Journal of Enterocolitis

Review

Efficacy and Safety of Mirikizumab for Induction and Maintenance of Remission in Ulcerative Colitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Gizem Dağcı[1], Adem Sarıca[2], Besim Fazıl Ağargün[1], Mehmet Akif Yağlı[1], Bilger Çavuş[1], Aslı Çiftçibaşı Örmeci[1], Kadir Demir[1], Selman Fatih Beşışık[1], Sabahattin Kaymakoglu[1], Filiz Akyüz[1]

[1]Department of Gastroenterology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Türkiye
[2]Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Türkiye

Cite this article as: Dağcı G, Sarıca A, Ağargün BF, et al. Efficacy and Safety of Mirikizumab for Induction and Maintenance of Remission in Ulcerative Colitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Enterocolitis.* 2026;5(2):43-52.

Corresponding author: Gizem Dağcı, e-mail: gizem.dagci@istanbul.edu.tr

Received: August 26, 2026 **Accepted:** September 15, 2026

DOI: 10.14744/Jenterocolitis.2026.381700

Abstract

Objective: Mirikizumab, a p19-directed anti-interleukin-23 monoclonal antibody, has been evaluated as induction and maintenance therapy for moderately to severely active ulcerative colitis (UC). We conducted a systematic review and meta-analysis of randomized, placebo-controlled trials to quantify its efficacy and safety.

Methods: PubMed, Web of Science, and Scopus were searched for randomized controlled trials of mirikizumab versus placebo in UC. Two independent RCT programs met the eligibility criteria: the Phase 2 trial (Sandborn et al.,10; comprising a 12-week double-blind induction period and a double-blind 52-week maintenance re-randomization of induction responders, with the latter reported through its ClinicalTrials.gov registry record) and the Phase 3 LUCENT program (D'Haens et al.11;LUCENT-1 induction and LUCENT-2 maintenance). Outcome data (clinical remission, clinical response, endoscopic remission/response, symptomatic remission, histologic remission, and serious adverse events [SAEs]) were extracted from the primary ClinicalTrials.gov results records (NCT02589665, NCT03518086, and NCT03524092) and pooled using random-effects (DerSimonian–Laird) meta-analysis of risk ratios (RRs).

Results: During induction (12 weeks), mirikizumab increased clinical remission (RR 2.45, 95% CI 1.03–5.83; I^2=56%), clinical response (RR 1.98, 95% CI 1.05–3.73), and endoscopic remission (RR 1.72, 95% CI 1.36–2.18; I^2=0%) compared with placebo. During maintenance (weeks 40–52), mirikizumab increased clinical remission (RR 1.98, 95% CI 1.51–2.61) and endoscopic remission (RR 2.03, 95% CI 1.59–2.59; I^2=0%). Serious adverse events were numerically less frequent with mirikizumab than with placebo during both induction (RR 0.56, 95% CI 0.32–0.99) and maintenance (RR 0.36, 95% CI 0.19–0.70).

Conclusion: Mirikizumab is significantly more effective than placebo in inducing and maintaining clinical, endoscopic, symptomatic, and histologic remission in moderately to severely active UC, with a favorable serious adverse event profile relative to placebo. The evidence base remains limited to two independent RCT programs; the wider confidence intervals and moderate-to-high heterogeneity observed for some induction outcomes reflect the small Phase 2 sample and should be interpreted cautiously.

Keywords: Biologic therapy, interleukin-23, meta-analysis, mirikizumab, systematic review, ulcerative colitis.

INTRODUCTION

Ulcerative colitis (UC) is a chronic immune-mediated inflammatory disease of the colon whose global incidence and prevalence have risen steadily in recent decades.[1] A growing number of biologic and small-molecule therapies are now available for its treatment. Interleukin-23 (IL-23), through its p19 subunit, is a key driver of Th17-mediated mucosal inflammation in UC, and selective p19 blockade has emerged as an effective therapeutic strategy.[2] Mirikizumab is a humanized IgG4 monoclonal antibody that selectively binds to the p19 subunit of IL-23, thereby blocking its interaction with the IL-23 receptor.[3]

Mirikizumab was evaluated in a randomized, placebo-controlled Phase 2 dose-ranging study and subsequently in the Phase 3 LUCENT program (LUCENT-1 induction and LUCENT-2 maintenance), leading to regulatory approval for moderately to severely active UC in adults. Several narrative reviews and at least one prior systematic review/meta-analysis conducted by Abu Elainein et al.[4] have summarized this evidence base. The present analysis independently re-extracts arm-level data directly from the primary trial registry records (ClinicalTrials.gov), rather than relying solely on published summary statistics, to provide a fully transparent and reproducible data-extraction table and updated pooled estimates of clinical, endoscopic, histologic, and safety outcomes, separately for the induction and maintenance phases.

Objectives (PICO)

Population: Adults with moderately to severely active ulcerative colitis.

Intervention: Mirikizumab (any studied intravenous induction dose or subcutaneous maintenance dose).

Comparator: Placebo.
Outcomes: Clinical remission, clinical response, endoscopic remission, endoscopic improvement/response, symptomatic remission, histologic remission, and serious adverse events.

Study design: Randomized, double-blind, placebo-controlled trials.

METHODS

This review followed the PRISMA 2020 reporting guidelines.5
This review was registered with PROSPERO (registration number CRD420261485281).

Search strategy

PubMed was searched using combinations of "mirikizumab," "LY3074828," "ulcerative colitis," and randomized controlled trial filters. Web of Science Core Collection was searched using the topic-field query: TS=(mirikizumab OR LY3074828) AND TS=("ulcerative colitis") AND TS=(randomi* OR placebo) AND TS=("phase 2" OR "phase 3" OR LUCENT) NOT TS=(subgroup OR "post hoc" OR "post-hoc" OR "real-world" OR "case report" OR "case series" OR review OR editorial), which was iteratively narrowed from an initial unrestricted search of 344 records to 30 records after applying randomized controlled trial and exclusion terms. Scopus was searched on August 22, 2026, using an analogous query restricted to the title, abstract, and keywords: TITLE-ABS-KEY(mirikizumab OR "LY3074828") AND TITLE-ABS-KEY("ulcerative colitis") AND TITLE-ABS-KEY(randomi* OR placebo) NOT TITLE-ABS-KEY(subgroup OR "post hoc" OR "post-hoc" OR "real-world" OR "case report" OR "case series" OR review OR editorial OR pharmacovigilance OR Crohn), returning 35 records; every record corresponded to one of the four already identified primary trial reports or was a secondary, mechanistic, or commentary analysis of those reports, confirming that no additional eligible randomized controlled trial was identified. As a further supplementary check, the Cochrane Central Register of Controlled Trials (CENTRAL) was also searched for "mirikizumab AND ulcerative colitis," returning 246 trial records; every record corresponded to one of the four already identified primary trial reports, a conference abstract or biomarker subanalysis of those reports, or an unrelated combination-therapy trial (e.g., mirikizumab plus tirzepatide or eltrekibart), confirming that no eligible placebo-controlled RCT had been missed.

Eligibility criteria

Randomized, double-blind, placebo-controlled trials of mirikizumab in adults with moderately to severely active UC reporting at least one efficacy or safety outcome of interest were eligible. Conference abstracts were included only when no corresponding full-text publication existed; when data from an abstract were superseded by a full-text report of the same trial, only the full-text data were extracted. Studies of mirikizumab in Crohn's disease, pharmacokinetic/exposure–response modeling studies, nonrandomized or open-label extension studies without a placebo comparator, and secondary, subgroup, or post hoc analyses of already included trials were excluded from quantitative pooling.

Data extraction

Arm-level participant counts and outcome event counts were extracted directly from the sponsor-submitted results records on ClinicalTrials.gov for each trial (NCT02589665, NCT03518086, and NCT03524092), which report exact per-arm percentages and denominators from which integer event counts were derived for all prespecified efficacy outcomes and adverse-event tables. This source was used in preference to secondary journal figures because it provides complete arm-by-arm denominators for every dose group, including doses not carried forward to Phase 3. Baseline demographic and disease characteristics (Table 1), which are not reported in the ClinicalTrials.gov registry records, were instead extracted directly from the original peer-reviewed trial publications.[6]

Risk of bias assessment

Risk of bias was assessed using the Cochrane RoB 2.0 tool across five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selective reporting. Assessments are summarized in Table 2.[7]

Table 1. Baseline demographic and disease characteristics of the induction-phase trials. *NR, not reported. Table 1a presents baseline characteristics for only the placebo and mirikizumab 200-mg arms of the Phase 2 trial—the two arms included in the pooled induction analyses (Table 3a)—and for both randomized arms of LUCENT-1. Baseline characteristics for the Phase 2 50-mg and 600-mg induction arms, which were not carried forward to Phase 3 and were not included in the pooled analyses, are available in the original publication (Sandborn et al.,10 Table 1).*

	Sandborn 2020 Placebo (n=63)	Sandborn 2020 Mirikizumab 200 mg (n=62)	LUCENT-1 Placebo (n=294)	LUCENT-1 Mirikizumab 300 mg (n=868)
Age, years, mean (SD)	42.6 (13.5)	43.4 (14.7)	41.3 (13.8)	42.9 (13.9)
Female sex, n (%)	27 (42.9)	25 (40.3)	129 (43.9)†	338 (38.9)
Disease duration, years, mean (SD)	9.5 (9.6)	9.0 (9.0)	6.9 (7.0)	7.2 (6.7)
Modified Mayo score (9-point), mean (SD)	6.7 (1.2)	6.4 (1.4)	NR	NR
Severe modified Mayo score, n/N (%)	NR	NR	155/293 (52.9)	463/868 (53.3)
Endoscopic subscore indicating severe disease, n/N (%)	47/63 (74.6)	41/62 (66.1)	200/293 (68.3)	574/868 (66.1)
C-reactive protein, median (IQR), mg/L	3.9 (1.1–11.2)	3.6 (1.4–13.7)	4.2 (1.2–9.5)	4.1 (1.5–9.6)
Fecal calprotectin, median (IQR), µg/g	1353 (618–2481)	1560 (399–2443)	1471.5 (626.5–2944.5)	1559.0 (634.0–3210.0)
Corticosteroid use at baseline, n (%)	33 (52.4)	25 (40.3)	113 (38.4)	351 (40.4)
Previous biologic/tofacitinib treatment failure, n (%)	NR	NR	118 (40.1)	361 (41.6)
IBDQ score, mean (SD)	124.1 (29.8)	133.0 (34.7)	NR	NR

IBDQ, Inflammatory Bowel Disease Questionnaire; IQR, interquartile range; NR, not reported; SD, standard deviation.

Table 2. Cochrane RoB 2.0 domain-level risk-of-bias assessment

Study	D1	D2	D3	D4	D5	Overall
Sandborn 2020 (Phase 2)	Low	Low	Some concerns	Low	Low	Some concerns
Phase 2 maintenance re-randomization (ClinicalTrials.gov record only)	Low	Low	Some concerns	Low	Low	Some concerns
D'Haens et al.11 2023, LUCENT-1 (induction)	Low	Low	Low	Low	Low	Low
D'Haens et al.11 2023, LUCENT-2 (maintenance)	Some concerns	Low	Low	Low	Low	Some concerns

D1, randomization process; D2, deviations from intended interventions; D3, missing outcome data; D4, measurement of the outcome; D5, selective reporting; RoB, risk of bias.

Table 3. Characteristics of the included trial reports

Trial (report)	Registry ID	Phase	Randomized arms (mirikizumab dose)/route vs placebo	Duration	Primary endpoint
Sandborn10 2020 (Phase 2, induction)	NCT02589665	Induction	Placebo (n=63); mirikizumab 50 mg (n=63), 42.9 (13.9) 200 mg (n=62), or 600 mg (n=61) IV at weeks 0, 4, and 8	12 weeks	Clinical remission (Mayo score)
Phase 2 maintenance re-randomization (ClinicalTrials.gov record only)	NCT02589665	Maintenance	Re-randomized induction responders: placebo (n=13); mirikizumab 200 mg SC Q4W (n=47) or Q12W (n=46)	52 weeks	Endoscopic/ symptomatic remission
D'Haens et al.11 2023, LUCENT-1 (Phase 3, induction)	NCT03518086	Induction	Randomized 3:1 to mirikizumab 300 mg IV (n=868) or placebo (n=294) at weeks 0, 4, and 8	12 weeks	Clinical remission (Mayo score)
D'Haens et al.,11 LUCENT-2 (Phase 3, maintenance)	NCT03524092	Maintenance	LUCENT-1 responders re-randomized 2:1 to mirikizumab 200 mg SC Q4W (n=365) or placebo (n=179)	40 weeks	Clinical remission (Mayo score)

Statistical analysis

For each outcome, study-level risk ratios (RRs) with 95% confidence intervals were calculated on the log scale; a continuity correction of 0.5 was applied to any study with a zero cell. When two independent trials contributed data for the same phase (induction or maintenance) and a comparable dose, estimates were pooled using the DerSimonian–Laird random-effects model.[8] This approach was selected because of the anticipated clinical heterogeneity in dose (200 mg vs 300 mg intravenous induction; 200 mg subcutaneous maintenance schedules) and design between the Phase 2 and Phase 3 programs. Heterogeneity was quantified using the I^2 statistic and τ^2. When only a single trial reported an outcome (e.g., histologic remission, reported only in the LUCENT program), the unpooled study-level RR is presented. All pooled estimates and forest plots were generated using Cochrane RevMan 5.4 (Review Manager, The Cochrane Collaboration), with the inverse-variance method for the random-effects model described above.

Certainty of evidence

The certainty of evidence for each outcome was rated using the GRADE framework.[9] Randomized evidence was initially rated as "high" and downgraded for risk of bias, inconsistency ($I^2 \geq 50\%$), indirectness, and imprecision according to prespecified rules detailed in Supplementary Table S1.

RESULTS

Study selection

The search and screening process is summarized in Figure 1 (PRISMA flow diagram). After removing records concerning Crohn's disease, pharmacokinetic bridging in healthy volunteers, a mismatched drug (guselkumab), nonrandomized pediatric studies, or secondary/subgroup analyses of already identified trials, two independent randomized, placebo-controlled RCT programs met the inclusion criteria: the Phase 2 trial (with induction reported by Sandborn et al.[10] and the double-blind maintenance re-randomization of induction responders reported only in the trial's ClinicalTrials.gov registry record, NCT02589665.10, rather than in a dedicated maintenance-phase journal publication) and the Phase 3 LUCENT program (D'Haens et al.11; comprising LUCENT-1 induction and LUCENT-2 maintenance.10,11).

Study characteristics

Table 3 summarizes the four trial reports arising from the two included RCT programs. The Phase 2 trial (NCT02589665) randomized 249 participants to placebo or mirikizumab 50, 200, or 600 mg intravenously every 4 weeks for a 12-week induction period; induction responders were re-randomized to placebo, 200 mg subcutaneously every 4 weeks, or 200 mg subcutaneously every 12 weeks for a 52-week maintenance period (n=13 in the placebo group, because only responders were re-randomized). LUCENT-1 (NCT03518086) randomized 1,281 participants in a 3:1 ratio to mirikizumab 300 mg intravenously or placebo for a 12-week induction period. LUCENT-2 (NCT03524092) re-randomized LUCENT-1 induction responders in a 2:1 ratio to continue mirikizumab 200 mg subcutaneously or switch to placebo for an additional 40 weeks. A related open-label substudy of the Phase 2 program, reporting rescue extended-induction and extended-maintenance treatment for the subset of patients who did not respond to blinded induction therapy (Sandborn et al.10), was identified but excluded from the quantitative synthesis because of its nonblinded, non-placebo-controlled design, consistent with the eligibility criteria in Section 2.2.

Baseline demographic and disease characteristics for the two induc-

Table 4. Pooled induction-phase efficacy outcomes (mirikizumab vs placebo, week 12). *Endoscopic improvement/response combines two nonidentically named endpoints (Phase 2 "endoscopic improvement" vs LUCENT "endoscopic response"). Both are based on a reduction in the Mayo endoscopic subscore; however, this definitional difference is a source of indirectness.*

Outcome	k	Mirikizumab (events/N)	Placebo (events/N)	RR (95% CI)	I^2
Clinical remission	2	224/930	42/357	2.45 (1.03–5.83)	56%
Clinical response	2	588/930	137/357	1.98 (1.05–3.73)	82%
Endoscopic remission	2	317/930	63/357	1.72 (1.36–2.18)	0%
Symptomatic remission	2	431/930	95/357	2.02 (1.20–3.41)	72%
Endoscopic improvement/response	2	500/930	110/357	2.43 (0.81–7.28)	79%
Histologic remission (Geboes)	1	254/868	46/294	1.87 (1.41–2.49)	N/A

CI, confidence interval; I^2, heterogeneity statistic; k, number of studies; N, total number of participants; RR, risk ratio.

Table 5. Pooled maintenance-phase efficacy outcomes (mirikizumab vs placebo, weeks 40–52). *Endoscopic improvement/response combines two nonidentically named endpoints (Phase 2 "endoscopic improvement" vs LUCENT "endoscopic response"). Both are based on a reduction in the Mayo endoscopic subscore; however, this definitional difference is a source of indirectness.*

Outcome	k	Mirikizumab (events/N)	Placebo (events/N)	RR (95% CI)	I^2
Clinical remission	1	182/365	45/179	1.98 (1.51–2.61)	N/A
Endoscopic remission	2	234/458	53/192	2.03 (1.59–2.59)	0%
Symptomatic remission	2	325/458	78/192	1.70 (1.35–2.13)	14%
Clinical response	1	293/365	88/179	1.63 (1.40–1.91)	N/A
Endoscopic improvement/response	2	314/458	75/192	1.80 (1.50–2.17)	0%
Histologic remission (Geboes)	1	177/365	44/179	1.97 (1.49–2.60)	N/A

CI, confidence interval; I^2, heterogeneity statistic; k, number of studies; N, total number of participants; RR, risk ratio.

Table 6. Pooled serious adverse events (mirikizumab vs placebo)

Outcome	k	Mirikizumab (events/N)	Placebo (events/N)	RR (95% CI)	I^2
Serious adverse events (induction)	2	29/1020	19/384	0.56 (0.32–0.99)	0%
Serious adverse events (maintenance)	2	16/482	18/205	0.36 (0.19–0.70)	0%

CI, confidence interval; I^2, heterogeneity statistic; k, number of studies; N, total number of participants; RR, risk ratio.

tion-phase trials, extracted directly from the original trial publications (Sandborn et al.,[10] Table 1; D'Haens et al.,[11] Table 1), are summarized in Table 1. Corresponding baseline data for the two maintenance-phase re-randomizations (the Phase 2 responders re-randomized to placebo or mirikizumab and LUCENT-2) were not included because the baseline characteristics of these re-randomized subsets were not separately reported in an accessible peer-reviewed source.

Risk of bias

All four trial reports (arising from the two included RCT programs) were judged to have a low risk of bias for the randomization process, except LUCENT-2, which was rated as having "some concerns" because its maintenance population comprised only re-randomized induction responders rather than a treatment-naive randomized cohort. The trials were also judged to have a low risk of bias for deviations from intended interventions and measurement of the outcome, based on centrally read, blinded endoscopy and standardized Mayo/Geboes scoring. The main source of "some concerns" was missing outcome data related to the small placebo arm retained in the Phase 2 maintenance extension (n=13) and the ME2 China cohorts excluded from the confirmatory efficacy analysis in LUCENT-1/2. Domain-level judgments are summarized graphically in Figure 2 and in full in Table 3.

Induction outcomes

Mirikizumab significantly increased clinical remission, clinical response, endoscopic remission, and symptomatic remission relative to placebo at week 12 (Table 4, Figures 3–6). Heterogeneity was low for endoscopic remission (I^2=0%) but moderate to high for clinical remission, clinical response, and endoscopic improvement/response (Figure 7), reflecting the disproportionately large treatment effect observed in the small Phase 2 200-mg arm (e.g., clinical remission, 22.6% vs 4.8%; RR≈4.7) compared with the more precisely estimated effect in the LUCENT-1 300-mg arm (24.2% vs 13.3%; RR≈1.8). Histologic remission, reported only in LUCENT-1, was significantly higher with mirikizumab than with placebo (29.3% vs 15.6%; RR 1.87, 95% CI 1.41–2.49, Figure 8), consistent with independently reported histologic resolution data across the LUCENT program.

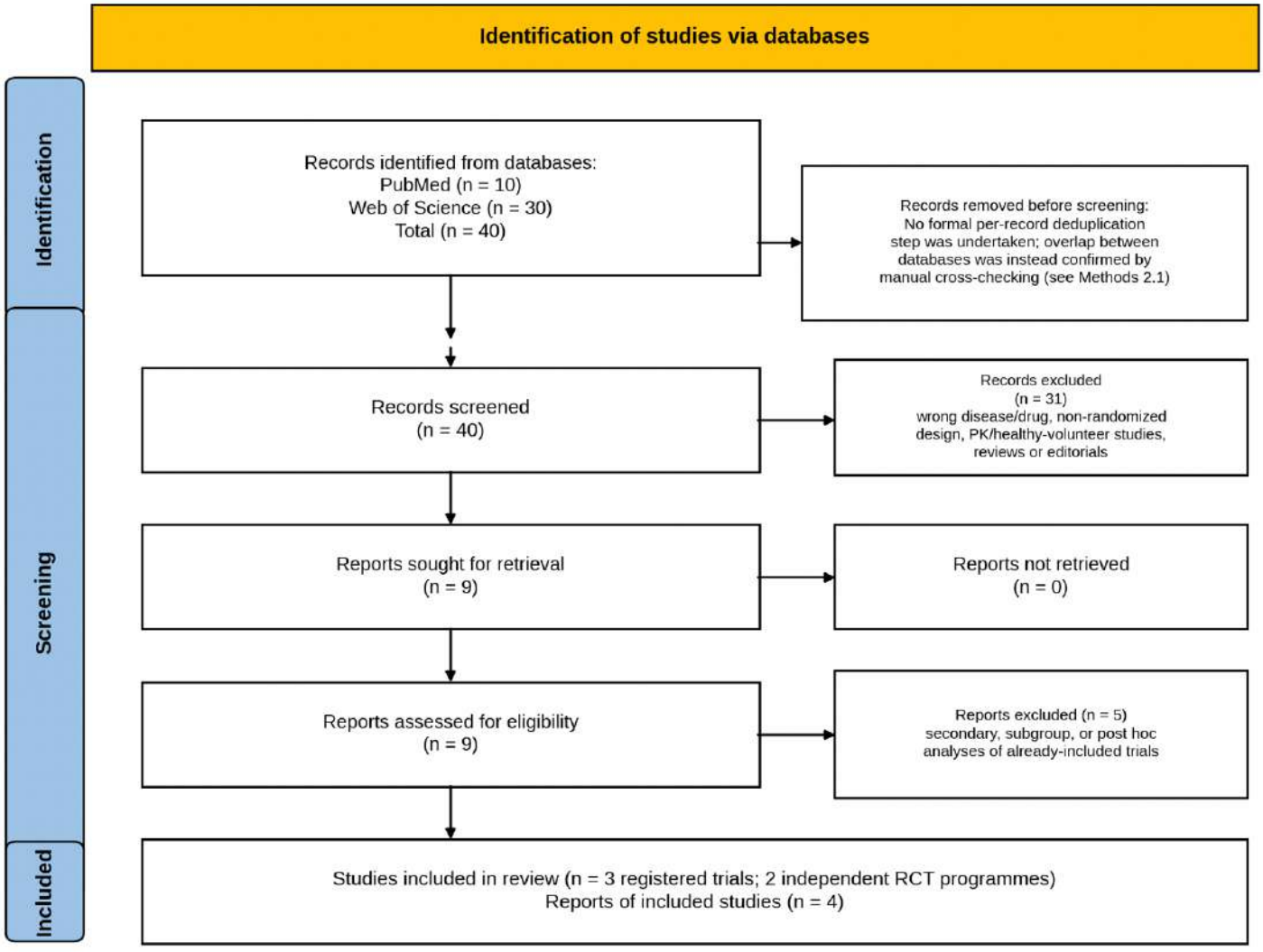

Figure 1. PRISMA 2020 flow diagram.

Maintenance outcomes

During the maintenance phase, mirikizumab was associated with approximately 1.6- to 2.0-fold higher rates of clinical remission, clinical response, endoscopic remission, endoscopic improvement/response, symptomatic remission, and histologic remission compared with placebo (Table 5, Figures 9-14).12 Heterogeneity was low when two trials contributed data (I^2=0–14%). Clinical remission and clinical response were reported only in LUCENT-2 because the Phase 2 maintenance extension did not reassess the Physician's Global Assessment component required for the full Mayo score definitions of clinical remission and response.

Safety

Serious adverse events were numerically less frequent with mirikizumab than with placebo during both induction (2.8% vs 5.3% pooled) and maintenance (3.3% vs 8.3% pooled), (Table 6, Figures 15-16) consistent with fewer disease-related complications (e.g., UC exacerbation, colectomy, hospitalization) among effectively treated patients rather than a direct drug-safety signal. No deaths were reported in any arm of any included trial. Discontinuation due to adverse events was numerically more frequent in the placebo arms of both LUCENT-1 (23/321 vs 15/958) and the Phase 2 induction trial.[13]

Certainty of evidence (GRADE)

Applying the GRADE criteria, certainty was downgraded for risk of bias when the Phase 2 maintenance re-randomization, with its very small placebo arm (n=13) and associated missing-outcome-data concerns, contributed to an outcome; for inconsistency when $I^2 \geq 50\%$; for indirectness when the composite "endoscopic improvement/response" outcome combined two nonidentically named endpoints; and for imprecision when a 95% CI approached or crossed the null or when only a single trial was available. Certainty ranged from "high" for induction endoscopic remission, which was homogeneous, based on ample events, and had a CI far from the null, to "very low" for induction endoscopic improvement/response, for which the pooled 95% CI crossed the null in the presence of substantial heterogeneity. Most efficacy outcomes were rated as having "low" or "moderate" certainty, chiefly reflecting the small number of contributing trials and, for maintenance outcomes, the very small placebo arm (n=13) in the Phase 2 maintenance re-randomization. The full GRADE Summary-of-Findings table, including domain-by-domain ratings and rationale, is provided in Supplementary Table S1.

DISCUSSION

This meta-analysis, based on arm-level data extracted directly from

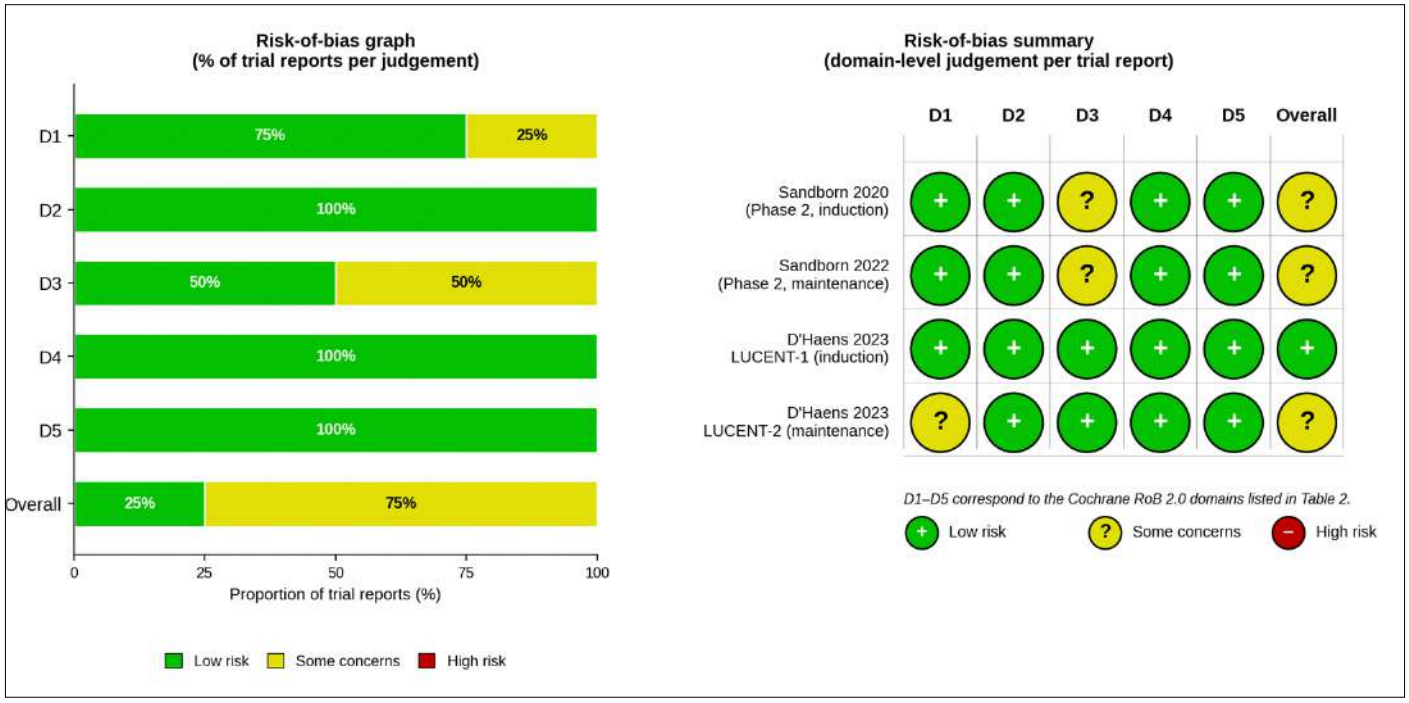

Figure 2. Risk-of-bias graph and summary (Cochrane Ro'B 2.0).

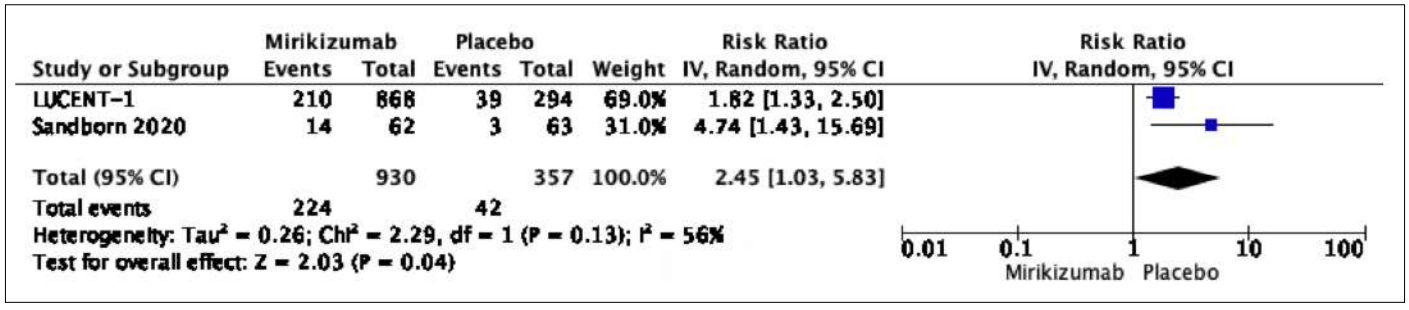

Figure 3. Forest plot of clinical remission during induction.

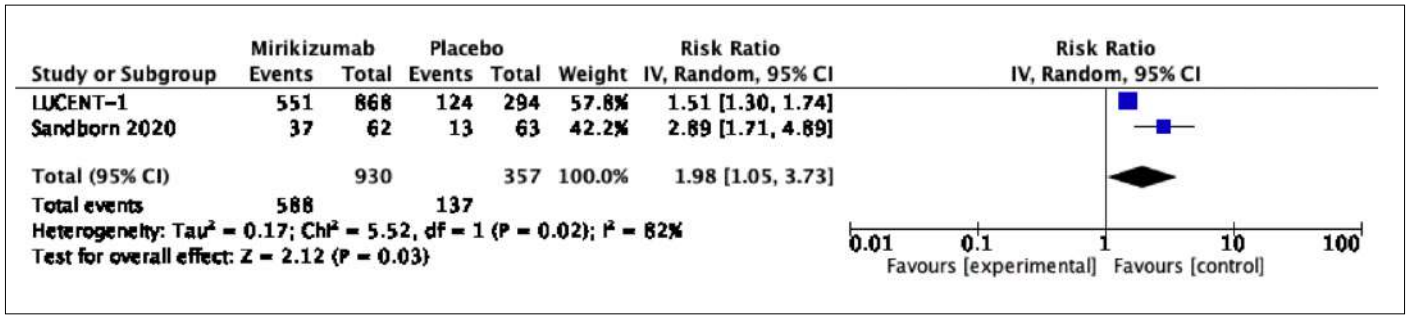

Figure 4. Forest plot of clinical response during induction.

primary trial registry records, confirms that mirikizumab significantly improves clinical, endoscopic, symptomatic, and histologic outcomes compared with placebo during both induction and maintenance treatment of moderately to severely active UC, with no signal of an increased risk of serious adverse events. However, for three induction outcomes—clinical remission (I^2=56%), clinical response (I^2=82%), and endoscopic improvement/response (I^2=79%)—this overall conclusion is based on moderately to highly heterogeneous pooled estimates and should therefore be interpreted as an average across a small, high-effect Phase 2 trial and a much larger, more conservative Phase 3

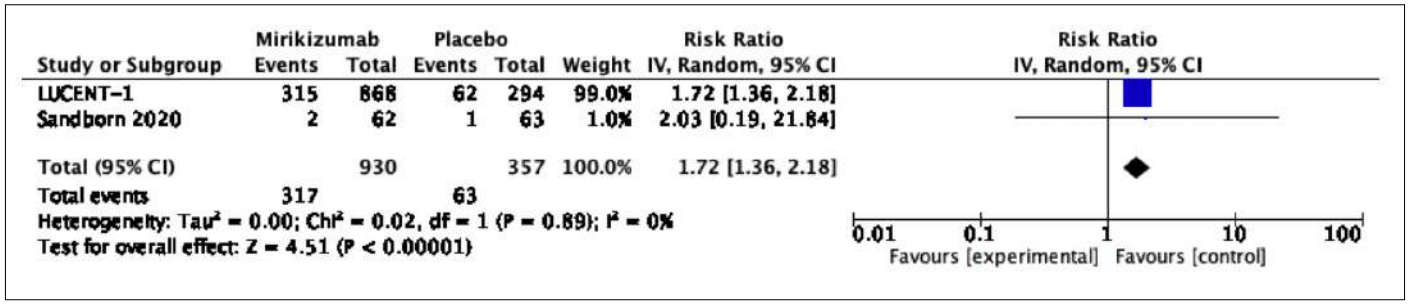

Figure 5. Forest plot of endoscopic remission during induction.

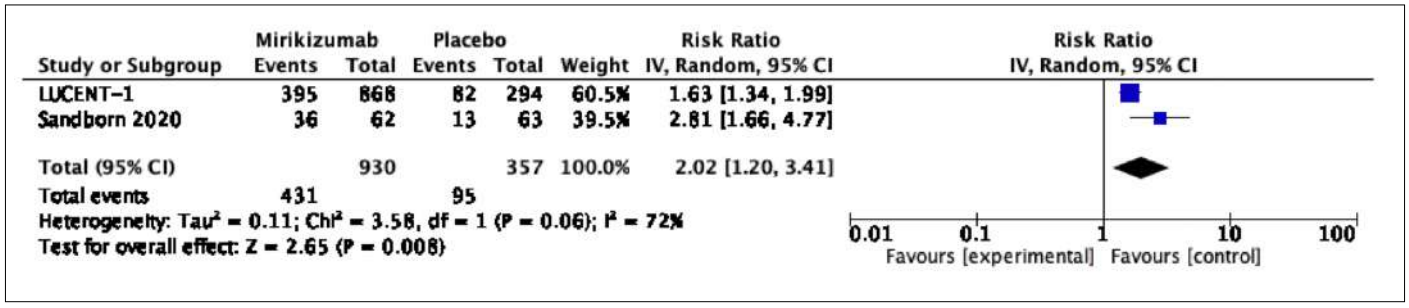

Figure 6. Forest plot of symptomatic remission during induction.

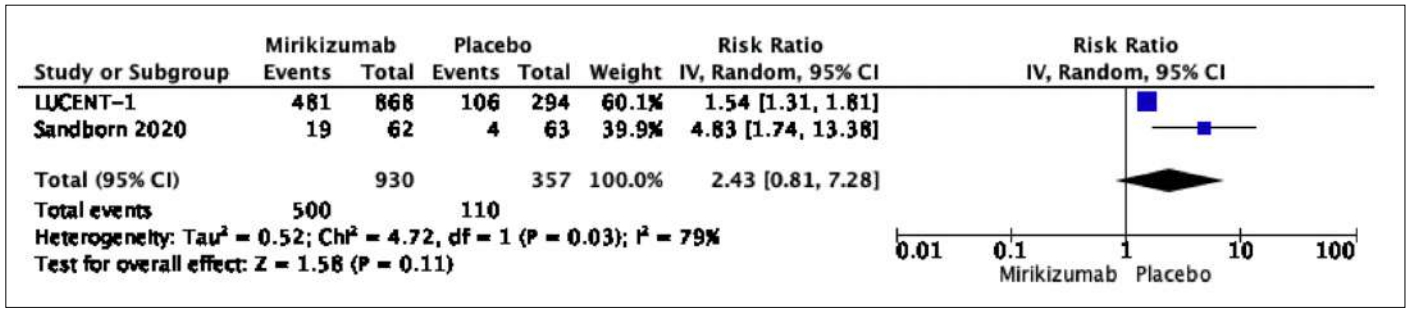

Figure 7. Forest plot of endoscopic improvement/response during induction. Endoscopic improvement/response combines two nonidentically named endpoints (Phase 2 "endoscopic improvement" vs LUCENT "endoscopic response"). Both are based on a reduction in the Mayo endoscopic subscore; however, this definitional difference is a source of indirectness.

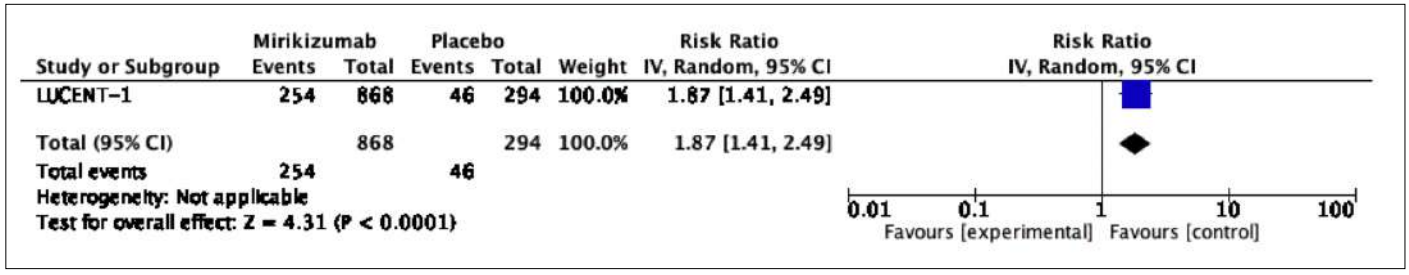

Figure 8. Forest plot of histologic remission during induction (single study, LUCENT-1).

trial rather than as a single homogeneous treatment effect (see Sections 3.4 and 4.2). Our pooled estimate for induction endoscopic remission (RR 1.72, 95% CI 1.36–2.18; I^2=0%) is numerically identical to that reported in the independent meta-analysis by Abu Elainein et al.[4] (RR 1.72, 95% CI 1.36–2.17; I^2=0%), despite the two analyses using different data-extraction sources (published article data vs ClinicalTrials.gov registry data).[4]

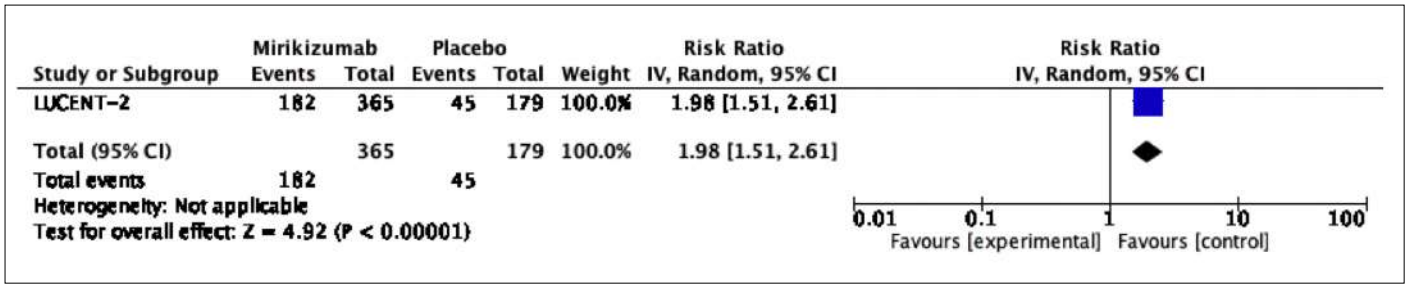

Figure 9. Forest plot of clinical remission during maintenance (single study, LUCENT-2).

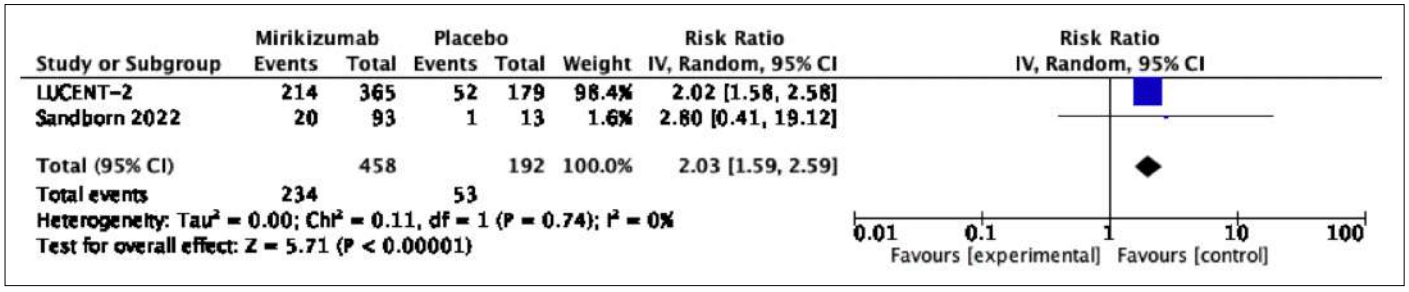

Figure 10. Forest plot of endoscopic remission during maintenance.

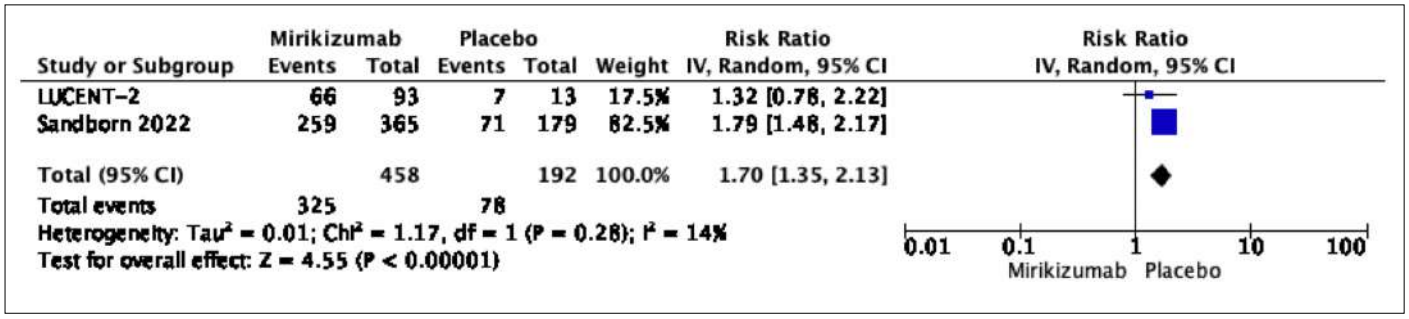

Figure 11. Forest plot of symptomatic remission during maintenance.

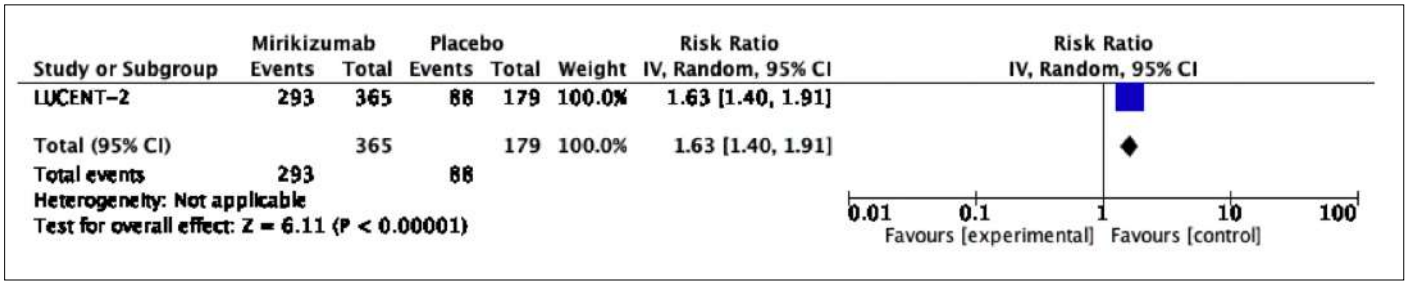

Figure 12. Forest plot of clinical response during maintenance (single study, LUCENT-2).'"

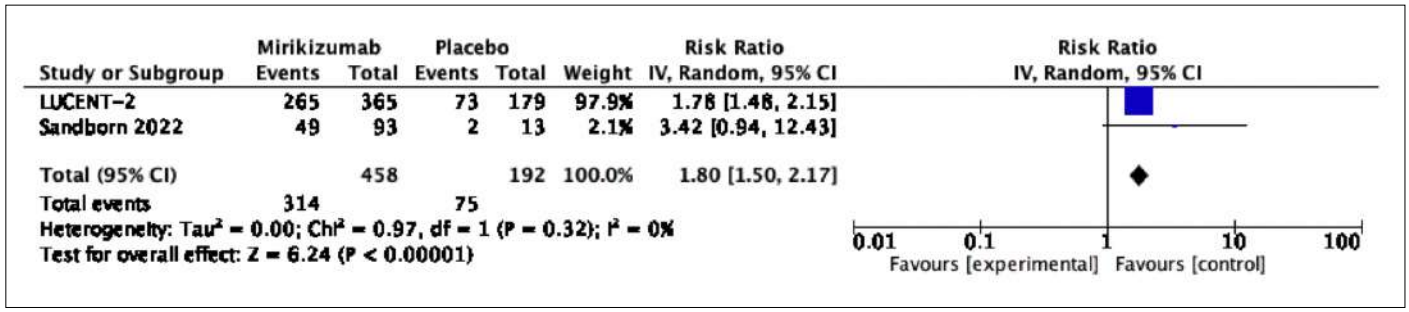

Figure 13. Forest plot of endoscopic improvement/response during maintenance. Endoscopic improvement/response combines two nonidentically named endpoints (Phase 2 "endoscopic improvement" vs LUCENT "endoscopic response"). Both are based on a reduction in the Mayo endoscopic subscore; however, this definitional difference is a source of indirectness.

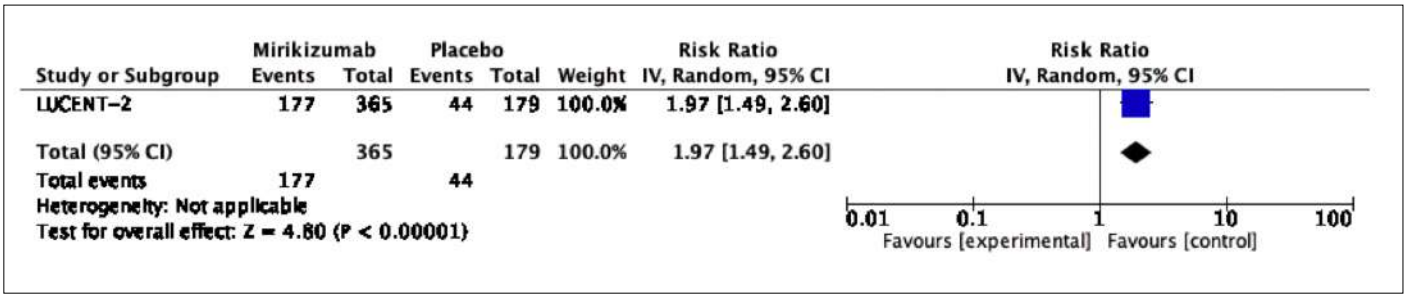

Figure 14. Forest plot of histologic remission during maintenance (single study, LUCENT-2).'

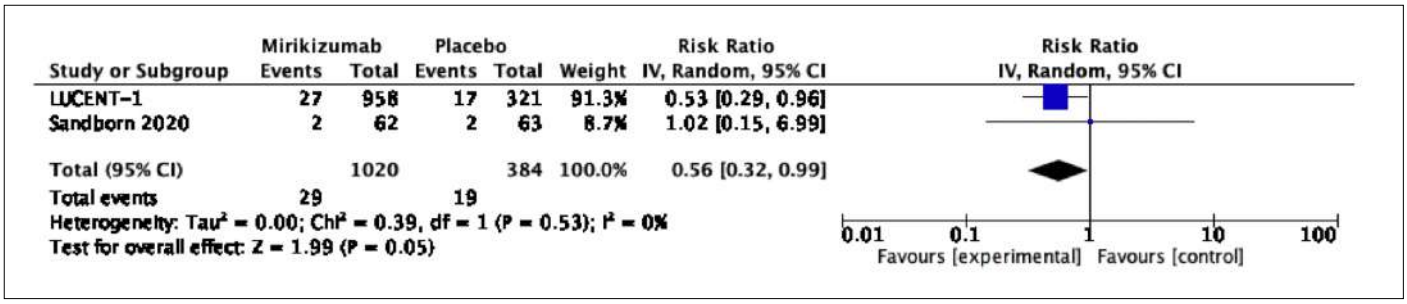

Figure 15. Forest plot of serious adverse events during induction.

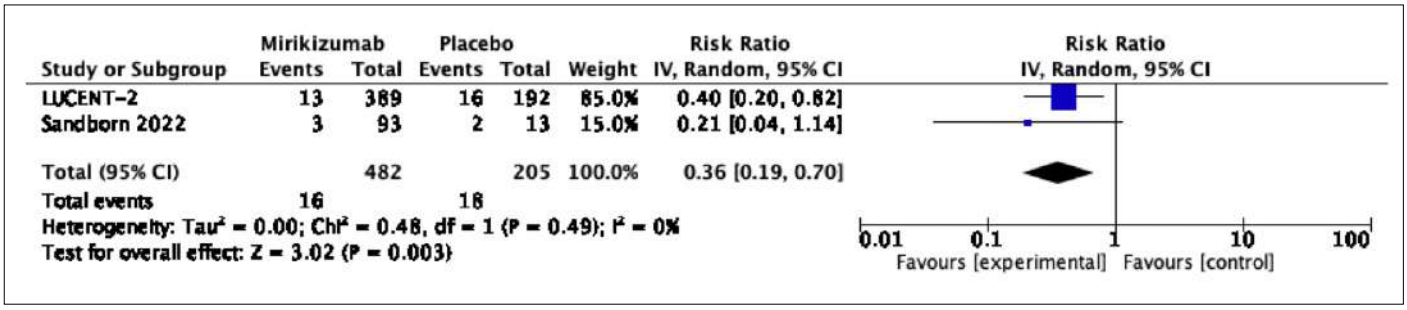

Figure 16. Forest plot of serious adverse events during maintenance.

Rather than simply reanalyzing the same data, our review provides a methodologically updated, GRADE-rated synthesis of the evidence, as detailed below. Our updated search (Section 2.1), conducted on August 22, 2026, postdates that of Abu Elainein et al.[4] by approximately 16 months and independently confirms that no additional eligible trial has since been published. This review necessarily draws on the same finite evidence base as Abu Elainein et al.,[4] currently comprising only two independent placebo-controlled RCT programs of mirikizumab in UC; our supplementary Cochrane Library search (Section 2.1) likewise confirmed that no additional eligible trial has become available. Some overlap in the underlying evidence base between contemporaneous systematic reviews addressing the same clinical question is expected and has been documented in the broader methodological literature.[14] The two analyses nonetheless differ methodologically in several respects that extend beyond simply reanalyzing the same trials: arm-level data were independently re-extracted directly from the primary ClinicalTrials.gov registry records rather than from published summary figures alone, yielding a fully transparent and reproducible extraction table (Table 1) across all tested dose groups, including doses not carried forward into Phase 3; risk of bias was assessed using the Cochrane RoB 2.0 tool rather than the older RoB1 tool; the approved clinical dosing regimen (300 mg IV induction/200 mg SC maintenance) was pooled as the primary comparison rather than combining all tested doses; a single prespecified random-effects model was applied throughout rather than switching between fixed- and random-effects models post hoc according to the observed I^2; and formal GRADE certainty-of-evidence ratings (Section 3.7) were assigned to every pooled outcome. Subgroup analysis according to prior biologic/JAK inhibitor exposure—a gap explicitly identified by Abu Elainein et al.4 as a priority for future research—was not undertaken in the present analysis and remains a direction for future work. Despite these methodological differences, both analyses reached the same overall conclusion that mirikizumab is superior to placebo.

The wider confidence intervals and greater heterogeneity observed for clinical remission, clinical response, and endoscopic improvement/response during induction are attributable to the small sample size and disproportionately large point estimate in the Phase 2 200-mg arm. Because random-effects pooling combines a small, high-variance early-phase trial with a much larger, more precise Phase 3 trial, the pooled

interval is appropriately wider. Clinicians should place greater weight on the LUCENT-1/2 (Phase 3, N>1,000) estimates when applying these results because these trials used the dose ultimately approved for clinical use (300 mg IV induction/200 mg SC maintenance) in a substantially larger and more representative population.

Limitations

This analysis has several limitations that warrant consideration. Only two independent RCT programs (four publications) were available for pooling; this reflects the current size of the evidence base for a relatively recently approved therapy rather than a limitation of the search strategy. The Phase 2 and Phase 3 trials used different mirikizumab doses/routes (200 mg vs 300 mg IV induction) and, in some instances, different clinical remission scoring conventions, introducing clinical heterogeneity that random-effects modeling only partially addresses. The Phase 2 maintenance placebo arm was very small (n=13), as it comprised only placebo-treated induction responders who were re-randomized, thereby limiting the precision of maintenance outcomes derived from that trial. Maintenance efficacy and safety should therefore be interpreted primarily in light of the LUCENT-2 results (placebo n=179 vs mirikizumab n=365), which provide a substantially larger and more precise basis for clinical inference. Long-term (>1 year) efficacy and safety data from the LUCENT-3 open-label extension were not pooled because that study lacked a placebo comparator beyond the initial randomized period. Study selection, data extraction, and GRADE certainty rating were divided between two authors (GD and AS), each following the prespecified eligibility, extraction, and rating rules described above, with the outputs reviewed by the other author before finalization. Because these steps were divided rather than independently duplicated, no formal disagreement-adjudication process was required; we acknowledge this as a deviation from best-practice duplicate review. The composite "endoscopic improvement/response" outcome combines two nonidentically named endpoints (Phase 2 "endoscopic improvement" vs LUCENT "endoscopic response"). Although both are based on a reduction in the Mayo endoscopic subscore, this definitional non-equivalence is a source of indirectness and likely contributes to the high heterogeneity and GRADE "very low"/"low" certainty ratings for this specific outcome (Section 3.7). Subgroup analysis according to prior biologic/JAK inhibitor exposure was not undertaken.

CONCLUSION

Mirikizumab is an effective and well-tolerated induction and maintenance therapy for moderately to severely active ulcerative colitis, with consistent benefits across clinical, endoscopic, symptomatic, and histologic domains. These conclusions are drawn from only two independent RCT programs; accordingly, the precision and generalizability of the pooled estimates are limited, and confirmatory evidence from additional independent trials and long-term real-world cohorts would strengthen confidence in these findings before they are considered definitive. Further head-to-head and longer-term randomized studies would help refine dose-specific effect estimates and clarify comparative efficacy against other advanced therapies.[15]

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept – B.F.A., M.A.Y., S.F.B.; Design – M.A.Y., K.D.; Supervision – G.D., B.F.A.; Resource – B.Ç.; Materials – A.S., B.F.A., K.D., S.K.; Data Collection and/or Processing – B.Ç., S.F.B., F.A.; Analysis and/or Interpretation – G.D., A.S., B.F.A., A.Ç.Ö., M.A.Y.; Literature Review – G.D., S.K.; Writing – A.S., M.A.Y., K.D.; Critical Review – B.Ç., F.A.

Trial Registration: PROSPERO (Registration Number CRD420261485281).

REFERENCES

1. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet. 2017;390(10114):2769-2778. Erratum in: Lancet. 2020;396(10256):e56. [CrossRef]
2. Neurath MF. IL-23 in inflammatory bowel diseases and colon cancer. Cytokine Growth Factor Rev. 2019;45:1-8. [CrossRef]
3. Feuerstein JD, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S; AGA Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. [CrossRef]
4. Elainein MAA, ElSherefy SS, Yousef NM, et al. Efficacy and safety of Mirikizumab for ulcerative colitis: a systematic review and meta-analysis of randomized controlled trials. BMC Gastroenterol. 2025;25(1):307. [CrossRef]
5. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. [CrossRef]
6. Sandborn WJ, Ferrante M, Bhandari BR, et al. Efficacy and Safety of Mirikizumab in a Randomized Phase 2 Study of Patients With Ulcerative Colitis. Gastroenterology. 2020;158(3):537-549.e10. [CrossRef]
7. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. [CrossRef]
8. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-188. [CrossRef]
9. Guyatt GH, Oxman AD, Vist GE, et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-926. [CrossRef]
10. Sandborn WJ, Ferrante M, Bhandari BR, et al. Efficacy and Safety of Continued Treatment With Mirikizumab in a Phase 2 Trial of Patients With Ulcerative Colitis. Clin Gastroenterol Hepatol. 2022;20(1):105-115.e14. [CrossRef]
11. D'Haens G, Dubinsky M, Kobayashi T, et al.; LUCENT Study Group. Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2023;388(26):2444-2455. Erratum in: N Engl J Med. 2023;389(8):772. [CrossRef]
12. Magro F, Pai RK, Kobayashi T, et al. Resolving Histological Inflammation in Ulcerative Colitis With Mirikizumab in the LUCENT Induction and Maintenance Trial Programmes. J Crohns Colitis. 2023;17(9):1457-1470. [CrossRef]
13. Ran Z, Chen Y, Miao Y, et al. Mirikizumab as Induction and Maintenance Therapy in Chinese Patients with Ulcerative Colitis: A Subpopulation Analysis of the Randomized, Global Phase 3 LUCENT-1 and LUCENT-2 Trials. BioDrugs. 2026;40(4):733-745. Erratum in: BioDrugs. 2026;40(4):759-761. [CrossRef]
14. Helfer B, Prosser A, Samara MT, et al. Recent meta-analyses neglect previous systematic reviews and meta-analyses about the same topic: a systematic examination. BMC Med. 2015;13:82. [CrossRef]
15. Ananthakrishnan AN, Murad MH, Scott FI, et al. Comparative Efficacy of Advanced Therapies for Management of Moderate-to-Severe Ulcerative Colitis: 2024 American Gastroenterological Association Evidence Synthesis. Gastroenterology. 2024;167(7):1460-1482. [CrossRef]

Supplementary Table 1. GRADE Summary of Findings for all 14 pooled and single-study outcomes

Phase	Outcome	RR (95% CI)	I^2	k	Certainty	Rationale
Induction	Clinical remission	2.45 (1.03–5.83)	56.3%	2	Low	I^2=56% (moderate-to-high inconsistency); lower CI bound (1.03) close to the null; relatively few events (~272).
Induction	Clinical response	1.98 (1.05–3.73)	81.9%	2	Low	I^2=82% (high inconsistency); lower CI bound (1.05) close to the null.
Induction	Endoscopic remission	1.72 (1.36–2.18)	0%	2	High	Homogeneous (I^2=0%), with ample events and a CI far from the null, indicating robust evidence.
Induction	Symptomatic remission	2.02 (1.20–3.41)	72.1%	2	Moderate	I^2=72% (high inconsistency); however, the lower CI bound (1.20) is sufficiently far from the null.
Induction	Endoscopic improvement/ response (composite)	2.43 (0.81–7.28)	78.8%	2	Very low	The 95% CI crosses the null (not statistically significant); Phase 2 "endoscopic improvement" and LUCENT-1 "endoscopic response" are nonidentically named endpoints (indirectness); I^2=79% (high inconsistency).
Induction	Histologic remission (single study)	1.87 (1.41–2.49)	N/A	1	Moderate	Reported only in LUCENT-1 (single-study default imprecision downgrade).
Induction	Serious adverse events (SAEs)	0.56 (0.32–0.99)	0%	2	Moderate	Rare events (~48 total events); upper CI bound (0.99) close to the null.
Maintenance	Clinical remission (single study, LUCENT-2)	1.98 (1.51–2.61)	N/A	1	Moderate	Reported only in LUCENT-2 (single-study default imprecision downgrade); low risk of bias (double-blind RCT).
Maintenance	Endoscopic remission	2.03 (1.59–2.59)	0%	2	Moderate	Includes the Phase 2 maintenance re-randomization (RoB 2.0: "some concerns," driven by its small placebo arm [n=13] and risk of missing outcome data); otherwise homogeneous, with a CI far from the null.
Maintenance	Symptomatic remission	1.70 (1.35–2.13)	14.4%	2	Moderate	Includes the Phase 2 maintenance re-randomization (RoB 2.0: "some concerns," due to the small placebo arm [n=13] and risk of missing outcome data).
Maintenance	Clinical response (single study, LUCENT-2)	1.63 (1.40–1.91)	N/A	1	Moderate	Reported only in LUCENT-2 (single-study default imprecision downgrade).
Maintenance	Endoscopic improvement/ response (composite)	1.80 (1.50–2.17)	0%	2	Low	Includes the Phase 2 maintenance re-randomization (RoB 2.0: "some concerns," due to the small placebo arm [n=13] and risk of missing outcome data); Phase 2 and LUCENT use nonidentically named endpoints (indirectness), although the CI is narrow and far from the null.
Maintenance	Histologic remission	1.97 (1.49–2.60)	N/A	1	Moderate	Reported only in LUCENT-2 (single-study default imprecision downgrade).
Maintenance	Serious adverse events (SAEs)	0.36 (0.19–0.70)	0%	2	Low	Includes the Phase 2 maintenance re-randomization (RoB 2.0: "some concerns," due to the small placebo arm [n=13] and risk of missing outcome data); rare events (~34 total events).

CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; I^2, heterogeneity statistic; k, number of contributing trials; N/A, not applicable; RCT, randomized controlled trial; RoB, risk of bias; RR, risk ratio; SAE, serious adverse event. Certainty was rated down from "high" for risk of bias, inconsistency ($I^2 \geq 50\%$), indirectness, and imprecision according to the prespecified rules described in Sections 2.6 and 3.7.