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Mirikizumab—A Narrative Review of LUCENT Trials

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Abstract

Introduction: Ulcerative colitis (UC) falls under the spectrum of inflammatory bowel disease, presents with bloody diarrhea and abdominal pain, and is diagnosed endoscopically with erosive lesions in the colon. Salicylates and steroids form the cornerstone of the treatment, but severe and resistant diseases warrant biological therapy. Methods: LUCENT 1 - 3 trials, for approval of Mirikizumab, a p-19 subunit antagonist on IL-23, were included in this review. Discussion: Mirikizumab outperformed placebo in the induction trial (LUCENT-1), with notably higher rates of clinical remission. In the maintenance phase (LUCENT-2), mirikizumab had sustained efficacy, with significant proportions achieving and maintaining clinical remission up to week 104. In LUCENT-3, which documented the 104-week follow-up period, mirikizumab exhibited lasting efficacy in maintaining clinical response and remission from weeks 52 to 104. Conclusions: This narrative review offers insight into the trial, its structure, and ultimate findings. Mirikizumab emerges as a potent biological therapy for UC.

Keywords

Mirikizumab, Ulcerative Colitis, LUCENT, p-19

1. Introduction

Ulcerative colitis, a chronic inflammatory condition affecting the colon, can lead to increased friability and erosive lesions in the bowel wall. It falls within the spectrum of inflammatory bowel diseases (IBD), along with Crohn's disease, collectively impacting over 2.4 million adults in the United States. UC is believed to affect 400 out of 100,000 Americans. These patients often experience bleeding due to these erosions. UC is considered idiopathic and is mediated by TH2 helper T cells [1] [2].

While corticosteroids and aminosalicylic acid derivatives were historically the

mainstays of UC treatment, the emergence of immunologic inhibitors has allowed for better disease management. TNF-alpha inhibitors were previously the drugs of choice for moderate to severe UC due to their higher efficacy rates. However, with a deeper understanding of the disease pathogenesis, drugs targeting specific interleukins involved in the disease process have gained the limelight in recent years [3].

IL-23 is a key cytokine in ulcerative colitis (UC) that promotes inflammation and inflammation in the colon. It is produced by tissue-resident myeloid cells and promotes Th17 cell differentiation, which produces pro-inflammatory cytokines like IL-17A. Blocking IL-23, either through the p40 or p19 subunit, has shown promise in treating UC, leading to remission, reduced inflammation, and improved quality of life. Monoclonal antibodies have been developed to target IL-23, targeting the p40 and p19 subunits respectively. Clinical trials have shown that IL-23 blockade can induce and maintain remission, reduce inflammatory indexes, promote mucosal healing, and improve UC patients' quality of life. Monoclonal antibodies like risankizumab, guselkumab, mirikizumab, and brazikumab specifically target the p19 subunit of IL-23, blocking its activity and reducing inflammation in UC. Ustekinumab (anti-p40) targets the shared p40 subunit of IL-12 and IL-23, effectively blocking both cytokines and reducing inflammation in UC.

This review centers on mirikizumab, a novel drug that targets interleukin-23 via its p19-directed antibody. Recently, mirikizumab underwent a multicentric phase 3 trial, the LUCENT trial, and has received FDA approval for managing moderate to severe UC. We have tried to compare and contrast the general UC population with the population studied in the LUCENT trials, while also exploring the potential future of UC therapeutics with regards to this drug.

2. Methods and Methodology

To extract data for this paper, the authors referred to the phase 3 LUCENT trial data, including the induction phase, maintenance phase, and the 104-week follow-up study. The search strategy included a thorough search through PubMed, Cochrane Library, Google Scholar, Embase, and Scopus. All studies referring to the use of Mirikizumab and Lucent trials were included. Even published abstracts were added to the narrative review. Studies not published in English and literature reviews were excluded.

3. Results of the Trial

Detailed information on the trials is shown in Tables 1-6.

Safety endpoints in LUCENT 3

1) Severe treatment-emergent adverse events were observed in 4.5% of patients.

2) 5.2% of individuals experienced serious adverse events during the specified period, and 2.8% (8 cases) of patients discontinued treatment due to adverse events.

3) Common treatment-emergent adverse events included pyrexia, diarrhea, injection site pain, abdominal pain, and gastroenteritis.

4) Treatment-emergent adverse events (TEAEs) occurred in 184 patients (63.7%).

Table 1. Overview of the LUCENT trials.

Trial	Drug	Population	Size and distribution
LUCENT 1—Induction phase	1) Mirikizumab vs placebo 2) p19-directed antibody against interleukin-23	1) 1281 2) underwent induction 3) Age—18 - 80 yrs	1) 3:1 mirikizumab to placebo 2) 300mg administered IV every 4 weeks for 12 weeks 3) Randomization stratified according to: a) Treatment failure with a biologic agent or tofacitinib (yes or no) b) Baseline glucocorticoid use (yes or no) c) Baseline disease activity (modified Mayo score of 4 to 6 or 7 to 9) d) Geographic region (North America, Europe, or other)
LUCENT 2—Maintenance phase	Mirikizumab vs placebo	544	1) 2:1 Mirikizumab to placebo 2) Received open-label mirikizumab (200 mg), administered subcutaneously every 4 weeks, through week 40. 3) Patients who showed response to placebo were continued on placebo 4) Extended induction - 300 mg SQ every 4 weeks for 12 weeks in the maintenance trial
LUCENT 3—Extension study	Mirikizumab only	368	Mirikizumab 200mg SQ every 4 weeks

Selection criteria [4] [5]	Exclusion criteria
1) Moderately to severely active ulcerative colitis, modified Mayo score of 4 to 9, endoscopic subscore of 2 to 3 2) Inadequate response to, a loss of response to, or an inability to take one or more glucocorticoids (referred to as corticosteroids in the trial protocol) or biological therapy/Janus kinase inhibitors 3) Patients were allowed to receive oral 5-aminosalicylic acid, oral glucocorticoids, or azathioprine, 6-mercaptopurine, and methotrexate at stable doses throughout the trial. 4) Non-responders to Mirikizumab or Placebo: a) Received open-label extended induction therapy with three additional doses of mirikizumab (300 mg), administered intravenously every 4 weeks. b) Reassessment at Week 12 of the Maintenance Trial (Week 24 Overall): c) Clinical response was reassessed compared to baseline of the induction trial.	1) Mayo score <4, endoscopic subscore of <2 2) previous exposure to anti–interleukin-12 and anti–interleukin-23 subunit p40 or anti–interleukin-23 subunit p19 antibodies 3) Patients who had treatment failure with three or more different biologic therapies
1) Clinical response in Lucent 1 • decrease of ≥2 points in the modified Mayo score and a ≥30% reduction from baseline • Plus either a ≥1 point reduction in the rectal bleeding subscore (range 0 to 3) or a rectal bleeding subscore of 0 or 1 2) Extended induction—Patients who had no response in the LUCENT 1 trial were allowed additional 12 weeks of induction in LUCENT 2	No clinical response in Lucent 1 Non-responders to Extended Induction therapy were withdrawn from the trial.

Continued

1) Induction Responders: a) Patients from LUCENT-1 who responded to mirikizumab induction treatment at week 12, continued on blinded mirikizumab in LUCENT-2 maintenance 2) Extended Induction Responders: a) Patients from LUCENT-2 who responded to extended induction mirikizumab treatment and completed the LUCENT-2 weeks 40 visit on open-label mirikizumab treatment. 3) Maintenance Remitters: a) Induction responders who achieved clinical remission at LUCENT-2 week 40 (week 52 continuous mirikizumab treatment). 4) Maintenance Responders: a) Induction responders who achieved clinical response at LUCENT-2 week 40 (week 52 continuous mirikizumab treatment). 5) Modified Intention-to-Treat Population: a) All patients who received any study treatment during the study, excluding those impacted by an electronic clinical outcome assessment transcription error in Poland and Turkey. 6) Reinduction Responders: a) Induction responders from LUCENT-1 who experienced a loss of response during LUCENT-2, received reinduction treatment during LUCENT-2, and benefited from mirikizumab treatment according to the investigator's opinion, then transitioned to LUCENT-3. 7) Safety Population: a) All patients who received any amount of study treatment, regardless of protocol adherence. 8) Induction Baseline Subgroups: a) Biologic Failed: Patients at LUCENT-1 induction baseline with prior inadequate response, loss of response, or intolerance to biologic therapy or Janus kinase inhibitors (tofacitinib). b) Not Biologic Failed: Patients at LUCENT-1 induction baseline not meeting the biologic-failed definition but who failed conventional therapy such as immunomodulators or corticosteroids.	1) Non responders after LUCENT 2 and extended induction in LUCENT 2 2) Patients on placebo, whether directly from LUCENT-2 or those assigned to placebo in LUCENT-2 from the induction responder population, were not included in the analysis. 3) Patients impacted by the electronic clinical outcome assessment transcription error in Poland and Turkey were excluded from the modified intention-to-treat population. This exclusion ensured data integrity by removing patients affected by data recording inaccuracies.

Table 2. Demographics of Ulcerative colitis and the LUCENT trial.

Demographics of the lucent 1 trial	Demographics of the lucent 2 trial	Demographics of the lucent 3 trial
1) n = 1162, Mirikizumab 868, Placebo 294), Total Randomized: 1281 patients	1) n = 816, 544 Mirikizumab induction responders, 272 on responders with extended induction treatment	1) 266 mirikizumab induction responders
2) Modified Intention-to-Treat Population: 1162 patients; Mirikizumab Group: 868 patients (300 mg IV), Placebo Group: 294 patients (IV)	2) Mirikizumab induction responders 365 continued on mirikizumab maintenance therapy, 324 completed 52 week maintenance	2) 102 extended induction responders
	3) Mirikizumab induction non responders 134 completed 52 weeks maintenance	
Mirikizumab—42.9 ± 13.94 Placebo—41.3 ± 13.8	Mirikizumab - median age 42 years	Induction responders—43.2 ± 13.98 Extended induction responders—45.9 ± 13.46

Continued

Mirikizumab—530 (61.1%) Placebo—165 (56.1%)	59% males	Induction responders—160 (60.2%) Extended induction responders—58 (56.9%)
Mirikizumab—451 (52.0%) Placebo—149 (50.7%)	-	Induction responders—152 (57.1%) Extended induction responders—56 (54.9%)
Mirikizumab—362 (41.7%) Placebo—117 (39.8%)	-	Induction responders—97 (36.46%) Extended induction responders—43 (42.15%)

Table 3. Induction trial endpoints.

Primary endpoint
Clinical remission defined as:
A) Stool-frequency subscore of 0 (scale 0 - 3) or 1 with a decrease of at least 1 point from baseline
B) Rectal-bleeding subscore of 0
C) Endoscopic subscore of 0 or 1 (excluding friability)
Secondary endpoint
Alternate Definition of Clinical Remission:
Stool-frequency subscore of 0 or 1
Rectal bleeding sub score of 0 or 1
Endoscopic subscore of 0 or 1 (excluding friability)
Clinical Response:
Decrease of ≥2 points and ≥30% from baseline in the modified Mayo score
Decrease of ≥2 points and ≥30% from baseline in the modified Mayo score
Rectal bleeding subscore of 0 or 1 or a decrease of ≥1 point from baseline
Endoscopic Remission:
Endoscopic subscore of 0 or 1 (excluding friability)
Remission of Symptoms
Stool-frequency subscore of 0 or 1 with a decrease of ≥1 point from baseline
Rectal-bleeding subscore of 0
Clinical Response in Patients with Treatment Failure: For patients who failed previous treatment with a biologic agent or tofacitinib Improvement in Bowel-Movement Urgency: Any reduction in the Urgency Numeric Rating Scale (NRS), an 11-point scale (0 = no urgency, 10 = worst possible urgency)

Table 4. LUCENT 2 maintenance trial end points.

Primary endpoints	Secondary endpoints
Clinical remission at week 40	**Major Secondary Endpoints at Week 40:**
	1) Alternate Definition of Clinical Remission
	2) Endoscopic Remission
	3) Glucocorticoid-Free Clinical Remission:
	a) Clinical remission at week 40

Continued

b) Symptom remission at week 28
c) No glucocorticoid use for ≥12 weeks before week 40
4) Histologic-Endoscopic Mucosal Remission:
a) Endoscopic remission
b) Geboes subscore of 0 for specific histologic grades
5) Improvement in Bowel-Movement Urgency: Any reduction in Urgency NRS score (scale 0 - 10)
6) Bowel-Urgency Remission: Urgency NRS score of 0 or 1 in patients with a baseline score of ≥3
7) Maintenance of Clinical Remission: Clinical remission in patients who had achieved remission during the induction trial
Additional Endpoints (not included in multiplicity-controlled testing):
1) Inflammatory Bowel Disease Questionnaire score
2) Levels of inflammatory biomarkers (C-reactive protein and fecal calprotectin)
3) Serum concentration of mirikizumab

LUCENT 3 endpoints [6]
1) Abdominal Pain ≥ 30% Improvement: At least a 30% change from induction baseline in Abdominal Pain Numeric Rating Scale score, with a score of at least 3 at baseline.
2) Abdominal Pain Severity: Change in Abdominal Pain Numeric Rating Scale score from induction baseline.
3) Alternate Clinical Remission: Stool frequency (SF) of 0 or 1; rectal bleeding (RB) of 0; and endoscopic subscore (ES) of 0 or 1 (excluding friability).
4) Bowel Urgency Clinically Meaningful Improvement: Decrease from induction baseline in Urgency Numeric Rating Scale score by at least 3 points in patients with a score of at least 3 at induction baseline.
5) Bowel Urgency Remission: Urgency Numeric Rating Scale score of 0 or 1.
6) Bowel Urgency Severity: Change in Urgency Numeric Rating Scale score from induction baseline.
7) Clinical Remission: Stool frequency (SF) of 0 or 1 with at least a 1-point decrease in modified Mayo score from induction baseline; rectal bleeding (RB) of 0; and endoscopic subscore (ES) of 0 or 1 (excluding friability).
8) Clinical Response: At least a 2-point and 30% decrease from induction baseline in modified Mayo score; rectal bleeding (RB) of 0 or 1, or at least a 1-point decrease from baseline.
9) Corticosteroid-Free Remission: Clinical remission with no corticosteroid use for at least 12 weeks.
10) Endoscopic Remission: Endoscopic subscore (ES) of 0 or 1 (excluding friability).
11) Histologic-Endoscopic Mucosal Improvement (HEMI): Geboes score of 3.1 or less, along with an endoscopic subscore (ES) of 0 or 1 (excluding friability); histologic improvement defined using the Geboes scoring system with specific criteria.

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12) Histologic-Endoscopic Mucosal Remission (HEMR): Geboes score of 2B.0 or less, along with an endoscopic subscore (ES) of 0 or 1 (excluding friability); histologic remission with resolution of neutrophils according to the Geboes scoring.

13) Inflammatory Bowel Disease Questionnaire (IBDQ) Remission: IBDQ total score of 170.1 or higher.

14) IBDQ Response: At least a 16-point improvement from the induction baseline in IBDQ total score.

15) IBDQ Severity: Change in IBDQ total score and domain scores from induction baseline.

16) RB Severity: Change in rectal bleeding modified Mayo score subscore from induction baseline.

17) SF Severity: Change in stool frequency modified Mayo score subscore from induction baseline.

18) Symptomatic Remission: Stool frequency (SF) of 0 or 1 with at least a 1-point decrease in modified Mayo score from induction baseline; rectal bleeding (RB) of 0.

Table 5. Outcomes of the trials.

	LUCENT 1	LUCENT 2	LUCENT 3 [8]
Primary outcomes	1) Clinical Remission at Week 12:	1) Clinical Remission at Week 40:	1) 74.5% of week 52 mirikizumab responders maintained clinical response at week 104.
	a) Mirikizumab Group: 24.2%	a) Mirikizumab Group: 49.9%	2) Remission rates: 54.0% clinical, 52.7% corticosteroid-free remission, 65.3% endoscopic, 47.7% HEMR, 67.8% symptomatic, and 50.2% bowel urgency.
	b) Placebo Group: 13.3%	b) Placebo Group: 25.1%	3) Improvement rates for HEMI and bowel urgency were 53.1% and 67.0%, respectively.
	c) Difference: 11.1 percentage points (99.875% CI 3.2 to 19.1, P-value: <0.001)	c) Difference: 23.2 percentage points, (95% CI 15.2 to 31.2 P-value: <0.001)	
	2) Alternative Definition of Clinical Remission: Mirikizumab Group: 25.6%, Placebo Group: 14.6%, P-value: <0.001	2) Alternative Definition of Clinical Remission: Mirikizumab Group: 54.9%, Placebo Group: 27.0%, P-value: <0.001	
Secondary outcomes	1) Favorable outcomes for mirikizumab group: P-value: <0.001 for all comparisons	1) Major Secondary Endpoints:	1) Sustained Maintenance: Responders at week 52 showed consistent maintenance rates at week 104 (65.6% to 87.2%).
	a) Clinical response	a) Significantly greater percentages in mirikizumab group (P-value: <0.001 for all comparisons):	2) Long-Term Symptom Improvement: Symptom reduction persisted from treatment initiation to week 104.

Continued

b) Endoscopic remission	i) Clinical remission	3) Extended Treatment Impact: Extended induction responders maintained remission rates ranging from 33.3% to 45.7% at week 104.
c) Remission of symptoms at weeks 4 and 12	ii) Glucocorticoid-free clinical remission	4) Reinduction Results: Over half of those needing reinduction achieved response and remission at week 104.
d) Clinical response in patients with previous treatment failure	iii) Maintenance of clinical remission	5) Enhanced Quality of Life:
e) Histologic-endoscopic mucosal improvement	iv) Endoscopic remission	a) Patients experienced sustained improvements in quality of life, with over 60 points of IBDQ total score improvement.
f) Bowel-movement urgency	v) Histologic–endoscopic mucosal remission	b) Response and remission rates remained stable at week 104, regardless of prior treatment history.
-	vi) Bowel-urgency remission	-
-	2) Glucocorticoid Use: Among mirikizumab-treated patients in clinical remission at week 40, 97.8% were not taking glucocorticoids	-
-	3) Urgency NRS Score: Improvement in Urgency NRS score remained stable throughout maintenance trial in mirikizumab group, placebo group showed loss of some improvement gained during induction trial	-
-	4) Subgroup Analysis: Greater proportions meeting endpoints in mirikizumab group among patients with treatment failure with biologic agents or tofacitinib	-
-	5) Additional Measures: Improvement observed in Inflammatory Bowel Disease Questionnaire score, C-reactive protein, and fecal calprotectin in mirikizumab group compared to placebo group	-
-	6) Response to Extended Induction Therapy: Among patients who did not respond to mirikizumab therapy in induction trial:	-
-	a) 53.7% had clinical response and 11.4% had clinical remission by week 12 of extended induction therapy	-
-	b) 72.2% of patients who received mirikizumab maintenance treatment maintained clinical remission	-
-	c) 36.1% had clinical remission at week 40	-

Table 6. Safety endpoints in LUCENT 1 and 2.

Overall incidence of adverse effects	Similar incidences observed in mirikizumab and placebo groups during induction and maintenance trials
Opportunistic infections	1) Herpes zoster, candidiasis, cytomegalovirus disease, intestinal tuberculosis 2) Occurred in 15 patients (6 during placebo-controlled periods and 9 during non–placebo-controlled periods)
Cancer	1) Reported in 8 patients during 52-week treatment period 2) Types included adenocarcinoma of colon (2 during induction trial), nonmelanoma skin cancer, gastric cancer, squamous-cell carcinoma, rectal cancer, Kaposi's sarcoma
Elevations of liver enzymes	1) More frequent in mirikizumab-treated patients 2) One patient met criteria for Hy's law, resolved after discontinuation of mirikizumab
Hypersensitivity reactions	More frequent in mirikizumab group during induction trial, no serious reactions observed
Injection site reactions	More frequent in mirikizumab group during placebo-controlled maintenance period, two cases of severe injection-site pain reported
Depression	1) Reported in four mirikizumab-treated patients during maintenance trial 2) Two cases occurred during open-label maintenance period in non-responders to initial induction therapy, one case involved attempted suicide in patient with a history of suicide attempts

a) Mild TEAEs: 99 (34.3%)
b) Moderate TEAEs: 72 (24.9%)
c) Severe TEAEs: 13 (4.5%)
5) Serious adverse events (SAEs) were reported in 15 patients (5.2%).
6) Most common TEAEs:
a) COVID-19: 35 cases (12.1%)
b) Ulcerative colitis: 22 cases (7.6%)
c) Arthralgia: 18 cases (6.2%)
d) Headache: 18 cases (6.2%)
e) Nasopharyngitis: 17 cases (5.9%)
7) Other common TEAEs:
a) Pyrexia: 13 cases (4.5%)
b) Diarrhea: 10 cases (3.5%)
c)Injection site pain: 10 cases (3.5%)
d)Abdominal pain: 9 cases (3.1%)
e) Gastroenteritis: 9 cases (3.1%)
8) Adverse events of special interest:
a) Infections (all): 87 cases (30.1%)
b) Injection site reactions: 16 cases (5.5%)

c) Hepatic events: 6 cases (2.1%)

d) Deaths: 0 cases

9) In the induction responder safety population during the 52-week period of LUCENT-3:

a) 1 patient (0.4%) experienced elevated alanine aminotransferase (≥3× the upper limit of normal).

b) 1 patient (0.4%) experienced elevated aspartate transaminase (≥3× the upper limit of normal). This patient was the same as the one with elevated alanine aminotransferase.

c) 2 patients (0.7%) had elevated bilirubin (≥2× upper limit of normal).

10) No patients had liver enzymes that were 5× or 10× the 2× upper limit of normal.

11) None of the patients met Hy's law criteria.

4. Discussion

Interleukin-23 (IL-23) plays a crucial role in the immune response linked to ulcerative colitis (UC). It is involved in the differentiation and maintenance of Th17 T helper cells, which produce inflammatory cytokines that contribute to the chronic inflammation that is characteristic of the disease. IL-23 consists of two subunits: p40, shared with IL-12, and p19, unique to IL-23. Advances in understanding the molecular mechanisms of UC have opened new avenues for therapeutic interventions targeting these pathways [7] [8].

Ustekinumab, an anti-p40 antibody, has previously been effective for moderate to severe UC. It targets the p40 subunit shared by IL-12 and IL-23, reducing pro-inflammatory cytokines and easing UC symptoms, offering an option for patients unresponsive to other treatments. This highlights the value of targeting specific immune components to improve disease management [9].

Mirikizumab, targets the p19 subunit of IL-23, crucial for its biological activity and interaction with its receptor. By blocking p19, mirikizumab effectively inhibits IL-23, reducing the inflammatory response and helping control the symptoms of ulcerative colitis. This targeted approach offers a more precise method of managing the disease compared to broader immunosuppressive treatments. After showing promise in phase 2 trials, mirikizumab recently underwent randomized multicentric phase 3 trials termed the LUCENT trials.

The LUCENT trials, including LUCENT-1, LUCENT-2, and LUCENT-3, investigated mirikizumab's effectiveness and safety for moderate to severe ulcerative colitis (UC). The induction dose was 300 mg given every 4 weeks followed by the maintenance dose of 200mg every 4 weeks. Mirikizumab outperformed placebo in the induction trial (LUCENT-1), with notably higher rates of clinical remission at week 12: 24.2% for the Mirikizumab group compared to 13.3% for the Placebo group ($p < 0.05$). In the maintenance phase (LUCENT-2), mirikizumab had sustained efficacy, with significant proportions achieving and maintaining clinical remission up to week 104: 49.9% for the Mirikizumab group versus 25.1% for the

placebo group ($p < 0.05$). Safety data revealed manageable adverse events, with fewer corticosteroid requirements among subjects and sustained improvements in quality of life among mirikizumab-treated patients. The drug had a relatively good side effect profile in the study population with sustained remission. This, in addition to the improvement in patients who had failed a prior biologic therapy may help clinicians to manage the condition better with there being very few treatment options for the management of such patients.

In LUCENT-3, which documented the 104 week follow up period, mirikizumab exhibited lasting efficacy in maintaining clinical response and remission from week 52 to 104. Both biologic-failed and not-biologic-failed patients showed similar response rates, with 74.5% and 65.6% maintaining response and remission, respectively. Extended induction and reinduction therapies were effective strategies, contributing to sustained remission rates. Significant improvements in abdominal pain were observed, with over 75% of both induction and maintenance responders achieving a ≥30% improvement. Quality-of-life outcomes remained positive, emphasizing the benefits of mirikizumab therapy for long-term UC patients.

Mirikizumab demonstrates promising long-term effectiveness in treating moderate-to-severe ulcerative colitis (UC), sustaining improvements across various treatment goals like endoscopic improvement, stool frequency control, rectal bleeding management, and alleviation of bowel urgency and histological inflammation. Potential benefits for patients who are resistant to secondary therapy can be seen in its ability to maintain the efficacy of initial responders.

Additionally, mirikizumab also had a endoscopic endpoint analysis, something that was not performed for other contemporary drugs such as vedolizumab [9] and ustekinumab [10]. Safety findings were generally positive, with minimal adverse reactions and no significant long-term increase in liver enzyme levels observed during a 104-week treatment period. Studies have found that mirikizumab is more effective in treating patients with a biologic/JAKi naïve population than ustekinumab for response, remission, and mucosal healing. Despite prior biologic experience, a smaller number of patients may need to be treated with mirikizumab [11]. A systematic review of 14 randomized controlled trials (RCTs) compared the use of adalimumab, golimumab, infliximab, mirikizumab, vedolizumab, and ustekinumab compared to placebo or another biologic drug. Mirikizumab was found to be superior in clinical response and remission compared to placebo. Infliximab was found to be the most effective option in both clinical response and remission. Mirikizumab did not differ from other biologics in terms of clinical response and remission in patients with UC [12].

However, its applicability to a broader patient population is limited due to the exclusion criteria limiting the inclusion of patients with less extensive treatment failure history. While the trial was multicentric, there was not much data on generalizability of these results to a broader patient population including Asians, African-Americans and Hispanics. Due to the absence of direct comparisons with

other advanced treatments, the comparative effectiveness of mirikizumab remains unclear, although it has been shown to be effective across different endpoints, including endoscopic and histological remission.

5. Conclusion

Additional information on the increased efficacy and safety profile of Mirikizumab over three or four years may be gained by ongoing analyses from long-term extension studies, which will further enhance our understanding of its role in UC management. In order to provide a more detailed understanding of its efficacy, in particular as regards the goal of attaining an Endoscopic and Histologic remission, a key indicator of disease control and treatment success, Mirikizumab's comprehensive evaluation using endoscopic and histological assessment distinguishes it from other treatments for UC management studies. The study was funded by Eli Lilly, which may indicate a conflict of interest and only long-term side effect monitoring once it is used in clinical practice will help ascertain its utility in the management of ulcerative colitis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Nemeth, Z.H., Bogdanovski, D.A., Barratt-Stopper, P., Paglinco, S.R., Antonioli, L. and Rolandelli, R.H. (2017) Crohn's Disease and Ulcerative Colitis Show Unique Cytokine Profiles. *Cureus*, **9**, e1177. https://doi.org/10.7759/cureus.1177

[2] Gros, B. and Kaplan, G.G. (2023) Ulcerative Colitis in Adults: A Review. *JAMA*, **330**, 951-965. https://doi.org/10.1001/jama.2023.15389

[3] Ungaro, R., Mehandru, S., Allen, P.B., Peyrin-Biroulet, L. and Colombel, J. (2017) Ulcerative Colitis. *The Lancet*, **389**, 1756-1770. https://doi.org/10.1016/s0140-6736(16)32126-2

[4] D'Haens, G., Dubinsky, M., Kobayashi, T., Irving, P.M., Howaldt, S., Pokrotnieks, J., *et al.* (2023) Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis. *New England Journal of Medicine*, **388**, 2444-2455. https://doi.org/10.1056/nejmoa2207940

[5] Lewis, J.D., Parlett, L.E., Jonsson Funk, M.L., Brensinger, C., Pate, V., Wu, Q., *et al.* (2023) Incidence, Prevalence, and Racial and Ethnic Distribution of Inflammatory Bowel Disease in the United States. *Gastroenterology*, **165**, 1197-1205.E2. https://doi.org/10.1053/j.gastro.2023.07.003

[6] Sands, B.E., D'Haens, G., Clemow, D.B., Irving, P.M., Johns, J.T., Hunter Gibble, T., *et al.* (2024) Two-Year Efficacy and Safety of Mirikizumab Following 104 Weeks of Continuous Treatment for Ulcerative Colitis: Results from the LUCENT-3 Open-Label Extension Study. *Inflammatory Bowel Diseases*, **30**, 2245-2258. https://doi.org/10.1093/ibd/izae024

[7] Sewell, G.W. and Kaser, A. (2022) Interleukin-23 in the Pathogenesis of Inflammatory Bowel Disease and Implications for Therapeutic Intervention. *Journal of Crohn's and Colitis*, **16**, ii3-ii19. https://doi.org/10.1093/ecco-jcc/jjac034

[8] Tang, C., Chen, S., Qian, H. and Huang, W. (2012) Interleukin-23: As a Drug Target

for Autoimmune Inflammatory Diseases. *Immunology*, **135**, 112-124. https://doi.org/10.1111/j.1365-2567.2011.03522.x

[9] Loftus, E.V., Colombel, J.F., Feagan, B.G., *et al.* (2017) Long-Term Efficacy of Vedolizumab for Ulcerative Colitis. *Journal of Crohn's and Colitis*, **11**, 400-411.

[10] Panaccione, R., Danese, S., Sandborn, W.J., O'Brien, C.D., Zhou, Y., Zhang, H., *et al.* (2020) Ustekinumab Is Effective and Safe for Ulcerative Colitis through 2 Years of Maintenance Therapy. *Alimentary Pharmacology & Therapeutics*, **52**, 1658-1675. https://doi.org/10.1111/apt.16119

[11] Dignass, A., Redondo, I., Richards, M., *et al.* (2024) P105 Mirikizumab versus Ustekinumab in Moderately to Severely Active Ulcerative Colitis: Maintenance Number Needed to Treat from a Network Meta-Analysis. *Gut*, **73**, A113.1-A113. http://dx.doi.org/10.1136/gutjnl-2024-BSG.187

[12] Moćko, P., Koperny, M., Śladowska, K., Holko, P., Kowalska-Bobko, I. and Kawalec, P. (2024) Efficacy and Safety of Mirikizumab Compared with Currently Approved Biologic Drugs for the Treatment of Ulcerative Colitis: A Systematic Review and Network Meta-Analysis. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, **44**, 811-821. https://doi.org/10.1002/phar.4611