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Comparative Effectiveness of Risankizumab vs Other Biologics in Crohn's Disease: Long-Term and Quality-of-Life Outcomes after Inadequate Response to Prior Therapy

Monika Babczyńska, Agnieszka Buliszak, Piotr Marcjasz, Anna Bioły, Agnieszka Borończyk, Piotr Zając

Monika Babczyńska
Medical University of Silesia,
Ul. Poniatowskiego 15, 40-055 Katowice, Poland
e-mail: m.babczynska@gmail.com
https://orcid.org/0009-0007-8430-5838

Agnieszka Buliszak
Medical University of Silesia,
Ul. Poniatowskiego 15, 40-055 Katowice, Poland
e-mail: agnieszkaa.buliszak@gmail.com
https://orcid.org/0009-0002-2434-4775

Piotr Marcjasz
Medical University of Silesia,
Ul. Poniatowskiego 15, 40-055 Katowice, Poland
e-mail: mpmarcjasz@gmail.com
https://orcid.org/0009-0007-8247-5200

Anna Bioły
Medical University of Silesia,
Ul. Poniatowskiego 15, 40-055 Katowice, Poland
e-mail: biolyanna@gmail.com
https://orcid.org/0009-0005-2246-3537

Agnieszka Borończyk
Medical University of Silesia,
Ul. Poniatowskiego 15, 40-055 Katowice, Poland
e-mail: agawoj8@o2.pl
https://orcid.org/0009-0001-3866-9370

Piotr Zając
Upper Silesian Medical Center of Prof. Leszek Giec of the Silesian Medical University,
Ziołowa 45-47, 40-635 Katowice – Ochojec
e-mail: piotr512pz@gmail.com
https://orcid.org/0009-0004-1516-8487

ABSTRACT

Introduction and Purpose:

Crohn's disease (CD) is a chronic inflammatory condition with an unpredictable course. Despite the availability of biologics, many patients fail to achieve sustained remission. Risankizumab, an anti-IL-23 p19 monoclonal antibody, offers a new therapeutic option. This study compares risankizumab with other biologics (infliximab, adalimumab, ustekinumab, vedolizumab), focusing on long-term outcomes and quality of life.

Materials and Methods:

This review analyzes data from phase III trials (ADVANCE, MOTIVATE, FORTIFY), the SEQUENCE head-to-head trial with ustekinumab, and observational studies. Outcomes assessed include clinical remission, endoscopic response, safety, and health-related quality of life (IBDQ, SF-36, FACIT-F).

Brief Description of the State of Knowledge:

Biologics targeting TNF-α, integrins, or IL-12/23 are effective but limited by non-response or loss of response. Risankizumab selectively inhibits IL-23, sparing the IL-12/Th1 pathway. It has demonstrated higher remission and mucosal healing rates than placebo and maintains efficacy in patients previously exposed to multiple biologics.

Conclusions:

Risankizumab is a safe and effective option in moderate-to-severe CD, especially after failure of other biologics. It improves both clinical and endoscopic outcomes, as well as patient quality of life. Further direct comparisons are warranted to clarify its role in treatment algorithms.

Keywords: *Crohn's disease, biologic therapies, risankizumab, ustekinumab, quality of life, clinical remission, long-term outcomes*

INTRODUCTION

Crohn's disease (CD) is a chronic, inflammatory condition of the gastrointestinal tract with an unpredictable course, frequently affecting young individuals. It is characterized by alternating periods of exacerbation and remission, with persistent inflammation potentially leading to complications such as intestinal strictures, fistulas, and the need for surgical intervention. The introduction of biologic therapies—particularly infliximab in the late 1990s—marked a breakthrough in the treatment of CD, demonstrating high efficacy in inducing and maintaining remission as well as promoting mucosal healing [3]. Biologic agents have enabled many patients to avoid extensive intestinal resections and significantly improved long-term prognosis. However, primary and secondary non-response to therapy remains a major clinical challenge. It is estimated that approximately 30% of patients do not respond to initial anti-TNF induction therapy (primary non-response), while nearly half of initial responders eventually lose response or develop intolerance (secondary non-response). Moreover, some patients have contraindications or poor tolerance to specific drug classes—for example, infectious complications or reactivation of latent tuberculosis during anti-TNF treatment [3,8].

In recent years, novel classes of biologic agents targeting alternative inflammatory pathways have become available. Vedolizumab, an anti-α4β7 integrin monoclonal antibody, limits lymphocyte trafficking to the intestinal mucosa, exerting a predominantly gut-selective effect. Ustekinumab, an antibody targeting the p40 subunit shared by interleukins IL-12 and IL-23, inhibits signaling pathways involved in both Th1 and Th17 immune responses. Although no head-to-head comparisons were available at the time of their introduction, registry data and observational studies suggest that ustekinumab may offer superior clinical outcomes compared to vedolizumab in patients who previously failed anti-TNF therapy [2,9]. Nevertheless, a need remained for therapies more selectively targeting the IL-23 pathway, recognized as central to CD pathogenesis, particularly through Th17 cell polarization. Risankizumab, a selective IL-23 inhibitor that binds specifically to the p19 subunit, was developed to address this need. It has been approved for use in adults with moderate-to-severe CD who have not responded to or are intolerant of conventional or prior biologic therapies.

This review aims to summarize current evidence regarding the efficacy of risankizumab in comparison with other biologic therapies for CD, with particular focus on patients with an inadequate response to previous treatments—often those with multiple prior biologic failures. The mechanisms of action of available biologic agents, outcomes from pivotal clinical trials (including long-term data), mucosal healing, and health-related quality-of-life (HRQoL) effects are discussed. The objective is to compare risankizumab with adalimumab, infliximab, ustekinumab, and vedolizumab and to define its potential role within the therapeutic algorithm for CD. The central research question addresses whether risankizumab provides superior disease control and HRQoL improvements in treatment-refractory patients compared to established biologics, and what the long-term implications are regarding remission maintenance, prevention of complications, and safety.

STATE OF KNOWLEDGE

Characteristics and Pathogenesis of Crohn's Disease

Crohn's disease (CD) is a type of inflammatory bowel disease (IBD) characterized by transmural inflammation that can affect any segment of the gastrointestinal tract, most commonly the terminal ileum and colon. The clinical presentation includes abdominal pain, diarrhea (often chronic), weight loss, and in active disease also fever, fatigue, and extraintestinal manifestations involving joints, skin, or eyes. The pathogenesis of CD is complex and multifactorial, involving genetic predisposition, environmental factors (such as gut microbiota and smoking), and dysregulated immune responses. A key feature is abnormal, excessive activation of the immune system within the intestinal wall. This response is driven predominantly by Th1 and Th17 lymphocyte subsets, stimulated by pro-inflammatory cytokines including IL-12 and IL-23, which are produced

by dendritic cells and macrophages. IL-23, composed of p19 and p40 subunits, plays a critical role in the differentiation and maintenance of the Th17 response [10].

Activated Th1 and Th17 cells secrete interferon-γ, IL-17, and IL-21, which further stimulate downstream production of tumor necrosis factor-alpha (TNF-α), exacerbating inflammation and tissue damage. The presence of granulomas is a characteristic histological feature of CD and results from chronic stimulation by cytokines (e.g., TNF, interferon) and persistent macrophage activation [11, 12, 13].

Pharmacological management of CD focuses on suppression of this dysregulated immune response. Conventional treatment includes aminosalicylates, corticosteroids, and immunosuppressants (e.g., azathioprine, methotrexate), along with biologic therapies that have been available for over two decades. Biologic agents target specific inflammatory mediators. The first major class includes TNF-α inhibitors, which block this key cytokine in the inflammatory cascade. Currently approved anti-TNF agents for CD include infliximab (a chimeric IgG1 monoclonal antibody) and adalimumab (a fully human IgG1 antibody). These agents inhibit the binding of TNF-α to its receptors (TNFR1 and TNFR2) on effector cells, thereby reducing the release of other pro-inflammatory cytokines and recruitment of immune cells [15].

Another class includes integrin antagonists, such as vedolizumab—a monoclonal antibody against the α4β7 integrin on T lymphocytes. By blocking α4β7, vedolizumab prevents lymphocyte interaction with MAdCAM-1 expressed on intestinal endothelial cells, selectively limiting leukocyte trafficking to the gut and thereby reducing localized inflammation. Importantly, this “gut-selective” mechanism is associated with a lower incidence of systemic adverse effects [14, 15].

Ustekinumab is an IgG1 monoclonal antibody that binds the p40 subunit common to both IL-12 and IL-23, thereby inhibiting both Th1- and Th17-mediated inflammatory pathways—leading to suppression of chronic intestinal inflammation [2, 16].

Risankizumab, in contrast, specifically binds to the p19 subunit of IL-23 and selectively inhibits this cytokine. Mechanistically, risankizumab suppresses the Th17 response while sparing the IL-12/Th1 pathway. This selectivity may translate into a distinct efficacy and safety profile: by not inhibiting IL-12, risankizumab preserves certain Th1-mediated immune functions, which may be important in defending against intracellular pathogens [2, 17].

In summary, biologic therapies for CD target different points along the inflammatory cascade: TNF-α neutralization (infliximab, adalimumab), inhibition of lymphocyte migration (vedolizumab), blockade of IL-12/23 (ustekinumab), and selective inhibition of IL-23 (risankizumab). All these strategies aim to reduce inflammation and promote mucosal healing, though they differ in efficacy profiles across patient subgroups and in their safety characteristics.

Mechanisms of Action of Risankizumab and Other Biologic Therapies

Risankizumab is a human IgG1 monoclonal antibody that selectively binds to the p19 subunit of interleukin-23 (IL-23), thereby preventing its interaction with the IL-23 receptor. By blocking IL-23 signaling, risankizumab disrupts a critical pathway required for the survival and activation of Th17 cells. These Th17 lymphocytes play a significant role in sustaining intestinal inflammation through the secretion of pro-inflammatory cytokines such as IL-17 and IL-22, which contribute to epithelial barrier damage and recruitment of neutrophils. Additionally, risankizumab indirectly downregulates the production of other inflammatory mediators and chemokines that are dependent on the IL-23/Th17 axis. Unlike ustekinumab, risankizumab does not interfere with the IL-12/Th1 pathway—an aspect that may contribute to its specificity of action and potentially confer a more favorable safety profile, as IL-12/IFN-γ-dependent immunity remains preserved, which may be important in host defense against intracellular pathogens [17].

Ustekinumab, by contrast, targets the p40 subunit shared by both IL-12 and IL-23. This dual inhibition affects both the Th1 (IL-12–driven) and Th17 (IL-23–driven) immune responses. In the context of Crohn’s disease, it is thought that the IL-23–driven Th17 pathway is most critical to ustekinumab’s efficacy. Indeed, the clinical success of ustekinumab has validated the importance of IL-23/Th17 signaling in CD pathogenesis. As the first therapy directed at this axis, ustekinumab represented a breakthrough for patients who had failed TNF

inhibitors. Its effectiveness has been demonstrated in both biologic-naïve individuals and those with prior anti-TNF exposure. In clinical practice, ustekinumab is frequently used following anti-TNF failure or as a subsequent-line therapy in patients with refractory disease [18].

Infliximab and adalimumab are both IgG1 monoclonal antibodies directed against tumor necrosis factor-alpha (TNF-α). Infliximab is a chimeric antibody (human-murine), while adalimumab is fully human; however, their mechanism of action is essentially analogous. By binding to both soluble and transmembrane forms of TNF-α, these agents prevent the cytokine from interacting with its receptors, TNFR1 and TNFR2, located on the surface of effector cells. This blockade inhibits the TNF-mediated signaling cascade, including nuclear factor kappa B (NF-κB) activation, upregulation of adhesion molecules, production of additional pro-inflammatory cytokines (e.g., IL-1, IL-6), chemokines, and recruitment of inflammatory cells. Furthermore, infliximab and adalimumab may induce lysis of TNF-expressing cells (e.g., lymphocytes, macrophages) through complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC). Clinically, this results in rapid suppression of inflammation, with symptom improvement often observed after the initial doses. Due to their systemic action, anti-TNF agents also modulate extraintestinal manifestations of Crohn's disease and reduce systemic inflammatory markers [8].

Vedolizumab is a monoclonal antibody that targets the α4β7 integrin on T lymphocytes, which plays a key role in mediating lymphocyte trafficking from the bloodstream to organized lymphoid tissue in the gut (e.g., Peyer's patches) and inflamed intestinal sites. By blocking α4β7, vedolizumab reduces the migration of activated lymphocytes into the intestinal mucosa. Unlike natalizumab (another anti-integrin agent used in multiple sclerosis), vedolizumab does not block α4β1 integrin, thus offering greater selectivity for the gastrointestinal tract and minimizing interference with central nervous system immune surveillance. This gut-selective mechanism of action allows vedolizumab to reduce intestinal inflammation with relatively limited systemic immunosuppressive effects [19].

These mechanisms of action translate into differences in the onset of effect and safety profiles of individual agents. Anti-TNF therapies act relatively quickly and exert systemic effects, but they carry a risk of infections (e.g., tuberculosis, opportunistic infections) and immunogenicity (anti-drug antibody formation). Vedolizumab has a slower onset of action (often requiring several months to reach peak efficacy) and acts locally within the gut, which results in a lower risk of systemic infections but may limit its effectiveness in severe extraintestinal manifestations [8]. Ustekinumab and risankizumab typically require several weeks to achieve full therapeutic effect; however, their safety profiles have proven favorable in clinical trials—with a low incidence of serious adverse events comparable to placebo—making them attractive options even for patients with concerns about treatment tolerability [1].

Comparative Effectiveness and Long-Term Clinical Outcomes: Risankizumab vs. Other Biologic Therapies

Induction of remission: Historically, anti-TNF agents have demonstrated the highest efficacy in inducing clinical remission among biologic-naïve patients with Crohn's disease (CD). In pivotal trials, such as ACCENT (infliximab) and CLASSIC/GAIN (adalimumab), clinical remission (CDAI <150) was achieved in approximately 40–50% of patients within 4–6 weeks of therapy, significantly outperforming placebo. The SEAVUE trial, a head-to-head comparison of ustekinumab and adalimumab in biologic-naïve patients, revealed no statistically significant difference in remission rates after one year: 65% for ustekinumab vs. 61% for adalimumab, suggesting both TNF and IL-12/23 blockade can be highly effective as first-line options in appropriately selected patients [20].

In patients with inadequate response to anti-TNF agents—whether primary or secondary—switching to a therapy with a different mechanism of action is a common strategy, often involving ustekinumab or vedolizumab. Data from the ENEIDA registry (Versus-CD study) showed that, following anti-TNF failure, ustekinumab was more effective than vedolizumab. Clinical response, remission, and steroid-free remission rates were significantly higher with ustekinumab, and the treatment discontinuation rate was lower (hazard ratio for vedolizumab vs. ustekinumab discontinuation: 2.55; $p < 0.001$). After one year of therapy, both treatment persistence and remission rates favored ustekinumab. These findings suggest that IL-12/23 blockade may offer superior outcomes compared to integrin inhibition in the post–anti-TNF setting, although individual factors such as fistulizing disease or colonic vs. ileal involvement may influence treatment selection [21].

The efficacy of risankizumab has been evaluated in a comprehensive phase III clinical program, including two induction trials (ADVANCE and MOTIVATE) and one maintenance trial (FORTIFY). Participants included both biologic-naïve and biologic-experienced patients, including those previously treated with anti-TNF agents and ustekinumab. In the induction studies, risankizumab demonstrated significantly higher rates of clinical and endoscopic response compared to placebo as early as week 12. For example, in the ADVANCE trial, approximately 45% of patients receiving risankizumab 600 mg IV achieved clinical remission (CDAI <150), versus about 25% in the placebo group—a ~20% absolute difference favoring risankizumab. Similarly, endoscopic response (≥50% reduction in SES-CD) occurred more frequently in the risankizumab group. Notably, these benefits were observed even in biologic-experienced patients, although response rates were generally lower than in the biologic-naïve population. In the FORTIFY maintenance study, after 52 weeks of subcutaneous treatment, clinical remission was maintained in 52% of patients receiving risankizumab 360 mg every 8 weeks, compared with 41% of those switched to placebo [6]. This suggests that over half of induction responders sustain benefit during long-term risankizumab treatment. Additionally, endoscopic remission (defined as the absence of ulcerations) at one year was achieved in 21% of risankizumab-treated patients vs. 8% of placebo-treated patients, underscoring its mucosal healing potential [5]. Importantly, these trials enrolled a particularly difficult-to-treat population, with some patients having failed more than three prior biologics—further emphasizing the effectiveness of risankizumab in refractory clinical scenarios [4].

Real-world evidence is beginning to support these findings. In a multicenter retrospective study from Belgium, risankizumab was evaluated in a cohort of multi-refractory Crohn's disease (CD) patients, of whom 85% had previously received ≥4 advanced therapies and nearly 99% had prior exposure to ustekinumab. After 24 weeks of risankizumab treatment, the clinical response rate (defined as a reduction in symptom activity) was 61.8%, while clinical remission was achieved in 18.2% of patients. At week 52, clinical remission was maintained in 27.3%, and the clinical response persisted in approximately 58% of the cohort. Endoscopic improvement (≥50% reduction in SES-CD) was observed in 50% of patients within one year of treatment. Notably, 75% of patients did not require surgical intervention during the one-year follow-up period (surgery-free survival). These results reflect a particularly challenging patient population with severe disease refractory to multiple lines of treatment, highlighting the potential of risankizumab as a viable "last-line" medical therapy before surgery [5].

Earlier indirect comparisons suggested that risankizumab might be more effective than ustekinumab in inducing clinical remission in patients with moderate to severe Crohn's disease; however, these differences were not statistically significant. In terms of endoscopic response, risankizumab appeared to have an advantage over ustekinumab, likely attributable to its more selective inhibition of IL-23 via targeting the p19 subunit. Nevertheless, direct head-to-head clinical evidence has now provided more conclusive results. In the phase 3b SEQUENCE trial—a randomized clinical study—risankizumab was compared to ustekinumab in patients with moderate to severe CD who had previously failed anti-TNF therapy. After 24 weeks of treatment, 58.6% of patients receiving risankizumab achieved clinical remission, compared to 39.5% in the ustekinumab group. At week 48, endoscopic remission was observed in 31.8% of risankizumab-treated patients versus 16.2% in the ustekinumab arm. These differences were statistically significant in favor of risankizumab [7]. In conclusion, current head-to-head clinical trial data demonstrate the superior efficacy of risankizumab compared to ustekinumab in treating moderate-to-severe Crohn's disease, particularly regarding both clinical and endoscopic remission outcomes [7].

When it comes to adalimumab and infliximab, direct comparisons with risankizumab in previously biologic-experienced patients remain limited. Anti-TNF agents are typically administered as first- or second-line therapies, while risankizumab has only recently become available and is often reserved for patients who have failed anti-TNF and/or ustekinumab therapy. Nevertheless, anti-TNF agents remain highly effective in biologic-naïve patients, as demonstrated in the SEAVUE trial, where adalimumab was shown to be as effective as ustekinumab as a first-line biological option [20]. In contrast, among anti-TNF-refractory patients, better outcomes are generally achieved by switching to a drug with a different mechanism of action. In this context, risankizumab appears to be an excellent candidate, particularly considering that many patients who failed ustekinumab (which blocks IL-12/23) still responded to risankizumab [5].

Maintenance of remission and long-term outcomes**:** For all biologic therapies, maintaining remission after initial response and preventing disease-related complications remain key therapeutic goals. Long-term data suggest that continuing treatment significantly reduces the frequency of flares, hospitalizations, and the need for

surgical intervention. For example, vedolizumab treatment has been associated with over a 50% reduction in hospitalizations within 12 months of therapy initiation, compared to the year prior. In the case of anti-TNF agents, early intensive treatment ("top-down" approach) has been shown to decrease the risk of fistula formation and surgical intervention over the course of chronic disease.

As a newer agent, risankizumab currently has approximately one year of follow-up data from clinical trials and early real-world analyses. These findings indicate that most patients maintain a favorable therapeutic response during this period—a notable outcome given the heavily treatment-experienced nature of the cohort (with 20% having a history of ileostomy) [5]. The long-term safety profile of risankizumab also appears promising. No new safety signals have been identified, and the incidence of adverse events has been comparable to other biologics. A meta-analysis of IL-23 and IL-12/23 inhibitors even suggested that the risk of serious adverse events (SAEs) and treatment discontinuation due to AEs was lower than in placebo groups, supporting the favorable tolerability of these agents. Based on the current evidence, risankizumab appears to be at least as effective as other biologics used in Crohn's disease, particularly in inducing and maintaining remission in patients refractory to prior treatments. Its unique mechanism of selectively targeting IL-23 may offer advantages in mucosal healing and potentially in durability of response, although direct head-to-head comparisons are still needed. It is also essential to individualize therapy selection. For example, patients with complex fistulizing disease may benefit more from anti-TNF agents, which have established efficacy in fistula healing (supported by data for infliximab and adalimumab), whereas patients with predominant mucosal inflammation who have failed anti-TNF therapy may derive more benefit from risankizumab or ustekinumab. In many cases, sequential use of different biologics is necessary over the disease course, highlighting the importance of having multiple therapeutic options available. The introduction of risankizumab expands the treatment landscape and improves the likelihood of achieving effective disease control in patients who have previously failed available therapies [22, 23, 24].

Assessment of Health-Related Quality of Life Based on the Type of Therapy

Improvement in health-related quality of life (HRQoL) is, alongside clinical remission, one of the primary goals in the treatment of Crohn's disease (CD). Active disease is associated with significantly reduced quality of life due to debilitating symptoms (e.g., abdominal pain, diarrhea, fatigue), frequent hospitalizations, surgical procedures, and the broader impact of the disease on patients' mental health and social functioning. Biologic therapies, by reducing disease activity, lead to improvement in patients' overall well-being and functional status. HRQoL is most commonly assessed using standardized questionnaires such as the Inflammatory Bowel Disease Questionnaire (IBDQ) or general instruments like the SF-36 [25, 26].

Clinical trials of risankizumab have included quality-of-life assessments. In the induction studies (ADVANCE, MOTIVATE), a significantly higher proportion of patients achieved a clinically meaningful improvement in IBDQ scores after 12 weeks of risankizumab therapy compared to placebo (e.g., 70–75% vs 48% in ADVANCE; $p \leq 0.001$). In terms of fatigue, assessed using the FACIT-F scale, response rates were also higher with risankizumab (~48–51% vs 34–36% with placebo; $p < 0.05$). Patients receiving risankizumab also reported greater improvements in physical and mental health domains of the SF-36, as well as less interference of the disease with work productivity. Importantly, these benefits were sustained at week 52 in the maintenance phase (FORTIFY), indicating that effective long-term disease control translates into durable HRQoL improvements [6].

Similar HRQoL benefits have been observed with other biologic agents, provided that treatment is clinically effective. For instance, in a 152-week open-label study, patients receiving vedolizumab showed sustained improvement in IBDQ scores from baseline. Furthermore, successful biologic therapy has been shown to reduce the prevalence of anxiety and depression among patients with IBD—an important dimension of quality of life. Conversely, therapeutic failure or secondary loss of response often leads to deterioration in HRQoL—patients requiring treatment escalation or surgery report lower HRQoL scores, highlighting the need to maintain remission through effective therapy [6, 27]. It is worth noting that direct comparative data on HRQoL between biologic therapies are currently lacking. However, it may be assumed that superior efficacy in disease control is likely to be accompanied by greater improvements in HRQoL [28]. Given that risankizumab has demonstrated high efficacy in patients unresponsive to other treatments, it may substantially improve HRQoL by reducing disease activity in otherwise refractory cases. An additional factor is the route of administration and treatment convenience. Infliximab requires intravenous infusions in a hospital setting, whereas adalimumab, ustekinumab, and risankizumab are administered subcutaneously during the maintenance phase (risankizumab every 8 weeks,

ustekinumab every 8–12 weeks, adalimumab every 2 weeks). Less frequent injections and greater ease of administration may positively influence patients' perception of treatment and everyday functioning, although robust comparative data on this aspect remain limited [28, 29].

In summary, risankizumab therapy results in significant and sustained improvements in HRQoL for patients with Crohn's disease, comparable to other effective biologic therapies. Introducing risankizumab as a viable option in biologic-refractory patients offers an opportunity to regain disease control and improve daily functioning. Monitoring HRQoL should be an integral part of treatment evaluation—if HRQoL remains low despite biologic therapy, a change in treatment strategy (e.g., switching to another class of biologics) should be considered, even in the presence of partial objective response [30].

CONCLUSION

Advances in the understanding of the immunopathogenesis of Crohn's disease (CD) have led to the expansion of the therapeutic armamentarium with biologic agents targeting distinct pathways of the immune system. As a result, clinicians now have access to several biologic classes: anti-TNF agents (infliximab, adalimumab), anti-integrin agents (vedolizumab), anti-IL-12/23 (ustekinumab), and the most recent addition—anti-IL-23 (risankizumab). Despite therapeutic progress, a substantial proportion of patients still experience inadequate response or secondary loss of response over time. In such cases, switching to a biologic with a different mechanism of action is necessary.

Risankizumab has emerged as a breakthrough treatment option for patients with moderate-to-severe CD, particularly those who failed previous biologic therapies. Its efficacy in inducing remission and promoting mucosal healing has been demonstrated in phase III trials, with favorable outcomes maintained during long-term therapy (approximately 50% clinical remission at one year of maintenance). Among heavily pretreated patients, risankizumab has shown a clinically meaningful rate of both clinical and endoscopic responses, positioning it as a valuable therapeutic option before considering surgery. When compared to other biologics, risankizumab yields outcomes that are at least comparable. Anti-TNF agents remain the gold standard as first-line treatment in many patients, but after their failure, risankizumab (and ustekinumab) may offer higher remission rates than traditional escalation strategies or vedolizumab. Preliminary evidence suggests that risankizumab may surpass ustekinumab in specific endpoints, such as mucosal healing, although direct head-to-head comparisons are still needed. In terms of safety, anti-IL-23 agents have shown excellent tolerability. The safety profile of risankizumab is favorable and comparable to that of ustekinumab, with no increased risk of opportunistic infections or other serious adverse events compared to placebo—distinguishing it from older immunosuppressive therapies. Nevertheless, careful monitoring remains essential due to the inherent risk of immunosuppression associated with all biologics [5]. From the quality-of-life perspective, achieving and maintaining remission is paramount. Risankizumab significantly improves HRQoL metrics during induction and maintains this improvement over time. This is especially relevant for patients who have experienced long-term impairment from active disease—an effective new therapy may significantly shift their clinical outlook [6].

Future Directions**:** Long-term studies are needed to determine whether sustained remission with risankizumab can be achieved in a subset of patients, potentially allowing treatment de-escalation in the future. Furthermore, it remains to be seen whether inhibition of the IL-23 pathway can reduce the risk of structural complications such as strictures. An emerging area of interest is combination therapy—ongoing trials are evaluating dual blockade (e.g., TNF and IL-23) in refractory patients, aiming to enhance efficacy without compromising safety.

In conclusion, risankizumab has filled an important gap in the treatment landscape of Crohn's disease. For patients with inadequate response to existing therapies, it offers new hope for clinical improvement and better quality of life. Personalized treatment—selecting the right biologic at the right time for each patient—is critical for therapeutic success. With anti-TNF, anti-integrin, and anti-interleukin agents now available, clinicians can better tailor therapy to individual disease characteristics. Continued progress in this field—including the development of new agents and biomarkers to predict treatment response—will further support the ultimate goal: sustained steroid-free remission, optimal mucosal healing, and the highest possible quality of life for patients with Crohn's disease.

AUTHOR'S CONTRIBUTIONS

The authors confirm contribution to the papers as follows:
Conceptualization: Monika Babczyńska
Methodology: Monika Babczyńska and Piotr Marcjasz
Software: Anna Bioły and Agnieszka Borończyk
Check: Agnieszka Buliszak and Piotr Marcjasz
Formal Analysis: Agnieszka Borończyk and Monika Babczyńska
Investigation: Anna Bioły and Piotr Zając
Resources: Agnieszka Buliszak
Data curation: Piotr Zając
Writing - rough preparation: Piotr Marcjasz, Anna Bioły, Monika Babczyńska and Agnieszka Buliszak
Writing - review and editing: Anna Bioły, Agnieszka Buliszak, Piotr Marcjasz and Piotr Zając
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Supervision: Agnieszka Borończyk
Project administration: Piotr Zając
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