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MIRIKIZUMAB – THE EFFICACY OF TREATMENT IN INFLAMMATORY BOWEL DISEASE

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ABSTRACT

Mirikizumab is a humanized monoclonal antibody directed against the p19 subunit of interleukin IL-23. In recent years, it has been the subject of numerous clinical trials as
a potential new therapy for inflammatory bowel diseases, including Crohn's disease and ulcerative colitis. Additionally, mirikizumab has been evaluated in clinical trials as a possible treatment for plaque psoriasis. Clinical trial results in ulcerative colitis led to its approval in the European Union, the United States, Canada, and Japan for the treatment of adult patients with moderately to severely active disease. Despite promising clinical trial outcomes, mirikizumab has not yet been approved for the treatment of Crohn's disease. This review focuses on summarizing findings from clinical trials investigating mirikizumab in inflammatory bowel diseases. The information is derived from scientific publications indexed in PubMed, searched using the terms "mirikizumab" and "IL-23" and published up to February 2025, as well as from published clinical trial results on mirikizumab.

KEYWORDS

Mirikizumab, IL-23, IL-23R, P40, Ulcerative Colitis, Inflammatory Bowel Diseases

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1. Introduction

Interleukin-23 (IL-23) is a cytokine from the IL-12 family that contributes to the activation and maintenance of Th17 cells and promotes the cascade of inflammatory processes sustaining mucosal inflammation [1, 2]. It is produced by activated type 1 macrophages and dendritic cells**.** It consists of two subunits: p19 – specific to IL-23, and p40 – non-specific to IL-23, also present in other interleukins **[3].** IL-23 is associated with many inflammatory diseases such as inflammatory bowel disease (IBD), gastritis related to Helicobacter pylori infection, and rheumatoid arthritis. This is mainly due to its ability to induce a Th1-type immune response. The receptor for IL-23 (IL-23R) is composed of two subunits: IL-23Rα (the proper, IL-23-specific subunit) and IL-12Rβ1 (a subunit shared by IL-12 and IL-23 receptors) [1].

IL-23 binds to the IL-23R heterodimeric receptor complex. Upon binding, IL-23 activates the JAK-STAT signaling pathways, primarily involving STAT3, but also STAT4. Following the activation of Janus kinase 2 (Jak2) and tyrosine kinase 2 (TYK2), the STAT3-STAT4 dimer translocates into the nucleus, where it activates gene expression [3]. The interaction between IL-23 and IL-23R is undeniably necessary for eliciting biological effects in specific cell types [2]. IL-23 induces the differentiation of naïve CD4+ T cells into Th17 helper T cells leading to the activation of a pro-inflammatory cytokine cascade. Activation of this pathway leads to the production of proinflammatory cytokines such as interleukin-17 (IL - 17), interleukin-22 (IL-22), interleukin-6 (IL-6), interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), and interferon gamma (IFN-γ) [4, 5]. This is particularly relevant in the pathogenesis of inflammatory and autoimmune diseases such as rheumatoid arthritis, Crohn's disease, and psoriasis [6–9**].**

It is also worth noting that in patients suffering from inflammatory bowel diseases, elevated levels of both IL-23 and Th17 have been demonstrated in plasma and intestinal mucosa [10, 11]. Importantly, a specific antibody against interleukin-23 has shown potential to inhibit the initiation of inflammatory processes and to influence the underlying autoimmune disease linked to Th17 cell dysfunction [12]. A reduction in the severity of inflammation in IBD has also been confirmed as a result of IL-23 inhibition [13].

The development of inflammatory bowel diseases is multifactorial, with genetic, immunological, and environmental factors all contributing [14]. Genetic predisposition is supported by the familial occurrence of Crohn's disease and ulcerative colitis, observed in 5–10% of cases and there is identified susceptibility loci for these conditions on chromosomes 1, 5, 6, 12, 14, 16, and 19 [15].

Mirikizumab is a humanized monoclonal antibody targeting the p19 subunit of IL-23.

By binding to it, it prevents IL-23 from attaching to the IL-23R receptor, thereby blocking the activation of the IL-23–dependent inflammatory pathway. Unlike antibodies that target the p40 subunit, mirikizumab acts selectively – it does not affect other cytokines that utilize p40 (such as IL-12, IL-27, or IL-25) [16]. Thanks to this selectivity, the drug does not interfere with the body's natural defense mechanisms against pathogens and does not impair a proper immune response to health-threatening pathogens [12].

2. Materials and Method

An analysis of the available scientific literature on the PubMed platform was conducted, covering articles published up to February 2025, searched using the keywords"mirikizumab" and"IL-23." The aim of this study was to gather up-to-date and reliable information regarding the mechanism of action of mirikizumab and its effectiveness in the treatment of patients with inflammatory bowel disease.

Results

3. Mirikizumab in the treatment of ulcerative colitis.

Ulcerative colitis (UC) belongs to the group of inflammatory bowel diseases (IBD). It is an idiopathic inflammatory disease of the colon in which the inflammatory process involves the mucosa and submucosa of the large intestine—either the rectum alone or the rectum and colon. In most cases, it follows a chronic course, with long periods of remission interrupted by acute relapses. The inflammation begins in the rectum and then spreads continuously to the remaining parts of the colon.

Typical symptoms of UC include bloody diarrhea, abdominal pain, urgent need for defecation, and painful tenesmus. Mild UC is characterized by loss of the normal vascular pattern of the mucosa, superficial erosions, and inflammatory exudate. In more severe forms, denuded mucosal areas and deep ulcerations may predominate. The diagnosis of ulcerative colitis is primarily based on endoscopy with biopsy. The goals of therapy are induction and maintenance of remission, reduction of complication risk, and improvement of quality of life [17-19].

The incidence of UC ranges from 4.9 to 505 cases per 100, 000 people. For comparison, in North America it is 37.5 to 248.6 cases per 100, 000 people [19]. The disease most commonly affects young individuals, regardless of sex. According to available statistics, the peak onset occurs between the ages of 20 and 40.

Ulcerative colitis begins suddenly and insidiously, with typical symptoms including diarrhea with blood in the stool, abdominal pain, painful tenesmus, and an urgent need for defecation. During active colitis, significant bleeding may occur, and bowel movement frequency can reach up to 20 times per day. In patients whose disease is limited to the rectum, bowel habits may remain normal, and constipation may even occur—making rectal bleeding the only symptom.

The pathogenesis of ulcerative colitis remains poorly understood [20]. Observations in UC patients have demonstrated increased IL-23 expression, excessive activity of Th17 cells, and abnormalities in the IL-23/Th17 axis [21].

The primary therapeutic goal is mucosal healing, meaning resolution of inflammatory changes. Initial therapy consists of monotherapy or combination treatment with 5-aminosalicylic acid (5-ASA) and glucocorticosteroids. In patients who do not respond due to intolerance or resistance to first-line therapy, as well as those with more advanced disease, biological treatment is used. Unfortunately, in many patients the response to therapy is insufficient, or over time treatment efficacy is lost altogether [22].

3.1. Mirikizumab in Phase II and III clinical trials in ulcerative colitis.

Phase II Clinical Trial in the Treatment of UC began in December 2015, with patient recruitment conducted between January 2016 and September 2017. This study was

a continuation of the I6T-MC-AMAC (AMAC) trial, which was a double-blind study conducted across 75 sites in 14 countries [23]. After 12 weeks of therapy with intravenous mirikizumab administered at doses of 50 mg, 200 mg, or 600 mg, or placebo, mirikizumab demonstrated a favorable safety profile in patients with moderate-to-severe ulcerative colitis. Patient assignment to the respective dose groups was randomized.

Eligibility criteria included: age 18–75 years; a confirmed diagnosis of ulcerative colitis for at least 3 months established both endoscopically and histopathologically; and endoscopic evidence of disease in a colonic segment of at least 15 cm. Additionally, patient recruitment was based on the Mayo score, a tool used to assess ulcerative colitis activity. The Mayo score consists of four subscales (stool frequency, rectal bleeding,

endoscopic findings assessed by sigmoidoscopy/colonoscopy, and physician's global assessment), each scored from 0–3.

The maximum possible score is 12, with higher scores indicating more severe disease [24]. Patients were required to have a score between 6 and 12, corresponding to moderate-to-severe disease.

Exclusion criteria included: a high likelihood of requiring surgical intervention, history of colectomy, presence of colostomy or ileostomy, intestinal stricture, or prior biologic therapy targeting IL-23.

At week 12, clinical remission was observed in 3 of 63 patients in the placebo group, compared with 10 of 63 patients receiving 50 mg mirikizumab, 14 of 62 patients receiving 200 mg, and 7 of 61 patients receiving 600 mg. Clinical response was achieved by 26 patients in the 50 mg group, 37 in the 200 mg group, and 30 in the 600 mg group, compared with 13 of 63 patients in the placebo group. Endoscopic improvement at week 12 was noted in 15 of 63 patients receiving 50 mg mirikizumab, 19 of 62 receiving 200 mg, and 8 of 61 receiving 600 mg, compared with 4 of 63 in the placebo group (Table 1) [23].

Following the 12-week induction phase, patients who achieved a clinical response were offered extended therapy and assigned to one of two maintenance groups: the first received 200 mg mirikizumab subcutaneously every 4 weeks, and the second received 200 mg subcutaneously every 12 weeks. Additionally, 13 placebo patients who had shown clinical response continued treatment with their current therapeutic regimen. At week 52, 22 of 47 patients in the 4-week dosing group and 17 of 46 patients in the 12-week dosing group achieved clinical remission [23].

It should also be noted that patients who did not respond during the initial induction phase were offered an extended 12-week induction with mirikizumab. During this period, patients received intravenous mirikizumab at doses of either 600 mg (n = 20) or 1000 mg (n = 64) every 4 weeks.

Table 1. Summary of key efficacy results from Phase II clinical trials.

Grupa	Mirikizumab 50 mg (n= 63)	Mirikizumab 200 mg (n= 62)	Mirikizumab 600 mg (n= 61)	Placebo (n=63)
Clinical remission at week 12 (% [95% CI])	**10** (15, 9% [6, 8-24, 9], p = 0, 066)	**14** (22, 6% [12, 2-33, 0], p = 0, 004)	**7** (11, 5% [3, 5-19, 5], p = 0, 142)	**3** (4, 8%)
Improvement in endoscopic examination (% [95% CI])	**15** (23, 8% [13, 3-34, 3], p = 0, 012)	**19** (30, 6% [23, 3-34, 3], p = 0, 0007)	**8** (13, 1% [4, 6-21, 6], p = 0, 215)	**4** (6, 3%)
Clinical response (% [95% CI])	**26** (41, 3% [29, 1-53, 4], p = 0, 014)	**37** (59, 7% [47, 5-71, 9], p < 0, 001)	**30** (49, 2% [36, 6-61, 7], p = 0, 001)	**13** (20, 6%)

In the final week of the second treatment phase, patients who demonstrated a clinical response continued therapy with 200 mg mirikizumab administered subcutaneously [23].

Among participants who had not responded to initial induction therapy with mirikizumab, approximately half of those receiving 600 mg for an additional 12 weeks, and 43.8% of those receiving 1000 mg, achieved a measurable clinical response. Rates of clinical remission were 15.0% and 9.4%, respectively. Endoscopic improvement was observed in 20.0% of patients in the 600 mg group and in 15.6% of patients in the 1000 mg group.

In the subgroup of patients who did not achieve a clinical response after the first 12-week induction but showed clinical response at week 24 and continued on subcutaneous mirikizumab 200 mg, clinical response was recorded in 65.8%, clinical remission in 26.3%, and endoscopic improvement at week 52 in 34.2% [25, 26].

The Phase II trial therefore demonstrated that mirikizumab effectively induced both clinical response and remission and maintained efficacy through week 52 in a significant proportion of patients, including those who had previously failed biologic therapy. These promising results in moderate-to-severe ulcerative colitis provided the rationale for progression into Phase III trials.

LUCENT-1 Trial was a randomized, multicenter, parallel-group, double-blind, placebo-controlled study of 12 weeks of mirikizumab induction therapy [27]. Eligible patients were adults aged 18–80 years with a Mayo score between 4 and 9 points and an endoscopic subscore of at least 2 [28, 29]. Patients were

randomized to receive intravenous mirikizumab 300 mg (868 patients) or placebo (294 patients). Treatment was administered at weeks 0, 4, and 8, with the primary endpoint assessed at week 12. In total, 1, 281 patients were enrolled. Of these, 544 patients who achieved a clinical response to mirikizumab were re-randomized into the maintenance trial [28, 29].

After 12 weeks of induction, clinical remission was achieved in 24.2% of patients treated with mirikizumab versus 13.3% in the placebo group (P = 0.00006). Clinical response was significantly higher with mirikizumab compared to placebo (63.5% vs. 42.2%; P < 0.00001). Mirikizumab also demonstrated superiority in endoscopic outcomes: endoscopic remission was achieved in 36.3% of treated patients compared to 21.1% in placebo (P < 0.00001). Histologic improvement of the colonic mucosa was reported in 27.1% of patients on mirikizumab versus 13.9% on placebo (P < 0.00001) [28, 30].

LUCENT-2 Trial included 544 patients who had achieved a clinical response in LUCENT-1. Response was defined as a decrease of at least 2 points and 30% in the Mayo score from baseline, along with improvement in rectal bleeding. These patients were re-randomized to receive either mirikizumab 200 mg subcutaneously every 4 weeks (365 patients) or placebo (179 patients) for 40 weeks. Patients in the placebo group who had previously responded to induction continued placebo during this phase [29, 30][Table 2].

The primary endpoint was maintenance of clinical remission at week 40. Results showed clear superiority of mirikizumab, with nearly half of patients (49.9%) remaining in remission compared with only 25.1% in the placebo group. Additionally, patients who did not respond during LUCENT-1 were eligible for extended induction in LUCENT-2, receiving three additional intravenous doses of mirikizumab 300 mg every 4 weeks. Of the 272 patients undergoing extended induction, 53.7% achieved a clinical response and approximately 11% achieved remission at week 12. Among these, 144 patients entered the mirikizumab maintenance phase, and the majority (72.2%) maintained clinical remission [30, 31].

Overall, significantly more patients achieved remission with mirikizumab than placebo—both at week 12 of induction (24.2% vs. 13.3%) and at week 40 of maintenance therapy (49.9% vs. 25.1%). These differences were statistically significant, and all key secondary endpoints were also met [30].

In safety profile the most common adverse events with mirikizumab included nasopharyngitis (cold-like symptoms, upper respiratory tract infections) and arthralgia, occurring more frequently than in the placebo group. Among 1, 217 patients who had ever received mirikizumab during induction, maintenance, or open-label extension, 15 experienced opportunistic infections, including 6 cases of herpes zoster. Eight patients developed malignancies, including 3 cases of colorectal cancer. In contrast, in the placebo induction group, only one case of herpes zoster was reported, and no malignancies occurred [30].

Table 2. Summary of key efficacy results from Phase III clinical trials

Grupa	**Mirikizumab** (n= 868)	**Placebo** (n=294)	**Difference (%)**	**Parameter p**
Clinical remission at week 12 (% pacjentów)	210 (24, 2%)	39 (13, 3%)	10, 9	0, 00006
Clinical response (% pacjentów)	551 (63, 5%)	124 (42, 2%)	21, 3	< 0, 00001
Endoscopic remission (% of patients)	315 (36, 3%)	62 (21, 1%)	15, 2	< 0, 00001
Histological improvement (% of patients)	235 (27, 1%)	41 (13, 9%)	13, 2	< 0, 00001

LUCENT-3 is a long-term study designed to evaluate the efficacy and safety of mirikizumab in patients with moderate-to-severe ulcerative colitis. It includes participants who previously took part in the LUCENT-1 and LUCENT-2 trials. The overall study duration is planned for

3 years, with current data available up to 2 years (104 weeks) [32]. This interim analysis included only those patients who had achieved either clinical response or remission at week 52 (the end of LUCENT-2) [33].

All participants received mirikizumab 200 mg subcutaneously every 4 weeks. Among patients who had achieved clinical response after one year of therapy, 74.5% maintained this effect at two years, and more than half (54%) were in clinical remission. Among those who had already achieved remission at week 52, outcomes were even more favorable: 76.6% maintained clinical response, and 65.6% remained in remission at week 104 [34].

As of February 2025, the study is ongoing and continues to collect long-term data [31–33, 27]. However, the highly promising results obtained in Phase II and III studies in adult patients supported regulatory approval of mirikizumab in the European Union, the United States, Canada, and Japan [34–37].

3.2. Mirikizumab in the treatment of Crohn's disease.

Crohn's Disease is a chronic inflammatory bowel disease that can affect any part of

the gastrointestinal tract, though it most commonly involves the terminal ileum or the colon. The disease occurs predominantly in highly developed countries such as those in Western Europe and the United States. It most frequently affects young individuals between the ages of 15 and 25, with a slightly higher prevalence among women.

A hallmark of Crohn's disease (CD) is that inflammation is not continuous but rather segmental, transmural, and asymmetrical. The disease is progressive, often leading to intestinal damage and disability.

Histopathological examination in CD does not reveal pathognomonic features.

In approximately 60% of patients, caseating granulomas may be observed.

The most common symptoms reported by patients include abdominal pain and chronic diarrhea. At the time of diagnosis, most patients present with inflammatory disease only. Unfortunately, over time, some patients develop complications such as abscesses, fistulas, and intestinal strictures, which often require surgical intervention.

The current primary therapeutic goals in CD are to achieve long-term, deep remission, thereby preventing complications and reducing the likelihood of disease progression [38, 39]. Present pharmacological strategies focus on targeting the IL-23/Th17 pathway, within which mirikizumab plays a therapeutic role [11].

3.3. Mirikizumab in Phase II and III clinical trials in Crohn's disease.

The SERENITY Trial was a randomized, double-blind, placebo-controlled, multicenter Phase II study lasting 52 weeks that evaluated the efficacy of mirikizumab in patients with moderate-to-severe Crohn's disease. The trial enrolled 191 adult patients with inadequate response to standard therapies, including corticosteroids, immunosuppressants, or biologics. Patients were randomized to receive intravenous mirikizumab at doses of 200 mg, 600 mg, or 1000 mg every four weeks for the first 12 weeks, or placebo [40].

At week 12, endoscopic response was achieved in 25.8% of patients receiving 200 mg, 37.5% of those receiving 600 mg, and 43.8% of those receiving 1000 mg, compared with only 10.9% in the placebo group. Endoscopic remission was observed in 15.6% of patients in the 600 mg group and 20.3% in the 1000 mg group, compared with 1.6% in placebo; the 200 mg dose showed no superiority over placebo. Additional analyses confirmed clinical improvement, including reductions in CDAI (Crohn's Disease Activity Index), stool frequency, and abdominal pain. For higher doses, beneficial effects were evident as early as week 4, with clear superiority over placebo by week 12 across all measures [41].

In the maintenance phase, patients who had responded to induction continued intravenous therapy at the same dose or were switched to subcutaneous mirikizumab 300 mg every four weeks until week 52. Results were comparable between groups, with approximately 58% of patients achieving endoscopic improvement [42].

Given the promising results of the Phase II trial, mirikizumab advanced to Phase III evaluation. The VIVID-1 Trial, a large Phase III randomized, double-blind, placebo-controlled study, assessed the efficacy of mirikizumab in patients with moderate-to-severe Crohn's disease. More than 1, 000 patients aged 15–80 years were enrolled, all of whom had an inadequate response to, or intolerance of, conventional or biologic therapies. Exclusion criteria included other forms of inflammatory bowel disease, short bowel syndrome, active abscesses, or prior exposure to anti–IL-23 therapy [43].

Patients were randomized to three groups: mirikizumab (induction with intravenous dosing followed by subcutaneous administration), ustekinumab, or placebo. The two co-primary endpoints were early clinical response at week 12 and sustained endoscopic and clinical improvement at week 52.

Results demonstrated clear efficacy. At week 12, 38% of patients in the mirikizumab group achieved clinical response, and 38% maintained endoscopic improvement at week 52, compared with only 9% in the placebo group. Similarly, 45.4% of patients receiving mirikizumab achieved clinical remission at week 52 (following an initial week 12 response), versus 19.6% in the placebo group [44]. All key secondary endpoints—including endoscopic remission and sustained long-term response—were also met [45].

When compared with ustekinumab, mirikizumab showed comparable efficacy, further supporting its therapeutic potential [46].

The VIVID-2 Trial is currently ongoing to assess the long-term efficacy and safety of mirikizumab [47]. Importantly, the VIVID program led to FDA approval of mirikizumab for the treatment of moderate-to-severe Crohn's disease in adults [47].

In the European Union, mirikizumab has not yet received full approval for Crohn's disease. However, on December 13, 2024, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion based on promising Phase III results, confirming efficacy in adult patients with moderate-to-severe CD [48].

4. Discussion

Interleukin-23 (IL-23) plays a key role in regulating the immune system, particularly in inflammatory mechanisms. It is a heterodimeric cytokine that binds to the IL-23 receptor

(IL-23R) and activates the Jak-Stat signaling pathway, thereby enhancing the production of proinflammatory cytokines. IL-23 is especially important in the differentiation of naïve CD4+ T lymphocytes into Th17 cells, which leads to increased secretion of inflammatory mediators such as IL-17, IL-6, and TNF. In inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, elevated levels of IL-23 and Th17 cells are observed in the intestinal mucosa.

Blocking IL-23 activity represents a promising therapeutic strategy to reduce inflammation. Mirikizumab, a humanized monoclonal antibody targeting the p19 subunit of IL-23, has demonstrated high efficacy in the treatment of moderate-to-severe ulcerative colitis. Phase II and III clinical trials confirmed that the drug promotes induction of clinical remission, endoscopic improvement, and clinical response, including in patients who had not responded adequately to prior therapies, including biologics. Moreover, therapeutic benefits were maintained during long-term maintenance treatment.

The results of these studies led to the approval of mirikizumab for the treatment of ulcerative colitis in the European Union, the United States, Canada, and Japan. At the same time, findings from the VIVID-1 trial highlight the drug's potential in the treatment of Crohn's disease, although it has not yet been approved for this indication. Further studies with mirikizumab are necessary to fully assess its efficacy and safety in this patient population.

Authors' contributions:

All authors contributed to the article.

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REFERENCES

1. Tan ZY, Bealgey KW, Fang Y, Gong YM, Bao S. Interleukin-23: immunological roles and clinical implications. Int. J. Biochem. Cell Biol. 2009, 41(4), 733-5 DOI: 10.1016/j.biocel.2008.04.027
2. Duvallet E, Semerano L, Assier E, Falgarone G, Boissier MC. Interleukin-23: a key cytokine in inflammatory diseases. Ann. Med. 2011, 43(7), 503- 11, DOI:10.3109/07853890.2011.577093
3. Tian Z, Zhao Q, Teng X. Anti-IL23/12 agents and JAK inhibitors for inflammatory bowel disease. Front. Immunol. 2024, 15, Art. No: 1393463. DOI: 10.3389/fimmu.2024.1393463
4. Geremia A, Arancibia-Cárcamo CV, Fleming MPP, Rust N, Singh B, Mortensen NJ, Travis SPL, Powrie F. IL-23–responsive innate lymphoid cells are increased in inflammatory bowel disease. J Exp Med (2011) 208 (6): 1127–1133. doi.org/10.1084/jem.20101712
5. McGovern D, Powrie F. The IL23 axis plays a key role in the pathogenesis of IBD. Gut 2007; Oct; 56(10):1333–1336. doi: 10.1136/gut.2006.115402
6. Tang, C, Chen S, Qian H, Huang W. Interleukin-23: as a drug target for autoimmune inflammatory diseases. Immunology 2012, 135(2), 112-124. DOI: 10.1111/j.1365-2567.2011.03522.x
7. Aggarwal S, Ghilardi N, Xie M.H, de Sauvage F.J, Gurney A.L. Interleukin-23 promotes a distinct CD4 T cell activation state characterized by the production of interleukin-17. J. Biol. Chem. 2003, 278(3), 1910-1914. DOI:10.1074/jbc.M207577200
8. Aggarwal, S, Gurney A.L. IL-17: prototype member of an emerging cytokine family. J. Leukoc. Biol. 2002, 71(1), 1-8. DOI: 10.1189/jlb.71.1.1
9. Yen D, Cheung J, Scheerens H, et al.. IL-23 is essential for T cell-mediated colitis and promotes inflammation via IL-17 and IL-6. J Clin Invest 2006; 116: 1310-6.
10. Levin A.A, Gottlieb A.B. Specific targeting of interleukin-23p19 as effective treatment for psoriasis. J. Am. Acad. Dermatol. 2014, 70(3), 555-561. DOI: 10.1016/j.jaad.2013.10.043
11. Lees C.W, Barrett J.C, Parkes M, Satsangi J. New IBD genetics: common pathways with other diseases. Gut 2011, 60(12), 739-753 DOI:10.1136/gut.2009.199679
12. Steere B, Beidler C, Martin A, Bright, S, Kikly K, Benschop R.J. Generation and Characterization of Mirikizumab, a Humanized Monoclonal Antibody Targeting the p19 Subunit of IL-23. J. Pharmacol. Exp. Ther. 2023, 387(2), 180-187. DOI:10.1124/jpet.122.001512
13. Elson CO, Cong Y, Weaver CT, Schoeb TR, McClanahan TK, Fick RB, et al. Monoclonal anti-interleukin 23 reverses active colitis in a T cell-mediated model in mice. Gastroenterology 2007, 132(7), 2359-70. DOI:10.1053/j.gastro.2007.03.104
14. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. Gastroenterology 1998; 115: 182-205.
15. Ahmad T, Tamboli CP, Jewell D, Colombel JF. Clinical relevance of advances in genetics and pharmacogenetics of IBD. Gastoenterology 2004; 126: 1533-49.
16. Hammerhøj A, Boye TL, Langholz, E, Nielsen OH. Mirikizumab (Omvoh™) for ulcerative colitis. Trends Pharmacol. Sci. 2024, 45(3), 281-2. DOI:10.1016/j.tips.2024.01.001
17. Rao SS, Holdsworth CD, Read NW. Symptoms and stool patterns in patients with ulcerative colitis. Gut 1988, 29(3), 342-5. DOI:10.1136/gut.29.3.342
18. Feuerstein JD Cheifetz AS. Ulcerative colitis: epidemiology, diagnosis, and management. Mayo Clin. Proc. 2014, 89(11), 1553-1563. DOI:10.1016/j.mayocp.2014.07.002
19. Tontini GE, Vecchi M, Pastorelli L, Neurath MF, Neumann H. Differential diagnosis in inflammatory bowel disease colitis: state of the art and future perspectives. World J. Gastroenterol. 2015, 21(1), 21-46. DOI:10.3748/wjg.v21.i1.21
20. Danese S, Fiocchi C. Etiopathogenesis of inflammatory bowel diseases. World J. Gastroenterol. 2006, 12(30), 4807-12. DOI:10.3748/wjg.v12.i30.4807
21. Dragasevic S, Stankovic B, Sokic-Milutinovic A, Milosavljevic T, Milovanovic T, Lukic S, et al. Importance of TLR9-IL23-IL17 axis in inflammatory bowel disease development: Gene expression profiling study. Clin. Immunol. 2018, 197, 86-95. DOI:10.1016/j.clim.2018.09.001
22. Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, et al. ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. J. Crohns Colitis 2021, 16(1), 2-17. DOI:10.1093/ecco-jcc/jjab178

23. Sandborn WJ, Ferrante M, Bhandari BR, Berliba E, Feagan BG, Hibi T, 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. DOI: 10.1053/j.gastro.2019.08.043
24. Sandborn WJ, Sands, BE, Vermeire S, Leung Y, Guo X, Modesto I, et al. Modified Mayo score versus Mayo score for evaluation of treatment efficacy in patients with ulcerative colitis: data from the tofacitinib OCTAVE program. Therap. Adv. Gastroenterol. 2022, 15, Art. No: 7562848221136331. DOI: 10.1177/17562848221136331
25. Sandborn WJ, Ferrante M, Bhandari BR, Berliba E, Hibi T, D'Haens GR, 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. DOI: 10.1016/j.cgh.2020.09.028
26. II phase clinical trial of mirikizumab in UC [accesed and cited 2024 27.07]. Available from: https://clinicaltrials.gov/study/NCT02589665.
27. Badanie LUCENT-1 - III faza badań klinicznych mirikizumabu w leczeniu UC [accesed and cited 2024 27.07]. Available from: https://clinicaltrials.gov/study/NCT03518086.
28. D'Haens G, Kobayashi T, Morris N, Lissoos T, Hoover A, Li X, et al. OP26 Efficacy and safety of mirikizumab as induction therapy in patients with moderately to severely active Ulcerative Colitis: Results from the Phase 3 LUCENT-1 study. J. Crohns Colitis 2022, 16(Supplement_1), i028-i029. DOI: 10.1093/ecco-jcc/jjab232.025
29. Efficacy and Safety of Mirikizumab as Induction Therapy in Patients With Moderately to Severely Active Ulcerative Colitis: Results From the Phase 3 LUCENT-1 Study. Gastroenterol. Hepatol. 2022; 18(4 Suppl 1), 7-8.
30. D'Haens G, Dubinsky M, Kobayashi T, Irving PM, Howaldt S, Pokrotnieks J, et al. Mirikizumab as induction and maintenance therapy for ulcerative colitis. N. Engl. J. Med. 2023, 388(26), 2444-2455. DOI:10.1056/NEJMoa2207940
31. A Maintenance Study of Mirikizumab in Participants With Moderately to Severely Active Ulcerative Colitis (LUCENT 2). [accesed and cited 2024 27.07]. Available from: https://clinicaltrials.gov/study/NCT03524092
32. A Study to Evaluate the Long-Term Efficacy and Safety of Mirikizumab in Participants With Moderately to Severely Active Ulcerative Colitis (LUCENT 3). [accesed and cited 2024 27.07]. Available from: https://clinicaltrials.gov/study/NCT03519945.
33. Sands BE, D'Haens, G, Clemow, DB, Irving, PM, Johns, JT, Hunter, T, et al. 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. Inflamm. Bowel Dis. 2024, 30(6), 1044-1045. DOI: 10.1093/ibd/izae024
34. Information provided by the European Medicines Agency (EMA) concerning Omvoh (mirikizumab). Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/omvoh
35. The decision of the Japanese Pharmaceuticals and Medical Devices Agency to approve Omvoh (mirikizumab) for marketing in Japan for the treatment of moderate to severe UC in adults. Available from: https://www.pmda.go.jp/PmdaSearch/iyakuDetail/GeneralList/23994A5.
36. FDA Approves Lilly's Omvoh™ (mirikizumab-mrkz), A First-in-Class Treatment for Adults with Moderately to Severely Active Ulcerative Colitis. Available from: https://investor.lilly.com/news-releases/news-release-details/fda-approves-lillys-omvohtm-mirikizumab-mrkz-first-class
37. Summary Basis of Decision (SBD) documents provide information related to the original authorization of a product - Canada. Available from: https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SBD1695821197450.
38. Baumgart DC, Sandborn WJ. Crohn's disease. The Lancet. 2012, 380(9853), 1590-605.DOI:10.1016/S0140-6736(12)60026-9
39. Shanahan F. Crohn's disease. The Lancet. 2002, 359(9300), 62-9. DOI: 10.1016/S0140-6736(02)07284-7
40. A Study of Mirikizumab (LY3074828) in Participants With Active Crohn's Disease (SERENITY). Available from: https://clinicaltrials.gov/study/NCT02891226.
41. Avedillo-Salas A, Corral-Cativiela S, Fanlo-Villacampa A, Vicente-Romero J. The Efficacy and Safety of Biologic Drugs in the Treatment of Moderate-Severe Crohn's Disease: A Systematic Review. Pharmaceuticals (Basel) 2023, 16(11), ARt. No: 1581. DOI: 10.3390/ph16111581
42. Sands BE, Peyrin-Biroulet L, Kierkus J, Higgins PDR, Fischer M, Jairath V, et al. Efficacy and Safety of Mirikizumab in a Randomized Phase 2 Study of Patients With Crohn's Disease. Gastroenterology 2022, 162(2), 495-508. DOI:10.1053/j.gastro.2021.10.050
43. A Study of Mirikizumab (LY3074828) in Participants With Crohn's Disease (VIVID-1). Available from: https://clinicaltrials.gov/study/NCT03926130.
44. Aslam M, Ali MH, Irfan H. Mirikizumab: A promising breakthrough in Crohn's disease treatment. Health Sci. Rep. 2024, 7(8), Art. No: e2294. DOI:10.1002/hsr2.2294
45. Ferrante M, Danese S, Chen M, D'Haens G, Ghosh S, Hisamatsu T, et al. OP05 Primary efficacy and safety of mirikizumab in moderate to severe Crohn's Disease: results of the treat-through VIVID 1 study. J. Crohns Colitis 2024, 18(Supplement_1), i7-i9. DOI: 10.1093/ecco-jcc/jjad212.0005
46. Jairath V, Sands BE, Bossuyt P, Farraye F, Ferrante M, Hisamatsu T, et al. OP35 Efficacy of mirikizumab in comparison to ustekinumab in patients with moderate to severe Crohn's disease: Results from the phase 3 VIVID 1 study. J. Crohns Colitis 2024, 18(Supplement_1), i62-i4. DOI:10.1093/ecco-jcc/jjad212.0035
47. A Long-term Extension Study of Mirikizumab (LY3074828) in Participants With Crohn's Disease (VIVID-2). Available from: https://clinicaltrials.gov/study/NCT04232553.
48. Omvoh - opinion on variation to marketing authorization. Available from: https://www.ema.europa.eu/en/medicines/human/variation/omvoh