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Mirikizumab Is Safe and Effective for Moderate-to-Severe Crohn's Disease

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IBD

This summary reviews Ferrante M, D'Haens G, Jairath V, et al. Efficacy and safety of mirikizumab in patients with moderately-to-severely active Crohn's disease: A phase 3, multicentre, randomised, double-blind, placebo-controlled and active-controlled, treat-through study. Lancet. 2024;404(10470):2423-2436. .

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STRUCTURED ABSTRACT

Question: Is mirikizumab safe and effect for moderate-to-severe Crohn's disease?

Design: Phase 3, randomized, placebo and active-controlled treat-through trial.[1]

Setting: The study took place in 324 centers across 33 countries.

Patients: Overall, 1,150 adults of aged 18-80 years with moderate-to-severe Crohn's disease and prior exposure to 1 or more biologic or conventional therapies were included.

Exposure or Interventions: Patients were randomized 6:3:2 to mirikizumab 900

mg induction followed by 300 mg every 4 weeks maintenance, ustekinumab 6 mg/kg induction followed by 90 mg every-8 weeks maintenance, or placebo.

Outcomes: Co-primary endpoints were the composite of patient-reported outcome (PRO) clinical response at week 12 with endoscopic response at week 52 (endoscopic response-composite), and composite of PRO clinical response at week 12 with Crohn's Disease Activity Index (CDAI) clinical remission at week 52 (CDAI clinical remission-composite).

Data Analysis: Adjusted risk differences were calculated and comparisons were performed using the Cochran-Mantel-Haenszel test with non-responder imputation.

Funding: Eli Lilly and Company.

Results: Both co-primary endpoints were met for mirikizumab versus placebo: endoscopic response-composite 38.0% vs 9.0% (P <0.01) and CDAI clinical remission-composite 45.4% versus 19.6% (P <0.01) (Figure 1A). Results were similar regardless of prior exposure to biologics. Mirikizumab demonstrated non-inferiority versus ustekinumab for clinical remission by CDAI at week 52 (Figure 1B). In patients with prior biologic therapy failures, mirikizumab showed numerically higher response rates versus ustekinumab that were not statistically significant. Adverse events for mirikizumab were less common than for placebo and consistent with the known, favorable safety profile of mirikizumab.

COMMENTARY

Why Is This Important?

This study demonstrates both the efficacy and favorable safety profile of another therapy in the IL-23 inhibitor class for Crohn's disease. Importantly, the study demonstrated efficacy regardless of prior bio exposure, indicating that this would be a reasonable option in patients with prior biologic failures. The treat-through design rather than re-randomization after induction mimics clinical practice, and therefore the outcomes observed in the study may be more likely to reflect real-world outcomes. The study also utilized an active control arm, demonstrating non-inferiority to ustekinumab for clinical remission.

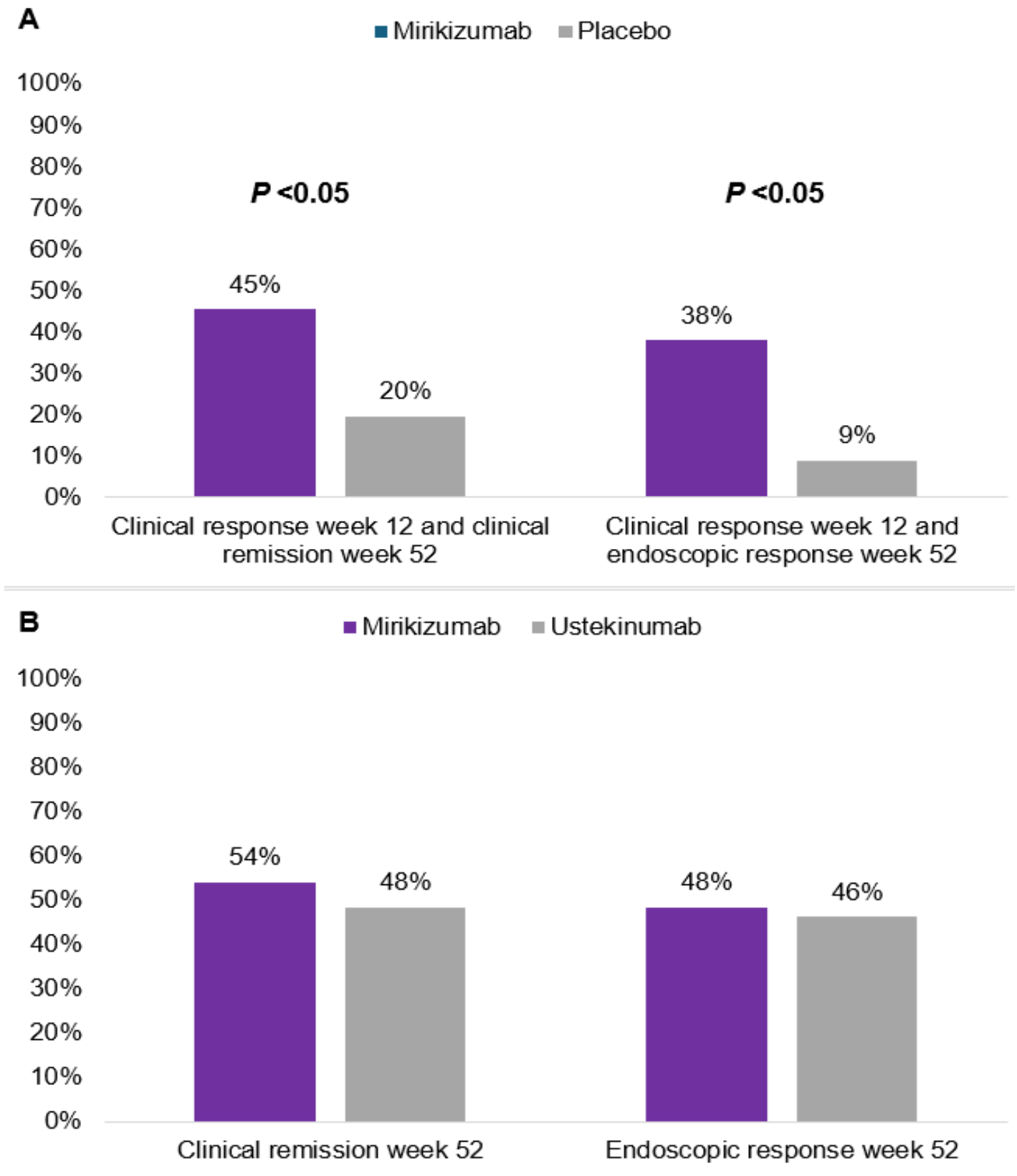

Figure 1. A. Coprimary endpoints for mirikizumab vs placebo. B. Mirikizumab vs Ustekinumab comparisons.

Key Study Findings

The study found that at week 12, a higher proportion of patients receiving mirikizumab achieved a PRO clinical response compared to placebo. At week 52, more patients on mirikizumab reached endoscopic response and CDAI clinical remission compared to placebo. Mirikizumab also demonstrated non-inferiority to ustekinumab in achieving clinical remission and endoscopic response at week 52.

In the bio-exposed population, more patients treated with mirikizumab achieved CDAI clinical remission and endoscopic response compared to those receiving ustekinumab, but this did not reach statistical significance. Patients treated with mirikizumab did achieve significantly more improvements in baseline fecal calprotectin and C-reactive protein compared to those receiving ustekinumab.

The safety of mirikizumab was consistent with its known profile in ulcerative colitis. The most common adverse events included COVID-19, anemia, arthralgia, headache, upper respiratory tract infection, nasopharyngitis, and injection site reactions

Caution

The study used composite endpoints which can be difficult to interpret for real-world practice. Additionally, the study was not powered to detect significant differences between mirikizumab and ustekinumab for bio-exposed patients, which requires further study. Extended intravenous induction or re-induction were not investigated for patients with partial response or loss of response, and this will be investigated in future long-term extension studies.

My Practice

In my practice, I am increasingly utilizing IL-23 inhibitors such as risankizumab as both first and second-line therapies for moderate-to-severe Crohn's disease due to their demonstrated efficacy in both clinical trials and real-world studies.[2-4] It is quite helpful to have another available agent approved in this treatment class. In most instances, I will likely choose mirikizumab over ustekinumab given the numerical improvements in clinical, endoscopic, and biochemical parameters favoring mirikizumab among the bio-exposed, though many of these results did not achieve statistical significance. However, I would need to see head-to-head data before I would consider mirikizumab over risankizumab for Crohn's disease.

For Future Research

Given the expansion of the IL-23 class (including ustekinumab, mirikizumab, risankizumab, and guselkumab), we need additional head-to-head data both within and outside of this treatment class to help guide positioning of advanced therapies. Data is also needed regarding the effectiveness of one IL-23 inhibitor after failure of another (e.g. the effectiveness of mirikizumab after

risankizumab failure and vice versa).

Conflict of Interest

Dr. Dalal has research grant support from Janssen and Pfizer and has served as a consultant for Janssen, Takeda, and Centaur Labs.

Note: The author of this summary is active on social media. Tag him to discuss this EBGI piece.

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