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Changes in health-related quality of life and associations with improvements in clinical efficacy: a Phase 2 study of mirikizumab in patients with ulcerative colitis

Marla C Dubinsky,[1] Vipul Jairath ,[2,3,4] Brian G Feagan,[2,3,4] April N Naegeli,[5] Jay Tuttle,[6] Nathan Morris,[5] Mingyang Shan,[5] Vipin Arora,[5] Trevor Lissoos,[5] Noah Agada,[5] Toshifumi Hibi,[7] Bruce E Sands[8]

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For numbered affiliations see end of article.

Correspondence to
Dr Marla C Dubinsky;
marla.dubinsky@mssm.edu

ABSTRACT

Objective Mirikizumab, a monoclonal antibody targeting the interleukin-23 p19 subunit, was effective in a Phase 2 study (NCT02589665) of moderately-to-severely active ulcerative colitis (UC). We studied mirikizumab's impact on health-related quality of life (HRQoL).

Design HRQoL was evaluated using the Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-Item Short Form Health Survey (SF-36) Physical Component Score (PCS) and Mental Component Score (MCS). Mixed effects models for repeated measures compared score changes between mirikizumab and placebo groups. Additional analyses evaluated associations between HRQoL score changes and achievement of efficacy endpoints at weeks 12 and 52.

Results At week 12, IBDQ improved compared with placebo for all mirikizumab groups except mirikizumab 50 mg (50 mg, p=0.073; 200 mg, p<0.001; 600 mg, p<0.001). SF-36 PCS was significantly higher in all mirikizumab groups at week 12 (50 mg, p=0.011; 200 mg, p=0.022; 600 mg, p=0.002); MCS was significantly higher in mirikizumab 200 and 600 mg groups compared with placebo (50 mg, p=0.429; 200 mg, p=0.028; 600 mg, p<0.001). Achievement of clinical response and remission were associated with greater HRQoL improvements at week 12. Improvements in HRQoL scores were sustained through week 52. Of the clinical symptoms evaluated, reduction in rectal bleeding was associated with greater improvements in IBDQ and SF-36 scores.

Conclusion Mirikizumab improved HRQoL in patients with moderately-to-severely active UC.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Mirikizumab, an anti-IL-23p19 monoclonal antibody, has demonstrated safety and efficacy in the treatment of patients with moderately-to-severely active ulcerative colitis (UC).

WHAT THIS STUDY ADDS

⇒ Mirikizumab treatment resulted in improvements in health-related quality of life (HRQoL) in patients with UC as early as Week 12 and was associated with achievement of clinical response or remission. These improvements were sustained through week 52.

⇒ Rectal bleeding is the clinical endpoint most strongly associated with improvements in HRQoL.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Improvements in clinical symptoms such as rectal bleeding remain an important treatment goal impacting overall HRQoL in UC.

INTRODUCTION

Ulcerative colitis (UC), a chronic inflammatory disease of the colon and rectum, presents with symptoms of rectal bleeding, increased stool frequency, and bowel urgency, which negatively impact health-related quality of life (HRQoL).[1]

The goals of medical management of UC are to induce and sustain remission, defined by control of symptoms and endoscopic improvements, ultimately preventing disease progression and complications.[1 2] However, the disease burden extends beyond intestinal symptoms in such a way that the well-being of patients is compromised due to limitations in educational, work, or recreational activities. Negative aspects of UC frequently include depression, anxiety, and isolation.[3] Measuring the effects of therapeutic agents on HRQoL is therefore part of UC management.

Interleukin (IL)-23, a member of the IL-12 cytokine family, plays an essential role in the maintenance and amplification of T helper 17 (Th17) cells and stimulation of innate immune cells, which are important in the pathogenesis of chronic inflammatory

diseases.[4–7] Mirikizumab (LY3074828), a humanised immunoglobulin G4 (IgG4)-variant monoclonal antibody that binds to the p19 subunit of IL-23, has demonstrated clinical efficacy in psoriasis, Crohn's disease, and UC with a favourable safety profile.[8–10] In a Phase 2, 52-week, randomised clinical trial in patients with moderate-to-active UC (NCT02589665), mirikizumab demonstrated efficacy, was well-tolerated, and significantly reduced rectal bleeding, stool frequency, and bowel urgency.[11]

We evaluated the effect of mirikizumab on HRQoL as part of a Phase 2 placebo-controlled dose-finding study conducted in patients with moderately-to-severely active UC. Associations between changes in HRQoL and clinical efficacy endpoints were also assessed.

METHODS

Study design and participants

Study I6T-MC-AMAC (NCT02589665) was a Phase 2 multicentre, randomised, double-blind, parallel-arm, placebo-controlled trial conducted in 14 countries. The trial design has been described previously.[10] In summary, patients with moderately-to-severely active UC were randomly assigned 1:1:1:1 to receive placebo, 50 mg mirikizumab exposure-based (EB) dosing, 200 mg mirikizumab EB dosing, or a 600 mg mirikizumab fixed dose with administration of study drug as an intravenous infusion at weeks 0, 4 and 8. EB dosing is a strategy where the dose is increased based on the observed concentration of drug in a patient's system after the initial starting dose. Patients could receive oral 5-aminosalicylic acid, corticosteroids (≤20 mg/day prednisone equivalent), or thiopurines; they must have failed ≥1 conventional UC therapy; and could either be biologic-naive or have had previous biological use. At week 12, patients who achieved clinical response were eligible to continue into the maintenance period, where mirikizumab responders were rerandomised to receive mirikizumab 200 mg subcutaneously (SC) every 4 weeks or every 12 weeks while placebo responders continued with placebo (online supplemental figure 1).

Objectives

The primary objective of this analysis was to evaluate mirikizumab's effects on HRQoL compared with placebo in the induction and maintenance periods of the study (baseline to week 12 and weeks 12–52, respectively). Secondary objectives were to assess the association between changes in HRQoL and clinical efficacy endpoints, including symptoms of UC such as bowel urgency, rectal bleeding, stool frequency and endoscopy at weeks 12 and 52. Additionally, exploratory analyses were conducted to evaluate the relative contribution of disease activity index components to changes in HRQoL scores.

Outcome measures

HRQoL was assessed using the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ) and the general Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard (SF-36).[3 12–14] These patient-reported questionnaires were administered according to the study schedule in countries where the questionnaires have been translated into the native language of the region and linguistically validated. The IBDQ is a 32-item questionnaire measuring four domains of subjects' lives: symptoms directly related to primary bowel disturbance, systemic symptoms, emotional function and social function. Responses for each item are graded on a 7-point Likert scale in which 7 denotes 'not a problem at all' and 1 denotes 'a very severe problem'. Each domain is scored as a sum of the items (bowel symptoms (10 items), systemic symptoms (5 items), emotional function (12 items) and social function (5 items)) in the respective domain. If only one question within a domain was not answered, the missing question was imputed to the mean of the remaining questions within the domain. The domain subscore was considered missing if two or more questions were unanswered. The total IBDQ score, a sum of all 32 items, ranges from 32 to 224 with higher scores indicating a better HRQoL.[12 15] The total IBDQ score was considered missing if a domain's subscore was missing. A total IBDQ score greater than or equal to 170 points was considered the threshold for IBDQ remission.[3] The minimal clinically important difference (MCID) was defined as an improvement of 16 points or more in the total IBDQ score.[3]

SF-36 is a 36-item self-administrated questionnaire designed to assess health in the areas of physical functioning, role-physical, role-emotional, bodily pain, vitality, social functioning, mental health, and general health.[14 16] Mental and physical well-being are represented as the Mental Component Summary (MCS) and Physical Component Summary (PCS) scores, respectively. Responses are graded on Likert scales of varying lengths. The summary scores range from 0 to 100 and were normalised to healthy US population scores. Higher scores indicate better levels of function and/or better health. An improvement of 5 points or more (score decrease) was defined as the MCID for the SF-36 PCS and MCS scores.[17] The SF-36 has demonstrated validity and reliability in the context of UC.[13 14 17]

The modified Mayo score (MMS) assessed UC disease activity. The MMS is the sum of three components of the Mayo score[18]: stool frequency, rectal bleeding, and endoscopic scores, giving a maximum total score of 9. The stool frequency subscore reports the number of stools in a 24-hour period relative to the normal number of stools for that patient in the same period on a 4-point scale. The rectal bleeding subscore reports the most severe amount of blood passed per rectum for a 24-hour period on a 4-point scale. The endoscopic score is a physician-reported measure that reports the worst appearance of the mucosa on flexible sigmoidoscopy or colonoscopy on a 4-point scale. Bowel urgency was reported daily by patients as the presence or absence of urgency over a 24-hour period.[11]

Clinical efficacy endpoints

Changes in HRQoL were categorised as clinical response (decrease in 9-point Mayo subscore (rectal bleeding, stool frequency, and centrally read endoscopy) inclusive of ≥2 points and ≥35% from baseline with either a decrease of rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or (1), clinical remission (stool frequency remission: Mayo stool frequency=0 or 1 with ≥1 point decrease from baseline; rectal bleeding remission: Mayo rectal bleeding=0; endoscopic remission: Mayo endoscopy=0 or (1), and absence of bowel urgency (no urgency for 3 days prior to week 12 and week 52 visit dates).

Statistical analysis

HRQoL outcomes were assessed in the intent-to-treat (ITT) population, which includes all randomised patients. The maintenance period analysis population was a subset of the ITT population that demonstrated clinical response at week 12, including mirikizumab responders rerandomised to one of the two maintenance arms and placebo responders continuing to receive placebo. Placebo results from the maintenance period were not summarised, as mirikizumab responders were not rerandomised to placebo. Descriptive statistics summarised differences in demographic and baseline disease characteristics among the ITT population treatment groups.

A mixed-effect model for repeated measures (MMRM) compared each HRQoL measure from baseline to week 12 with treatment, visit, geographical region, prior biological experience, treatment-visit interaction, and baseline value as factors. A similar MMRM that compared HRQoL measures across treatment groups in the maintenance period (weeks 12–52) was fitted with treatment, maintenance period visits, geographical region, prior biological experience, treatment-visit interaction, and baseline value as factors. An unstructured covariance matrix was used for each model. Type III tests for the least square means were used for statistical comparisons between treatment groups. No imputation was performed prior to implementing the MMRM.

The proportions of patients achieving IBDQ remission, IBDQ MCID, SF-36 MCS MCID, and SF-36 PCS MCID at weeks 12 and 52 were compared between treatment groups using logistic regression models with treatment, geographical region, and prior biological experience as fixed effects. Non-responder imputation was used to impute missing remission or MCID status. The 95% CI of the response rate difference was calculated using the Newcombe-Wilson method without continuity correction.

Additional post-hoc analyses assessed the association between HRQoL improvement and achievement of clinical efficacy endpoints at weeks 12 and 52 by pooling patients and clinical responders in the ITT population. Analysis of covariance (ANCOVA) models compared changes from baseline to week 12 for each HRQoL measure between patients who achieved and did not achieve clinical response, clinical remission, stool frequency remission, rectal bleeding remission, and absence of bowel urgency. Each ANCOVA model treated the HRQoL measure as the outcome and included the clinical endpoint component, geographical region, prior biological experience, age, gender, and baseline value of the HRQoL measure as independent variables. A similar set of models were used to examine changes from baseline to week 52 among clinical responders at week 12 who continued into the maintenance period. Type III tests for the least square means were used for the statistical comparisons between clinical efficacy outcome groups.

Non-responder imputation was used to impute missing clinical improvement criteria and modified baseline observation carried forward (mBOCF)[19] imputed missing HRQoL values in the ANCOVA models. Patients with missing bowel urgency data were imputed as having bowel urgency present at that visit.

Multivariable linear models were fitted to assess the relative proportion of variation in HRQoL measures at week 12 that could potentially be explained by achievement of clinical endpoints. Each linear model took the week 12 Mayo stool frequency score, rectal bleeding score, endoscopy score, absence of bowel urgency status, geographical region, prior biological experience, age, gender, and baseline value of the HRQoL measure into account. The coefficient of partial determination, or the partial R^2, was compared between urgency status, stool frequency, rectal bleeding, and endoscopy scores. Missing Mayo score components and HRQoL scores were imputed by mBOCF.

RESULTS

Study population

In this study, 249 patients were randomly assigned to receive placebo (N=63), 50 mg mirikizumab EB dosing (N=63), 200 mg mirikizumab EB dosing (N=62) or 600 mg mirikizumab fixed dose (N=61). There were no clinically important differences between groups in terms of demographics, baseline characteristics, or concomitant therapies received.[10] In patients treated with mirikizumab 50 mg EB, 200 mg EB and 600 mg fixed dose, the average duration of UC was 8.2, 9.0 and 6.0 years, respectively.[10] In patients receiving placebo, the average duration of UC was 9.5 years.[10] Notably, 63% (n/N=157/249) of patients had received prior treatment with a biologic. Mean baseline SF-36 PCS scores (placebo: 42.0; mirikizumab 50 mg EB: 41.8; mirikizumab 200 mg EB: 42.8; mirikizumab 600 mg fixed dose: 41.1) were numerically higher than mean SF-36 MCS scores (placebo: 39.8; mirikizumab 50 mg EB: 36.2; mirikizumab 200 mg EB: 41.1; mirikizumab 600 mg fixed dose: 40.3). Means of both SF-36 PCS and MCS scores in all treatment groups were below the United States population norm of 50 points.[13 17] Mean baseline IBDQ total scores were similar across the treatment groups.[10]

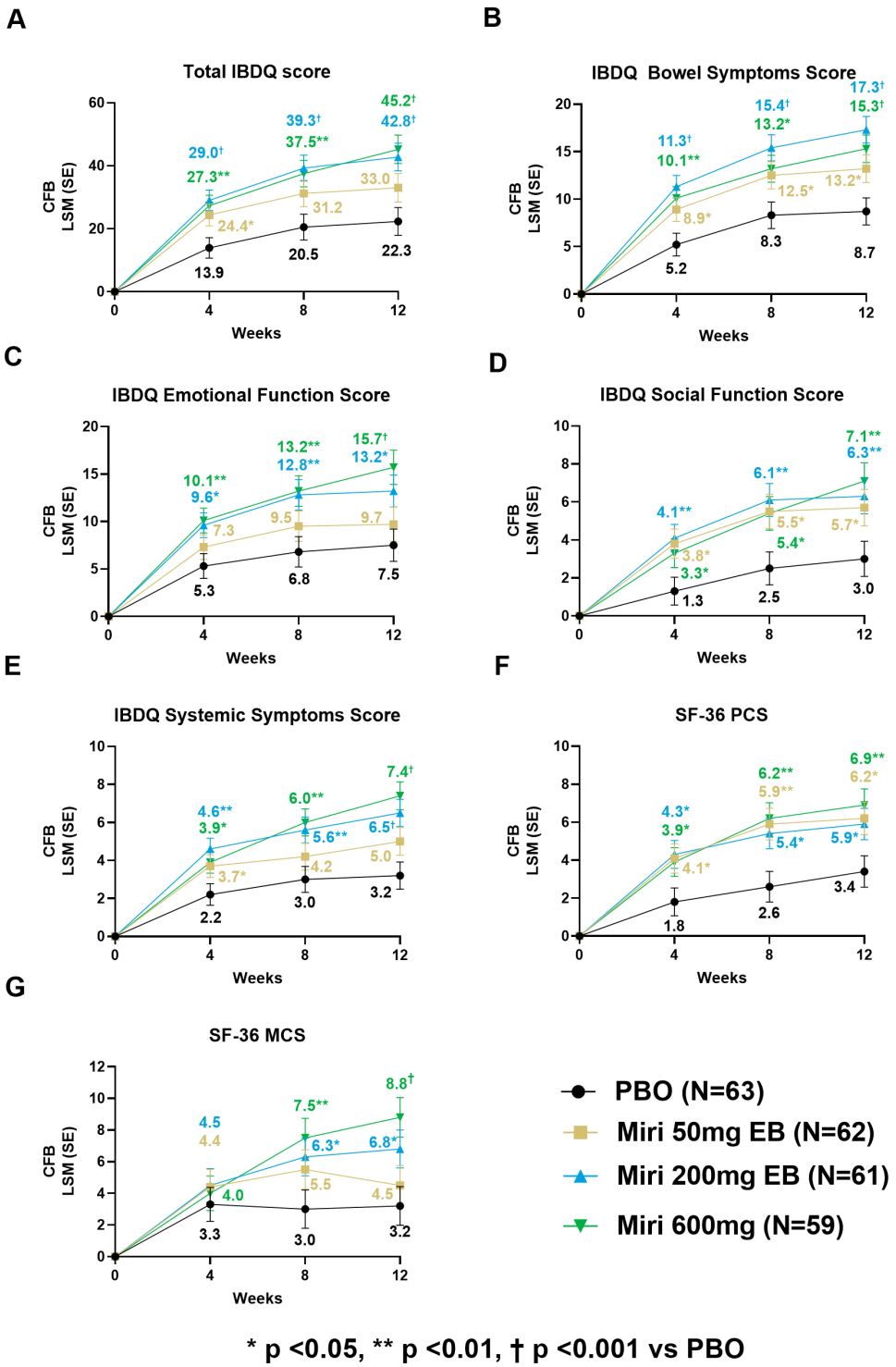

Figure 1 Change from baseline in HRQoL measures by treatment group: induction period. CFB, change from baseline; HRQoL, health-related quality of life; EB, exposure-based; IBDQ, Inflammatory Bowel Disease Questionnaire; LSM, least squares mean; MCS, Mental Component Score; miri, mirikizumab; n, number of patients in treatment group; PBO, placebo; PCS, Physical Component Score; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard.

HRQoL outcomes: induction period

At week 12, patients treated with mirikizumab 200 and 600 mg experienced significantly greater improvement in IBDQ total score from baseline versus placebo (figure 1A, online supplemental table 1). Significantly higher improvements in IBDQ bowel and social function scores from baseline to week 12 were observed across all mirikizumab treatment groups compared with placebo (figure 1B,D), while patients treated with mirikizumab 200 and 600 mg reported significantly greater improvements in IBDQ emotional and systemic symptom scores compared with placebo at week 12 (figure 1C,E).

The proportion of patients achieving IBDQ remission at week 12 was significantly higher among patients

receiving mirikizumab 200 mg (56.5%, p=0.003) and 600 mg (54.1%, p=0.009) compared with placebo (30.2%). Patients receiving mirikizumab 200 mg also had a significantly higher rate of achieving the IBDQ MCID than placebo (75.8% vs 50.8%, p=0.002).

Significantly greater improvements from baseline in SF-36 PCS were observed across all mirikizumab doses at week 12 compared with placebo (figure 1F, online supplemental table 1). Mirikizumab 200 and 600 mg groups had significantly greater improvement from baseline in SF-36 MCS (figure 1G). Compared with placebo, one or more of the mirikizumab dose groups had significant improvements in 7 of the 8 SF-36 domains (physical functioning, role-physical, role-emotional, social functioning, vitality, bodily pain, and mental health), while numerical improvements were observed in general health. Patients treated with mirikizumab 600 mg achieved the MCID for SF-36 PCS at a significantly greater rate than placebo (57.4% vs 38.1%, p=0.042). Similarly, a greater proportion of patients receiving mirikizumab 200 mg achieved the MCID for SF-36 MCS than placebo (54.8% vs 34.9%, p=0.021).

HRQoL outcomes: maintenance period

Patients with clinical response to mirikizumab at week 12 sustained improvements in HRQoL scores through week 52 in both the mirikizumab 200 mg SC every 4 weeks and every 12 weeks groups. Numerically greater changes from baseline were reported in the every 4 weeks group at week 52 for IBDQ total score, SF-36 PCS and SF-36 MCS (figure 2).

Among mirikizumab-treated patients who entered the study's maintenance period, greater than or equal to 80% achieved the MCID for improvement in IBDQ total score (% (95% CI): 200 mg every 4 weeks, 85.1 (74.9, 95.3); 200 mg every 12 weeks, 80.4 (69.0, 91.9)) and ≥67% achieved IBDQ remission (% (95% CI): 200 mg every 4 weeks, 68.1 (54.8, 81.4); 200 mg every 12 weeks, 67.4 (53.8, 80.9)) at week 52. A higher proportion of patients who achieved IBDQ remission at week 52 also achieved clinical remission at week 52 (% (CI) 75.0 (61.6%, 88.4%)) versus those without IBDQ remission at week 52 (% (CI): 25.0 (11.6%, 38.4%)).

At week 52, a significantly greater proportion of patients treated with mirikizumab 200 mg every 4 weeks met the MCID for SF-36 PCS than patients on mirikizumab 200 mg every 12 weeks (74.47% (62.0, 86.9) vs 54.35% (40.0, 68.7), p=0.03). Similar proportions of patients achieved the MCID for SF-36 MCS across both treatment groups (65.96% (52.4, 79.5) vs 52.17% (37.7, 66.6), p=0.21).

Clinical efficacy endpoints

At week 12, mirikizumab 200 and 600 groups demonstrated significant improvements from baseline for Mayo stool frequency and rectal bleeding (figure 3A,C). Absence of bowel urgency was reported in 39.3% of patients in the mirikizumab 200 mg group (p<0.05) and 43.1% of those in the mirikizumab 600 mg group (p<0.001; figure 3E). Patients receiving mirikizumab also experienced significant improvements from baseline on the Mayo endoscopic subscore compared with placebo (least squares mean±SE: placebo: −0.20±0.1, p=0.047; mirikizumab 50 mg: −0.52±0.1, p<0.001; mirikizumab 200 mg: −0.62±0.1, p<0.001 and mirikizumab 600 mg: −0.42±0.1, p<0.001).

At week 52, patients in the mirikizumab 200 mg every 4 weeks and every 12 weeks groups maintained improvement from baseline for Mayo stool frequency and rectal bleeding (figure 3B,D). At week 52, 67.4% of patients in the mirikizumab 200 mg every 4 weeks and 63.4% in the every 12 weeks group reported absence of bowel urgency (figure 3F).

Association between clinical efficacy endpoints and HRQoL outcomes

At week 12, patients achieving the clinical efficacy endpoints (endoscopy remission, Mayo stool frequency remission, Mayo rectal bleeding remission, and absence of bowel urgency) also reported greater improvement from baseline in the HRQoL outcome measures: IBDQ total and domain scores, SF-36 PCS, and SF-36 MCS (figure 4). These significant improvements in HRQoL measures for patients who achieved clinical endpoints over patients not meeting clinical endpoints were maintained at week 52, except for SF-36 (figure 5). The SF-36 PCS and IBDQ emotional, social, and systemic domain scores were also not meaningfully different between endoscopic remission groups at week 52 (figure 5).

Bowel urgency status, Mayo rectal bleeding subscore, and Mayo stool frequency subscore were symptomatic measures significantly associated with improvements in IBDQ total score (online supplemental figure 2B). The rectal bleeding subscore had the highest partial correlation with improvement in IBDQ total score and its four domain scores at week 12 after adjusting for other clinical measures (online supplemental figure 2A). Bowel urgency and stool frequency had similar magnitudes of relative importance to changes from baseline in the IBDQ total score and its four domain scores, which were each less in magnitude than rectal bleeding's correlation. The Mayo endoscopy subscore had the lowest correlation with IBDQ improvement among the clinical outcome measures at week 12.

Rectal bleeding also correlated the most with both SF-36 MCS and PCS at week 12 after adjusting for other clinical measures (online supplemental figure 2A). Following rectal bleeding, stool frequency showed greater association with SF-36 MCS and PCS than bowel urgency status. Stool frequency correlated significantly to improvement in SF-36 PCS but not MCS (online supplemental figure 2B). The Mayo endoscopy subscore had the lowest correlation with SF-36 MCS and PCS at week 12 (online supplemental figure 2A).

DISCUSSION

This analysis evaluated the effect of mirikizumab on HRQoL and the association between HRQoL changes

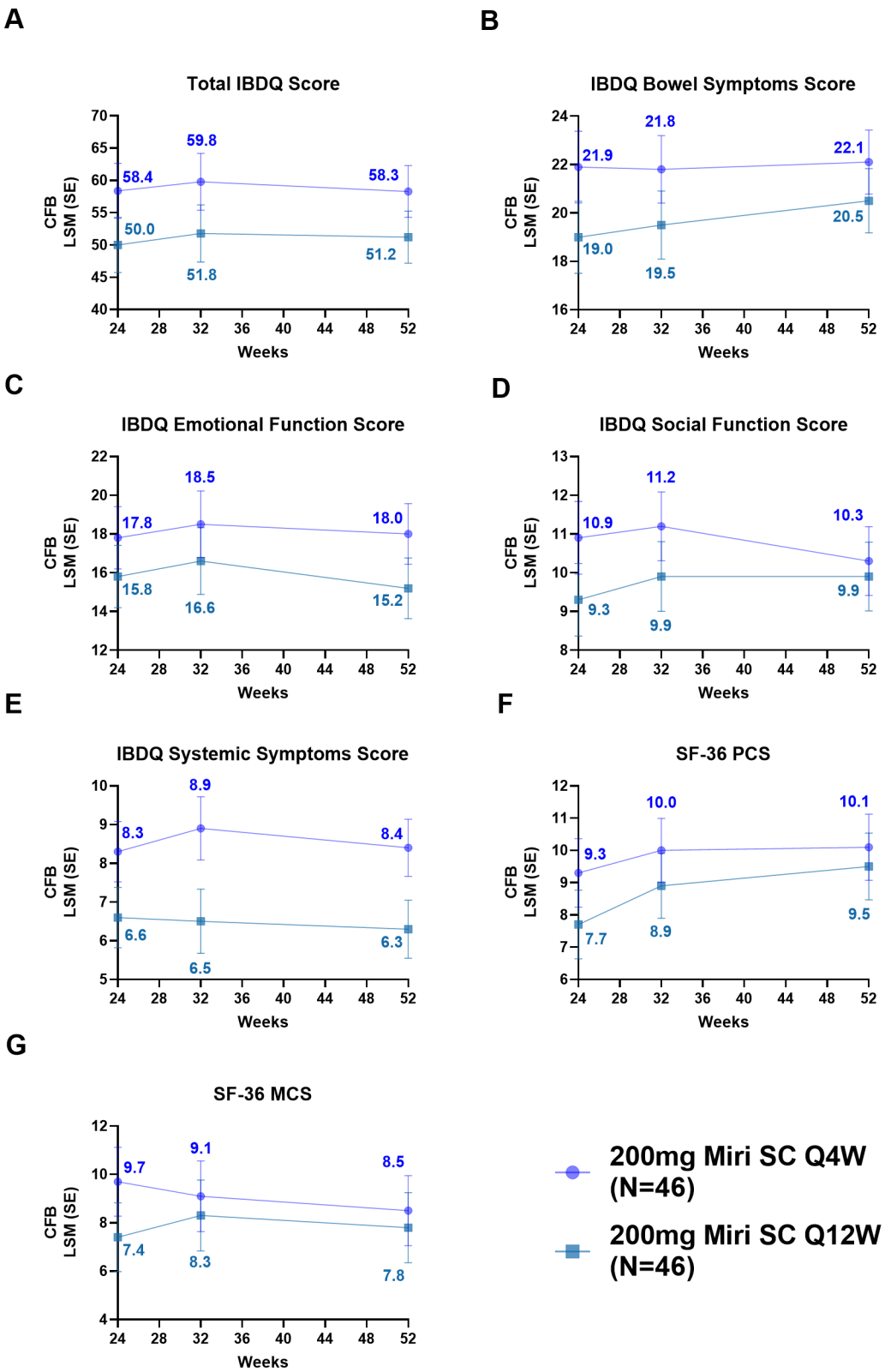

Figure 2 Change from baseline in HRQoL measures by treatment group: maintenance period. CFB, change from baseline; IBDQ, Inflammatory Bowel Disease Questionnaire; LSM, least squares mean; MCS, Mental Component Score; miri, mirikizumab; n, number of patients in treatment group; PCS, Physical Component Score; SC, subcutaneous; SF-36, 36-Item Short Form Health Survey Version 2 Standard.

and clinical efficacy endpoints, showing that treatment of moderate-to-severe UC with mirikizumab improves HRQoL. While multiple factors can influence HRQoL in UC, rectal bleeding had the highest relevance for both IBDQ and SF-36 scores followed by bowel urgency and stool frequency. In sum, all symptom-related measures

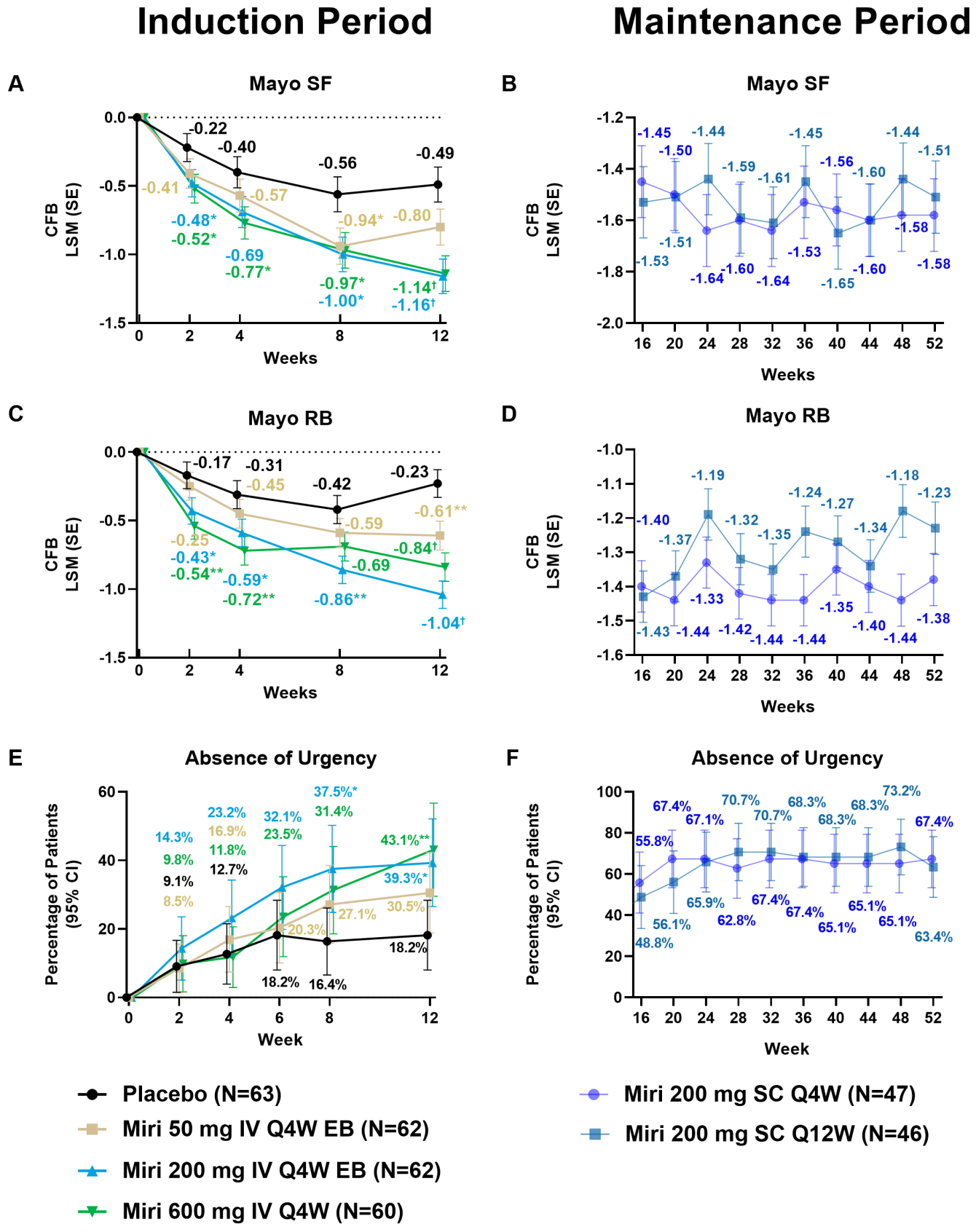

Figure 3 Comparison of CFBs in PRO symptom endpoints by treatment group: induction and maintenance periods. CFB, change from baseline; EB, exposure-based; IV, intravenous; LSM, least squares mean; miri, mirikizumab; n, number of patients in treatment group; Q4W, every 4 weeks; Q12W, every 12 weeks; RB, rectal bleeding; SC, subcutaneous; SF, stool frequency.

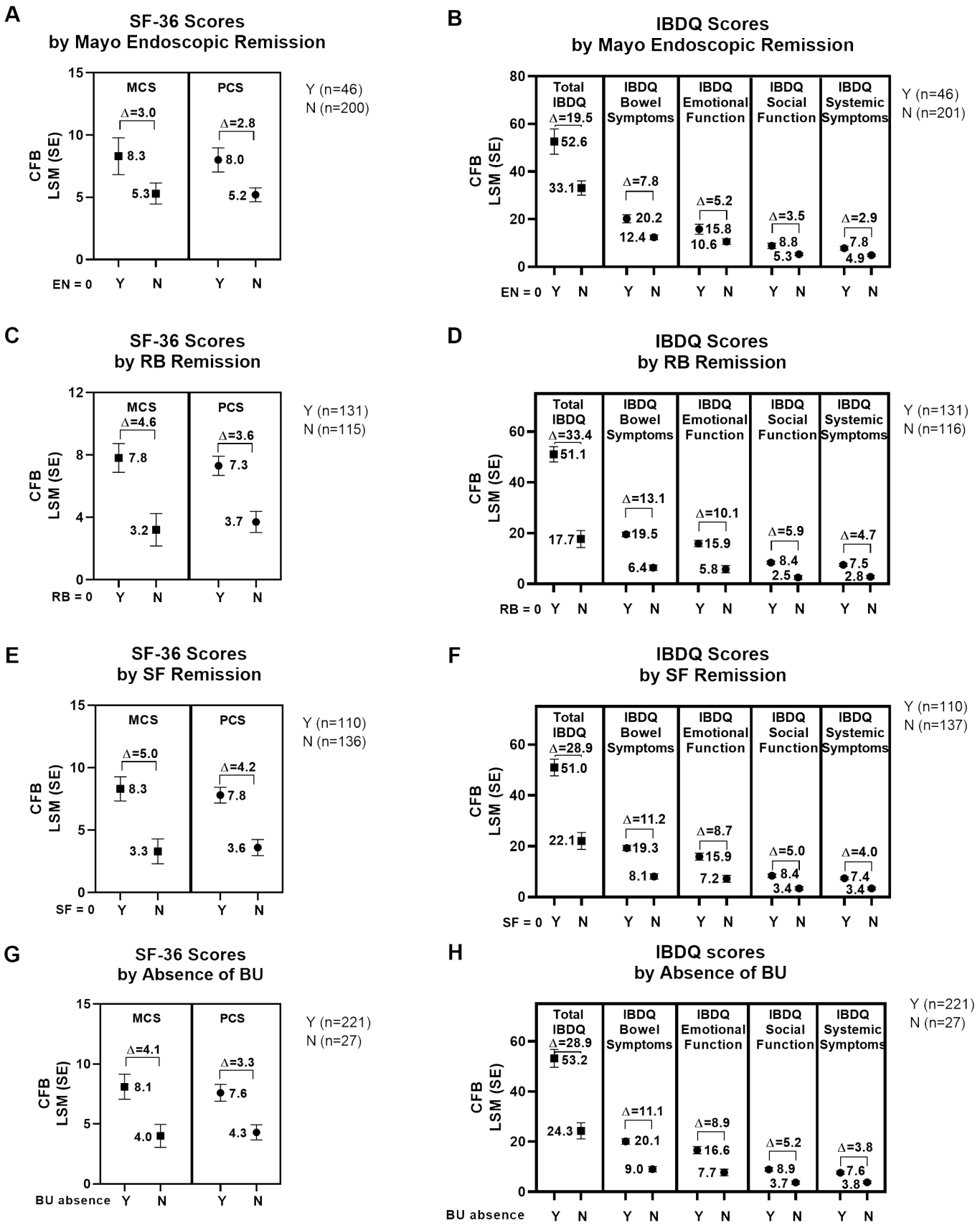

Figure 4 Effects of clinical efficacy endpoints on HRQoL measures at week 12. BU, bowel urgency; CFB, change from baseline; EN, Mayo endoscopic remission; IBDQ, Inflammatory Bowel Disease Questionnaire; LSM, least squares mean; MCS, Mental Component Score; miri, mirikizumab; n, no; n, number of patients in subgroup; PCS, Physical Component Score; RB, rectal bleeding; SC, subcutaneous; SF, stool frequency; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard; Y, yes.

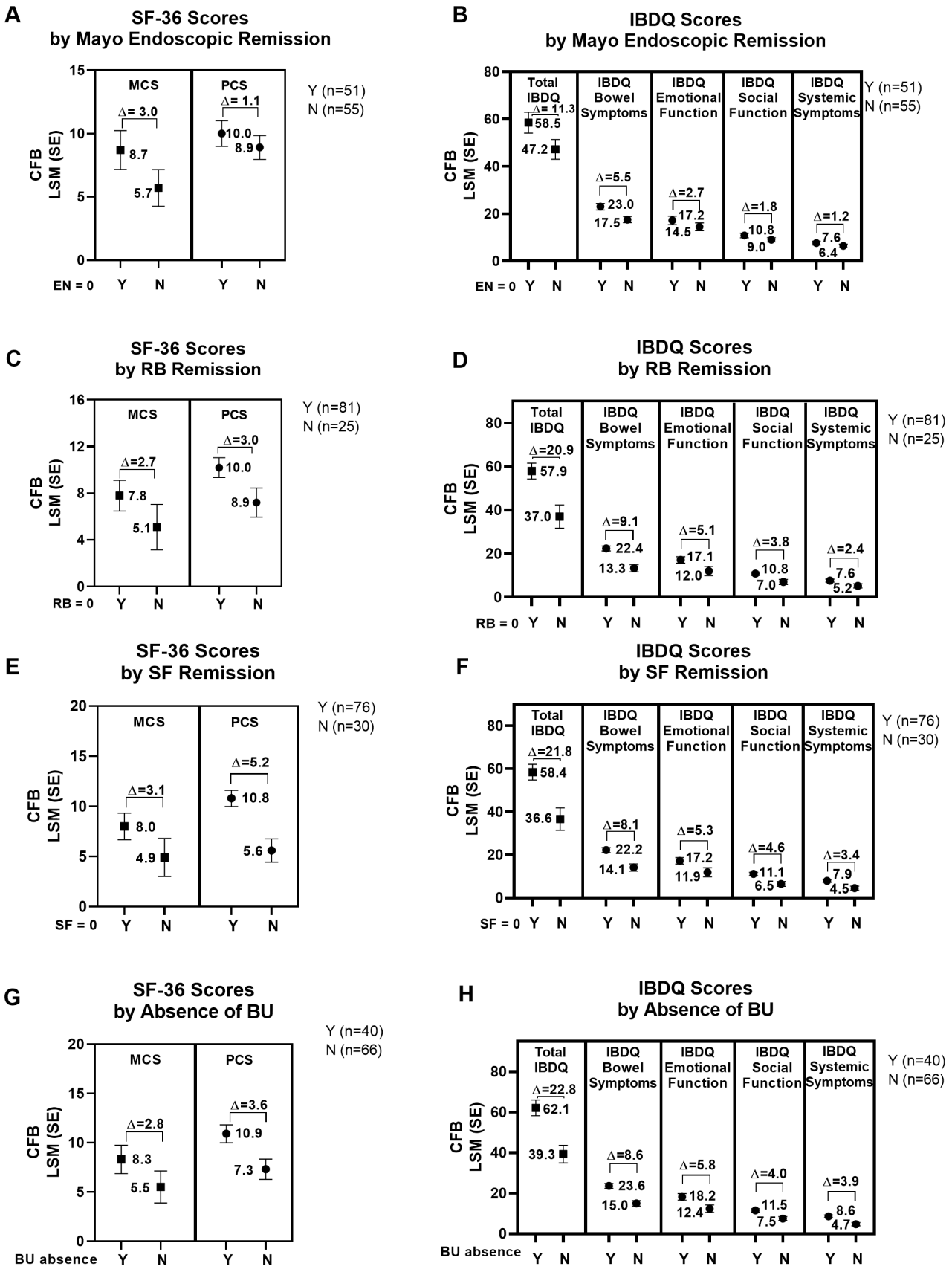

Figure 5 Effects of clinical efficacy endpoints on HRQoL measures at week 52. BU, bowel urgency; CFB, change from baseline; EN, Mayo endoscopic remission; HRQoL, health-related quality of life; IBDQ, Inflammatory Bowel Disease Questionnaire; LSM, least squares mean; MCS, Mental Component Score; miri, mirikizumab; N, no; n, number of patients in subgroup; PBO, placebo; PCS, Physical Component Score; RB, rectal bleeding; SC, subcutaneous; SF, stool frequency; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey Version 2 Standard; Y, yes.

evaluated, including bowel urgency, contributed to HRQoL improvements. These findings emphasise the need to develop effective treatments for UC that target patient-reported outcomes (PROs).

At study initiation, patients' IBDQ and SF-36 scores were consistent with moderate-to-severe UC as well as moderate-to-severe HRQoL impairments.[13] After induction with intravenous mirikizumab, HRQoL scores increased compared with placebo. At week 12, significantly greater proportions of patients receiving mirikizumab 200 mg versus placebo met the MCID in IBDQ total score (≥16 points) from baseline. By week 24, the mean IBDQ total score surpassed the threshold for remission (≥170 points),[3] and the mean IBDQ total score continued to improve through week 52. At week 52, more than 80% of patients receiving mirikizumab 200 mg met the MCID in IBDQ total score, demonstrating sustained and clinically meaningful improvements in HRQoL.

Mean baseline SF-36 MCS and PCS scores across treatment arms were at or approaching 1 standard deviation (10 points) below the average score for the general US population (50 points).[17] By week 52, the mean SF-36 MCS and PCS scores for both mirikizumab-treated groups that responded to induction therapy approached US population norms, which supports that effective induction therapy can improve patients' global well-being to approximate that of healthy controls.[17]

A dose–response relationship favouring every 4 weeks maintenance dosing vs every 12 weeks dosing was observed for the IBDQ total score and its domain subscores. This pattern was also observed in SF-36 scores; the mirikizumab every 4 weeks dosing group had numerically higher PCS and MCS scores versus the every 12 weeks group. These results were consistent with the week 52 primary endpoint of clinical remission, where the proportion of remitters among the mirikizumab every 4 weeks group was numerically greater than the every 12 weeks group.[10]

The symptomatic burden associated with UC negatively impacts HRQoL. Traditional symptomatic endpoints such as stool frequency and rectal bleeding have been included in evaluations of disease activity (eg, Mayo score), with improvements in these symptoms serving as an indicator of the benefits of therapeutic intervention. While bowel urgency is a common, bothersome and disruptive symptom experienced by UC patients,[20] it is not consistently assessed in UC clinical trials. Data on the association of bowel urgency with overall changes in HRQoL are limited.

This study was limited as the data were from a dose-finding Phase 2 trial enrolling a small and predominately white patient population, which may limit generalisability of these results.[10] In addition, SF-36 data from this international, multicentre trial were compared with US population norms, which may not be representative to other geographical regions.[17] Other limitations of this study are those inherent to post-hoc analyses of clinical trial data.

CONCLUSION

Treatment with mirikizumab improved disease-specific and general health HRQoL in patients with moderately-to-severely active UC as measured by IBDQ and SF-36 scores compared with placebo. These improvements were present after 12 weeks of induction mirikizumab treatment and were sustained among mirikizumab responders during an additional 40 weeks of maintenance therapy (SC mirikizumab 200 mg every 4 weeks or every 12 weeks). The present HRQoL results support previously reported efficacy data.[10] Patients' HRQoL is most impacted by symptoms, particularly rectal bleeding. Improvements in PROs such as rectal bleeding remain a critical treatment goal for UC. Larger, ongoing Phase 3 trials evaluating mirikizumab will provide future data on clinical efficacy and pharmacoeconomic benefits.

Author affiliations
[1]Department of Pediatrics, Icahn School of Medicine, New York, New York, USA
[2]Alimentiv, Inc, London, Ontario, Canada
[3]Department of Medicine, Western University, London, Ontario, Canada
[4]Department of Epidemiology and Biostatistics, Western University, London, Ontario, Canada
[5]Eli Lilly and Company, Indianapolis, Indiana, USA
[6]Lilly Biotechnology Center, San Diego, California, USA
[7]Center for Advanced IBD Research and Treatment, Kitasato Institute Hospital, Tokyo, Japan
[8]Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Contributors MCD: Guarantor. ANN, JT and MS: conception of the work. BGF, JT, MS and VA: design of the work. VA: acquisition of data for the work. VJ, BGF, MS and VA: analysis of data for the work. MCD, VJ, BGF, ANN, JT, TL, NM, MS, NA, TH and BES: interpretation of data for the work. BGF, ANN, JT and MS: drafting of the work. MCD, VJ, BGF, ANN, JT, NM, MS, VA, TL, NA, TH and BES: critical revision of the work for important intellectual content. MCD, VJ, BGF, ANN, JT and NM, MS, VA, TL, NA, TH and BES: final approval of the version to be submitted.

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Ethics approval This trial was compliant with the International Conference on Harmonisation (ICH) guidelines on good clinical practice. The study was approved by ERBs at individual sites. For example (one of many): Western Institutional Review Board1019 39th Avenue SEPuyallup, WA 98374-2115USAA full list of institutional ERBs is available upon request. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available on reasonable request. Lilly provides access to all individual participant data collected during the trial, after anonymisation, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the USA and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

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ORCID iD

Vipul Jairath http://orcid.org/0000-0001-8603-898X

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