined as Bristol Stool Scale Category 6 or 7) and/or abdominal pain ≥2 (on a 4-point scale) at baseline
  - SES-CD ≥7 for subjects with ileal-colonic disease or ≥4 for patients with isolated ileal disease
- Treatment history:
  - Inadequate response or intolerance to ≥1 conventional treatment or prior exposure to ≥1 biologic agent for the treatment of CD

Exclusion Criteria
- Strictures, stenoses, or any other manifestation that might require surgery
- Bowel resection, diversion, or placement of a stoma within 6 months; other intra-abdominal surgery within 3 months
- Previous exposure to any biologic therapy targeting the IL-23 p19 subunit, either licensed or investigational
  - After an amendment, a single prior induction dose of ustekinumab was allowed (USA only)

Assessments and Statistical Analyses

- SF-36 was assessed at baseline and Weeks 4, 12, 16, 24, 32, 44, and 52
- Due to small sample sizes, maintenance treatment arms were pooled for improvers:
  - IV-IV: Pooled maintenance intravenous (IV) treatment arms for patients at each mirikizumab induction dose level who achieved ≥1-point improvement in Simplified Endoscopic Activity Score for Crohn's Disease (SES-CD) at Week 12 who were re-randomized to continued induction IV treatment assignment during maintenance
  - IV-SC: Pooled maintenance subcutaneous (SC) treatment arms for patients at each mirikizumab induction dose level who achieved ≥1-point improvement in SES-CD at Week 12 who were re-randomized to mirikizumab 300 mg SC every 4 weeks during maintenance
- For statistical comparisons across induction treatment groups, a mixed-effects model of repeated measures was used, which included treatment, region, prior biologic CD therapy used, baseline score, and visit as factors/covariate and baseline-by-visit and treatment-by-visit as interactions
- Nominal p-values are presented and no multiplicity adjustments were made
- No statistical comparisons were made between mirikizumab treatment groups in the Maintenance Period

RESULTS

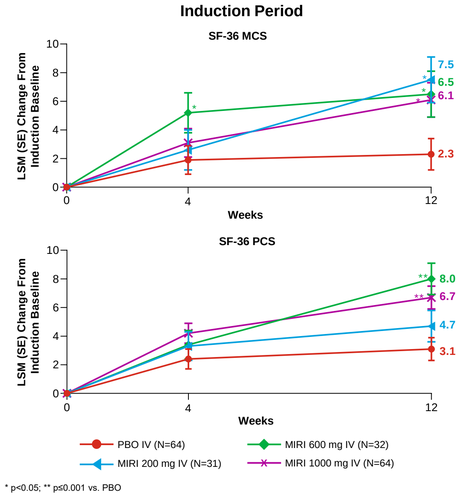
Baseline Demographics and Disease Characteristics by Induction Treatment and Maintenance Treatment Groups

	Induction Treatment Groups			
	PBO IV (N=64)	MIRI 200 mg IV (N=31)	MIRI 600 mg IV (N=32)	MIRI 1000 mg IV (N=64)
Age, years	39.0 (13.0)	38.1 (11.8)	40.4 (13.3)	37.7 (13.1)
Male, n (%)	28 (43.8)	17 (54.8)	14 (43.8)	34 (53.1)
Disease duration, years	10.2 (9.8)	8.9 (7.4)	10.8 (9.7)	8.6 (6.7)
Disease location, n (%)				
Ileal	11 (17.2)	6 (19.4)	5 (15.6)	11 (17.2)
Colonic	25 (39.1)	14 (45.2)	10 (31.3)	26 (40.6)
Ileal-colonic	28 (43.8)	11 (35.5)	17 (53.1)	27 (42.2)
CRP, mg/L, median (range)	6.8 (0-92)	7.4 (0-94)	6.8 (0-78)	4.5 (0-108)
SES-CD	11.9 (5.6)	14.4 (7.9)	15.2 (7.4)	13.1 (6.8)
Patient-reported outcomes				
Stool frequency	6.4 (3.1)	7.4 (3.0)	6.4 (3.8)	6.6 (5.5)
Abdominal pain	1.9 (0.6)	2.0 (0.6)	1.7 (0.7)	1.9 (0.6)
CDAI (0-600)	304.7 (93.1)	348.3 (92.1)	298.2 (103.7)	304.5 (94.4)
FACIT-F (13 items, 0-52)	21.9 (12.7)	19.3 (10.4)	28.2 (12.5)	24.1 (12.1)
SF-36 MCS[a]	37.0 (13.2)	35.2 (10.2)	41.1 (10.4)	40.4 (11.6)
SF-36 PCS[a]	38.9 (8.3)	38.4 (6.4)	42.9 (7.8)	39.5 (8.6)
	Maintenance Treatment Groups			
	PBO-MIRI 1000 mg IV (N=59)	NI MIRI 1000 mg IV (N=30)	All MIRI IV-IV (N=41)	All MIRI IV-SC (N=46)
SF-36 MCS[b]	37.2 (13.0)	38.0 (11.2)	41.9 (11.1)	38.7 (10.7)
SF-36 PCS[b]	39.5 (8.1)	40.8 (8.3)	41.1 (8.5)	38.1 (7.1)

Data are presented as mean (SD) unless stated otherwise
[a] At Induction Period baseline; [b] At Maintenance Period baseline

HRQoL Improved in Patients With Moderately to Severely Active CD Who Received Induction Treatment With MIRI vs. PBO

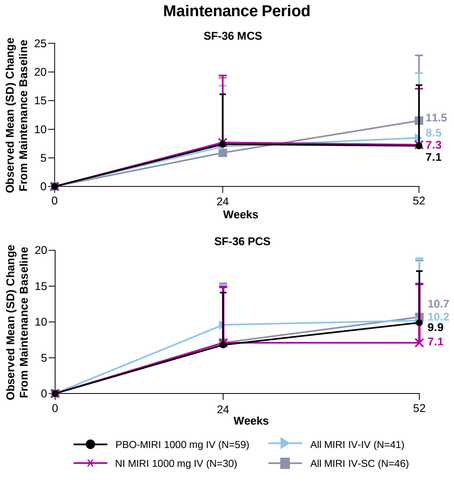
- At Week 4, numerical improvements in SF-36 MCS scores were observed for all mirikizumab dose groups and were statistically significant for the mirikizumab 600 mg IV group vs. placebo
- At Week 12, significant improvements in SF-36 MCS and PCS scores were observed in most mirikizumab dose groups



* p<0.05; ** p≤0.001 vs. PBO

Improvements in HRQoL Were Maintained or Increased Further During Maintenance Treatment With MIRI

- Numerical improvements in SF-36 MCS and PCS scores during maintenance treatment were evident, even among patients who did not achieve a ≥1-point improvement in SES-CD at Week 12 (non-improver group)



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ABBREVIATIONS

CD=Crohn's disease; CDAI=Crohn's Disease Activity Index; CRP=C-reactive protein; Endo NI=endoscopic non-improver; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; HRQoL=health-related quality of life; IL=interleukin; IV=intravenous; IV-IV=pooled maintenance IV treatment arms for patients at each MIRI induction dose level who achieved ≥1-point improvement in SES-CD at Week 12 who were re-randomized to continued induction IV treatment assignment during maintenance; IV-SC=pooled maintenance SC treatment arms for patients at each MIRI induction dose level who achieved ≥1-point improvement in SES-CD at Week 12 who were re-randomized to MIRI 300 mg SC every 4 weeks during maintenance; LSM=least squares mean; MCS=Mental Component Summary; MIRI=mirikizumab; NI=SES-CD non-improver (a patient who received MIRI during induction who did not achieve a ≥1-point improvement in SES-CD at Week 12); PBO=placebo; PCS=Physical Component Summary; Q4W=every 4 weeks; R1=randomization 1; R2=re-randomization after induction; SC=subcutaneous; SD=standard deviation; SE=standard error; SES-CD=Simplified Endoscopic Activity Score for Crohn's Disease; SF-36=36-Item Short Form Health Survey

DISCLOSURES

- **V. Jairath** has received grants and/or contracts from: AbbVie, Adare Pharmaceuticals, Atlantic Pharmaceuticals, Boehringer Ingelheim, Celgene/Bristol Myers Squibb, Eli Lilly and Company, Janssen, Seres Therapeutics, Takeda, UCB Pharma, and VHsquared; has received consulting fees from: AbbVie, Alimentiv, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris Pharmaceuticals, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos NV, Genentech, Gilead Sciences, GlaxoSmithKline, Janssen, Landos Biopharma, Merck, Mylan, Organon, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Ventyx Biosciences, and Vividion Therapeutics; has received payment or honoraria from: AbbVie, Ferring Pharmaceuticals, Galapagos NV, Janssen, Pfizer, and Takeda Pharmaceutical; and has participated on data safety monitoring or advisory boards for: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Fresenius Kabi, Gilead Sciences, Janssen, Mylan, Roche, and Takeda. **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 advisory and/or consultancy fees from: 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 Nichi-iko Pharmaceutical, and Zeria Pharmaceutical; has received research grants from: AbbVie, ActivAid, Alfresa Pharma, Bristol Myers Squibb, Eli Lilly Japan K.K., Ferring Pharmaceuticals, Gilead Sciences, Janssen Pharmaceuticals K.K., JMDC, Mochida Pharmaceutical, Nippon Kayaku, Pfizer Japan, and Takeda Nippon Kayaku; has received scholarship contributions from: Mitsubishi Tanabe Pharma, Nippon Kayaku, and Zeria Pharmaceutical; and belonged to study groups sponsored by: AbbVie, Alfresa Pharma, EA Pharma, JIMRO, Kyorin, MIYARISAN Pharmaceutical, Mochida Pharmaceutical, Otsuka, and Zeria Pharmaceutical; **L. Shan Chan**, **T. Hunter Gibble**, **H. Carlier**, and **M. Protic** are: employees and shareholders of: Eli Lilly and Company; **X. Zhou** is an employee of: Syneos Health under contract to Eli Lilly and Company; **D. T. Rubin** has been a consultant for: AbbVie, AbGenomics, Allergan, Biomica, Boehringer Ingelheim, Bristol Myers Squibb, Celgene/Syneos Health, Check-Cap, Dizal Pharma, Eli Lilly and Company, Galen/Atlantica, Genentech/Roche, Gilead Sciences, Ichnos Sciences, GlaxoSmithKline, InDex Pharmaceuticals, Janssen, Narrow River Management, Pfizer, Prometheus Therapeutics and Diagnostics, Reistone Biopharma, Shire, Takeda, and TechLab; has received grant support from: AbbVie, GenentechRoche, Janssen, Prometheus Therapeutics and Diagnostics, Shire, and Takeda; is a shareholder at: AbGenomics and Biomica; is on the Board of Trustees at: American College of Gastroenterology; is co-founder and CFO of: Cornerstones Health (non-profit); and is co-founder of: GoDuRn
- Medical writing assistance was provided by Joanna Best, 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