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Current Therapeutic Strategies for Inflammatory Bowel Disease: A Narrative Review

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Abstract

Background: Inflammatory bowel disease (IBD) is a chronic, relapsing disorder resulting from genetic, immune, microbial, and environmental factors. Therapeutic options have expanded from conventional drugs to biologic agents and targeted small molecules, enabling individualized management.

Aim: This narrative review aimed to summarize current treatment strategies for IBD, focusing on conventional therapies, biologics, targeted small molecules, antibiotics, and surgery.

Materials and Methods: A narrative literature review was conducted using PubMed, MEDLINE, Google Scholar, and the Journal of Education, Health and Sport (JEHS). Current

clinical guidelines, European Medicines Agency (EMA) product information, clinical studies, systematic reviews, and meta-analyses were reviewed, with attention to indications, efficacy, and safety.

Results: Biologic agents and targeted small molecules have broadened therapeutic options for moderate-to-severe IBD. Anti-TNF agents, vedolizumab, ustekinumab, selective IL-23 inhibitors, Janus kinase (JAK) inhibitors, and ozanimod act through different pathways and allow treatment to be adapted to disease phenotype, severity, and previous treatment exposure. Conventional therapies, including aminosalicylates, corticosteroids, thiopurines, and methotrexate, remain important in selected situations. Antibiotics retain a role in specific complications, while surgery remains essential in refractory disease and structural complications.

Conclusions: Contemporary IBD management follows an individualized, treat-to-target approach aimed at symptom control, objective inflammatory control, mucosal healing, and prevention of long-term complications. Despite therapeutic advances, uncertainties remain regarding treatment sequencing, predictors of response, long-term safety, and access to advanced therapies. Further research is needed to optimize personalized strategies and improve long-term outcomes.

Keywords: IBD; Crohn’s disease; ulcerative colitis; biological therapy; biological treatment; inflammatory bowel disease; TNF-alpha inhibitors

1. Introduction

Inflammatory bowel disease is an autoimmune disease and causes symptoms mainly in the digestive system, but also affects other systems due to impaired absorption of nutrients, as well as a number of extraintestinal complications resulting from an excessive immune response. A study using population data from the years 2012–2014 showed IBD prevalence of 157 per 100 000 individuals for Poland [1]. The onset of the disease most often occurs in adolescence and young adulthood. Approximately 25% of patients with IBD present before age 20 years [2]. Consequently, IBD not only reduces patients' quality of life but can also cause growth disorders in children. Therefore, it is crucial that treatment is not only effective but also causes minimal side effects, which can be particularly troublesome for children. The etiology is complex and involves the influence of environmental, genetic, and microbiological factors. Environmental factors appear to play a significant role, as the concordance rate for onset of the disease in monozygotic twins is only 50% [3]. The disease is more common in developed countries compared to developing countries [4]. Neonatal/infant factors, such as cesarean section, lack of

exposure to breast milk, and early exposure to antibiotics, play a significant role [5-8]. It should not be forgotten that the composition of the gut microbiome has a significant impact on the onset of the disease, and patients present with intestinal dysbiosis with overrepresentation and underrepresentation of specific taxa [9,10]. IBD is divided into ulcerative colitis and Crohn's disease. In ulcerative colitis, inflammatory lesions begin in the rectum and spread proximally without disruption [11]. Lesions can involve the entire colon and even the terminal ileum (backwash ileitis). In 40 to 70% of patients, mild inflammation also occurs in the upper gastrointestinal tract [12]. Crohn's disease lesions are discontinuous and can involve any area of the gastrointestinal tract, from the mouth to the anus. Gastrointestinal fissures, fistulas, and abscesses are common [12,13].

2. Material and methods

A literature review was conducted using the PubMed, Google Scholar, MEDLINE and Journal of Education, Health and Sport (JEHS) databases. Additionally, the EMA's Summary of Product Characteristics database was utilized. Current Polish IBD treatment guidelines were analyzed. Relevant studies and meta-analyses addressing various aspects of this complex and heterogeneous inflammatory bowel disease (IBD) were identified and analyzed. The following keywords and their combinations were used: “IBD”; “Crohn’s disease; Lesniowski-Crohn’s disease”; “ulcerative colitis”; “biological treatment”; “inflammatory bowel disease”; “TNF-alpha inhibitors”. The most up-to-date available data was used to present data on treatment regimens, guidelines, drug characteristics, their effects, and possible adverse effects.

3. Aim of the study

The aim of this study was to provide a comprehensive overview of the current therapeutic options available for the treatment of IBD, including anti-inflammatory, immunomodulatory, and biologic therapies, with a focus on their mechanisms of action, clinical efficacy, safety profiles, and current indications and approvals. Furthermore, the role of antibiotics and surgical procedures in current treatment was considered.

4. Treatment guidelines

The current goals of treatment are to (1) eliminate symptoms and restore quality of life, (2) restore normal growth, and (3) eliminate complications. Drugs used in treatment can generally be classified into those that induce remission, those that maintain remission, and those that act in both areas [11].

4.1. Treatment guidelines in Crohn disease

Recognized risk factors include: smoking, young age at the time of diagnosis, stenotic and fistulizing forms, and extensive intestinal involvement. The identification of at least two risk

factors for severe disease should prompt the selection of a more aggressive treatment strategy: earlier initiation of immunosuppressive therapy, as early as the first flare, and/or earlier consideration of biologic therapy [14-17].]The primary goal of treatment should be to achieve clinical remission (as assessed by the CDAI scale), as well as a decrease in CRP levels, healing of mucosal lesions as assessed by endoscopy and a decrease in fecal calprotectin levels. In patients without risk factors for severe disease who are in stable remission, fecal calprotectin levels should be measured every 6–12 months [18-32].

4.1.1. Induction therapy

In the event of a relapse, causes of symptoms other than exacerbations (e.g., infection, functional disorders) should be considered, and appropriate laboratory, imaging, and bacteriological tests should be performed [33-41]. In the first-line induction treatment of ChLC, glucocorticoids are used: systemic glucocorticoids (administered orally: prednisone and methylprednisolone; and administered intravenously: hydrocortisone) and budesonide. The use of budesonide in ChLC is limited to mild and moderate cases involving lesions located in the ileocecal region. In other cases, the first-line treatment is systemic steroids administered orally (at an initial dose equivalent to 0.75 mg/kg body weight or 40 mg of prednisone), and in selected cases, intravenously (e.g., hydrocortisone 300–400 mg/day in divided doses). Treatment with the initial dose should be continued for up to 4 weeks, after which the dose should be gradually reduced, and glucocorticoids should be discontinued after a maximum of 12 weeks [42-45]. In cases of steroid resistance, steroid dependence, or steroid intolerance, immunosuppressive drugs should be used. In more severe cases, biologics (anti-TNF agents, vedolizumab, ustekinumab) should be used as monotherapy or in combination with immunosuppressive drugs [46-48].

4.1.2. Maintenance therapy

In patients with a mild form of the disease, especially those with ileocecal involvement, a short history, and no risk factors for a severe course, if remission is achieved quickly, maintenance therapy may not be initiated. In such patients, clinical symptoms, calprotectin levels, and radiographic findings should be monitored [49]. Although mesalazine is a commonly used drug in the treatment of mild and moderate ChLC, numerous clinical trials and meta-analyses have failed to demonstrate its efficacy, both in remission induction and maintenance therapy. The only benefit may be a reduced risk of colorectal cancer [50-64]. If clinical remission has been achieved with glucocorticoids, immunosuppressive drugs are recommended for maintenance therapy: thiopurines or methotrexate. The first-line drugs for maintenance therapy are thiopurines (azathioprine at a dose of 2–2.5 mg/kg body weight or 6-mercaptopurine at a dose

of 1–1.5 mg/kg body weight) [43]. In cases of intolerance or contraindications to thiopurines, methotrexate is an alternative immunosuppressive drug (at a dose of 25 mg subcutaneously once a week for 12 weeks, followed by 15 mg subcutaneously or, alternatively, orally) [47]. If clinical remission has been achieved with biologic agents, these agents should be used for maintenance therapy, with a possible change in the route of administration from intravenous (used in induction therapy) to subcutaneous (used in maintenance therapy) [65-68].

4.2. Treatment guidelines in ulcerative colitis

When planning treatment, the following criteria should be taken into account: clinical disease activity (Mayo scale, PRO-2, Truelove-Witts criteria), endoscopic Mayo scale, as well as the extent of inflammatory changes in endoscopic assessment and the course of previous treatment [19,33,69,70].

4.2.1. Induction therapy

First-line treatment for exacerbations should be mesalazine, administered rectally and orally in cases of severe disease. For mild lesions (limited to the rectum), the dose is 1 g/day rectally, while for lesions involving the entire left half of the colon and more advanced disease, the dose is 3 g/day rectally in combination with oral medications. The daily dose of oral mesalazine is 4 g. An alternative to mesalazine is sulfasalazine [33,69,71]. If remission has not been achieved despite optimal use of mesalazine, treatment with topical steroids (budesonide) or systemic steroids, administered orally (prednisone, methylprednisolone), should be considered. Budesonide is administered at a dose of 9 mg per day, whereas prednisone at a dose of 0.5–1 mg/kg body weight (usually 40 mg/day). Budesonide is used to treat mild and moderate forms, however prednisone and methylprednisolone are used to treat moderate to severe cases. Unlike prednisone and prednisolone, budesonide has a primarily local effect due to the first-pass effect. Prednisone and prednisolone are used in induction therapy, which lasts 2–4 weeks, and are then gradually tapered off. The entire course of treatment should last no longer than 8–12 weeks [33,45,69,71-76]. For moderate to severe cases, high-dose mesalazine (administered orally and—if tolerated—topically) is recommended for induction therapy, in combination with systemic steroids (at the standard dose). In the most severe cases, molecularly targeted drugs (anti-TNF agents, vedolizumab, ustekinumab, tofacitinib) are used [33,69,71]. Acute severe ulcerative colitis (ASUC) is characterized by highly active inflammatory changes in the large intestine with severe intestinal symptoms and an accompanying systemic reaction. The Truelove-Witts criteria are used to diagnose ASUC. which is important to qualify the patient for hospital treatment. The diagnosis is based on the presence of 6 or more bloody stools per day accompanied by at least one systemic reaction marker, such as hemoglobin (Hb) < 10.5

g/dL, erythrocyte sedimentation rate (ESR) > 30 mm/h (or CRP > 30 mg/L), body temperature >37.8°C, and tachycardia > 90/min. To confirm ASUC, an endoscopic examination—a rectosigmoidoscopy without preparation—is recommended. Additional tests for patients with suspected ASUC also include a plain abdominal X-ray (to rule out toxic megacolon),to rule out an infectious cause of the exacerbation (primarily testing for infection with a toxin-producing strain of C. difficile), and laboratory tests (primarily a complete blood count, electrolyte levels, CRP, and creatinine). Intravenous steroid therapy in a hospital setting is recommended for patients who meet the Truelove-Witts criteria for an acute, severe exacerbation. Treatment with infliximab is recommended for patients who have not responded after 3 days of treatment with intravenous steroids. As an alternative to infliximab, cyclosporine may be used. In all cases, due to the increased risk of thromboembolic complications, low-molecular-weight heparin should be administered at a prophylactic dose. In selected patients, antibiotic therapy is sometimes also used as adjunctive treatment. Surgical treatment is recommended if no response is observed after an additional 5 days of therapy with cyclosporine or infliximab. Surgical treatment should always be considered if symptoms of toxic megacolon, massive bleeding, and/or signs of shock occur [33,70,71,77-80].

4.2.2. Maintenance treatment

If remission of a UC flare has been achieved with mesalazine, it should also be used for maintenance treatment. Mesalazine is also recommended for maintenance therapy in patients who have achieved remission with steroids and mesalazine. The minimum recommended oral dose is 2 g/day. As in exacerbations, the route of administration is rectal/oral or both, depending on the degree of involvement of the large intestine by the disease process. The lowest recommended oral dose is 2 g per day [33,69,71]. Maintenance therapy with thiopurines is recommended for selected patients who have achieved remission with steroids. In each patient, provided there are no contraindications, mesalazine should also be used as part of maintenance therapy. Azathioprine (at a dose of 2–2.5 mg/kg body weight) or 6-mercaptopurine (at a dose of 1–1.5 mg/kg body weight) is administered orally, in one or two divided doses. Thiopurines achieve their full therapeutic effect only after a long period of time (6–12 weeks); therefore, to control symptoms, steroid therapy should be maintained at the lowest effective dose until then (for the next 4–8 weeks), followed by an attempt to gradually taper the steroids (however, systemic steroid therapy should not last longer than 12 weeks) [33,69-71,77,81]. Maintenance therapy with infliximab is recommended if induction was achieved with this drug; however, if induction was achieved with cyclosporine, maintenance therapy should be conducted using thiopurines [82]. Molecularly targeted drugs (anti-TNF agents, vedolizumab, ustekinumab,

tofacitinib) are used in cases of primary failure, loss of efficacy, intolerance to other medications. They are also commonly used in cases of steroid resistance or steroid dependence, particularly in moderate-to-severe forms of the disease [33,69-71,77].

5. Types of treatment

5.1. Antiinflammatory treatment

Corticosteroids are effective in inducing remission but are not useful in maintaining remission because their long-term use is associated with a number of side effects.[11] Glucocorticoids reduce the number of T cells, monocytes, and eosinophils. They also reduce the binding of immunoglobulins to receptors on the cell surface and inhibit the synthesis or release of interleukins by reducing T-cell blastogenesis of T lymphocytes and reducing the intensity of the early immune response. They may also inhibit the penetration of immune complexes through basement membranes and reduce the concentration of complement components and immunoglobulins. In addition to their immunosuppressive effects, corticosteroids also suppress the hypothalamic-pituitary axis; therefore, be vigilant for secondary adrenal and pituitary insufficiency, as well as for adverse effects such as: psychiatric disorders, hyperglycemia, increased intracranial pressure, peptic ulcers, stretch marks, acne, muscle weakness, and osteoporosis [45]. Budesonide is characterized by a high first-pass effect (more than 90% of the drug is metabolized in the liver); therefore, its systemic effects are minimal, while it exhibits a strong local effect. A different effective treatment method for inducing remission with fewer side effects than glucocorticosteroids is exclusive enteral nutrition (EEN). The duration of therapy is usually 8 to 12 weeks. Furthermore, this form of treatment affects the healing of the mucosa. Adverse effects are primarily related to the insertion and presence of the nasogastric tube. Exclusive enteral nutrition (EEN) is also being used experimentally as a form of maintenance therapy, as nighttime feeding in addition to a normal daytime diet [83,84]. Another group of drugs effective in inducing and maintaining remission in IBD are aminosalicylates, which are primarily used in adults because few clinical trials have been conducted in children [85]. A large observational study showed that 30% of pediatric patients maintained remission when using aminosalicylates alone [86]. The most common drug in this group is mesalazine, which can cause nausea, headaches, fever, and rash. The active ingredient (mesalazine) is metabolized in the colon to form two metabolites: 5-aminosalicylic acid (mesalazine) and sulfapyridine. The active ingredient in this group of drugs is 5-aminosalicylic acid (5-ASA) and sulfapyridine is responsible for the side effects. Before starting treatment and during treatment, the following tests should be ordered: blood tests (complete blood count, AST, ALT, creatinine) and a general urinalysis (dipstick tests). It is

recommended to repeat these tests 14 days after the start of treatment, and then 2 to 3 times at 4-week intervals. If the results are within the normal range, subsequent tests should be performed every 3 months. If additional symptoms occur, the tests should be performed immediately. Rare side effects include headache, dizziness, myocarditis, pericarditis, abdominal pain, diarrhea, bloating, nausea, and vomiting [87].

5.2. Immunosuppressive treatment

Thiopurine drugs, such as azathioprine and its active metabolite, mercaptopurine (6-MP), are used as maintenance therapy because they have a delayed onset of action of several weeks. A large, multicenter, randomized clinical trial demonstrated that early (within the first 8 weeks) introduction of 6-MP reduces the need for corticosteroids and improves the maintenance of clinical remission in children [88]. Adverse effects include myelosuppression, elevated transaminases, and pancreatitis. During treatment with thiopurines, laboratory parameters should be monitored periodically, primarily complete blood count, alanine aminotransferase (ALT), and creatinine - ideally every 2 weeks for the first 2 months of treatment, and then at least every 3 months [49]. Furthermore, thiopurines increase the risk of lymphoma in the pediatric population by approximately 7.5-times [89]. In adult patients, thiopurines increase the risk of non-melanoma skin cancer, cervical cancer, and aggressive B-cell lymphoma, for which EBV is a risk factor. Therefore, thiopurines are not recommended for individuals who have not previously been infected with EBV, particularly young men (under 35 years of age). All patients should be under the care of a dermatologist, and women should also be under the care of a gynecologist. Mild leukopenia (white blood cell count above 3,500/μl) does not require a dose adjustment. If the white blood cell count remains below 3,500, the dose of thiopurine must be reduced; in cases of severe leukopenia (below 2,500, with lymphocytopenia < 1,000), the drug must be discontinued. An increase in transaminase levels to 3 times the upper limit of normal requires monitoring and possible dose adjustment, while a 5-fold increase above the upper limit of normal requires discontinuation of the drug. The efficacy of thiopurine therapy can be assessed after at least 6 weeks of treatment with a stable dose, while the optimal therapeutic effect is achieved after 12 weeks of therapy. Another immunomodulatory drug used to maintain remission in IBD is methotrexate, which can cause numerous health-threatening side effects and requires folic acid supplementation (1 mg daily or 5 mg once a week, 1–2 days after receiving a dose of methotrexate) [49]. Large retrospective cohort studies have confirmed its effectiveness in maintaining remission in 30% of children with IBD [90]. Particularly significant side effects of methotrexate, especially in young patients, include decreased fertility, decreased sperm count, menstrual irregularities, and amenorrhea.

Furthermore, methotrexate is toxic to the embryo and causes fetal defects and may cause miscarriage. Patients and their sexual partners should use effective contraceptive methods during methotrexate treatment and for at least three months after discontinuation. Methotrexate may cause leukopenia, elevated transaminase levels, acute liver atrophy, renal failure, hematuria. The use of methotrexate requires regular monitoring of kidney and liver function, urine test, blood counts and sometimes also assessment of methotrexate concentration in the blood [91]. A twofold increase in transaminase levels above the upper limit of normal is an indication to discontinue treatment until levels return to normal [49]. Any significant reduction in leukocyte or platelet counts is an indication for immediate discontinuation of the drug and the implementation of appropriate supportive treatment. During treatment, precipitation of methotrexate or its metabolites in the renal tubules is possible. Preventive measures include the administration of large amounts of fluids and urine alkalinization, which can be achieved by oral or intravenous administration of sodium bicarbonate or acetazolamide. In addition, methotrexate reduces resistance to infections, causing anorexia, dizziness and headaches, interstitial pneumonia, abdominal pain, joint pain, and chills [91].

5.3. Biological treatment and small molecule treatment

The treatment of IBD has been revolutionized by the introduction of biologics and small molecule drugs. The range of available therapies is still expanding. The main one, and the first to be introduced into treatment, is the group of tumor necrosis factor inhibitors (TNF-α inhibitors) [92]. These drugs include: infliximab - the first biologic drug approved in 1998 in the United States for the treatment of Crohn's disease and in 2005 for the treatment of ulcerative colitis, adalimumab, certolizumab (only for Crohn's disease, not registered in Poland for the treatment of IBD) and golimumab (only for ulcerative colitis) [92,93]. Other biological drugs include alpha 4 integrin inhibitors - vedolizumab; interleukins 12 and 23 inhibitor - ustekinumab; interleukin 23 inhibitors - mirikizumab, risankizumab [92], guselkumab and brazikumab [94]. The group of small molecule drugs includes: oral Janus kinase (JAK) inhibitors - tofacitinib, filgotinib, upadacitinib and sphingosine-1-phosphate receptor modulator - ozanimod [92]. In Crohn's disease, the most frequently mentioned indications for the introduction of biological treatment include: steroid-resistant or steroid-dependent disease, resistance to immunomodulators, severe course of the disease - also in the presence of negative prognostic factors, and the course of the disease with fistulas. Indications for the initiation of biological treatment in ulcerative colitis include: steroid-resistant severe colitis, steroid-dependent presence of active inflammation, steroid resistance, and resistance to immunomodulatory drugs [93]. Furthermore, an indication for initiating treatment with

biological drugs is the occurrence of side effects during treatment with immunomodulating drugs [49,82].

Biological drugs can be used both as monotherapy and in combination with immunomodulatory drugs [49,93]. Combination therapy with TNF-alpha inhibitors and immunosuppressive therapy has been shown to be effective in both Crohn's disease and ulcerative colitis [49,82,94]. The first study confirming the higher effectiveness of combined treatment with infliximab and azathioprine in Crohn's disease was the SONIC study from 2010. The combination of infliximab with azathioprine was found to be most effective in achieving clinical remission in moderate to severe Crohn's disease compared to aziatropine monotherapy and infliximab monotherapy [95]. Similar results have been shown for ulcerative colitis, with combination therapy with azatropine and infliximab increasing the chance of remission, resulting in better mucosal healing outcomes [96]. In both studies, the aim was to assess the effectiveness of achieving remission without the use of glucocorticosteroids [95,96]. Combination therapy also improves the effectiveness of therapy by reducing the risk of producing antibodies against infliximab, especially in the first year of treatment [82].

Tumor necrosis factor alpha (TNF-α) is a key pro-inflammatory cytokine involved in the pathogenesis of inflammatory bowel disease. Excessive TNF-α production promotes persistent intestinal inflammation, disrupts epithelial barrier function, and enhances the recruitment of inflammatory cells. Anti-TNF agents neutralize TNF-α activity, thereby reducing inflammatory signaling, limiting immune cell infiltration, and promoting mucosal healing. These mechanisms contribute to their effectiveness in inducing and maintaining remission in patients with Crohn's disease and ulcerative colitis [97]. Infliximab is one of the most commonly used biologic drugs for inflammatory bowel disease. Infliximab is indicated for the treatment of moderate to severe Crohn's disease and ulcerative colitis in patients who have not responded adequately to conventional therapy, and is registered for the treatment of both adults and children. It is effective in inducing and maintaining clinical remission, promoting mucosal healing, and reducing the need for corticosteroids and surgery. Currently, the drug is registered for intravenous and subcutaneous administration. The most frequently reported adverse effects include infections, infusion-related reactions, headache, abdominal pain, and upper respiratory tract infections [98]. Other side effects include a slight oncological risk, mainly an increased risk of developing skin melanoma [82]. Due to the increased risk of immunogenicity, it is recommended to initiate treatment with infliximab in combination whenever there are no contraindications to immunomodulatory treatment with thiopurines [49]. Adalimumab is also an IgG1 monoclonal antibody directed against the TNF factor [99], but it is a human antibody,

which is why it is characterized by lower immunogenicity compared to infliximab [82]. For this reason, it does not require the use of thiopurines in combination therapy during the induction phase of therapy, and should therefore be chosen when there are contraindications to thiopurine therapy or when side effects occur [49]. Adalimumab is also approved for the treatment of both inflammatory bowel disease in both the adult and pediatric populations. The most common side effects include upper respiratory tract infections, local reactions after injection, headaches, muscles and bones pain. Adalimumab is administered by subcutaneous injection [99]. Golimumab is an anti-TNF IgG1 antibody approved for the treatment of ulcerative colitis, for treatment of adults and children over 2 years of age, weighing at least 15 kg [100]. Golimamab's side effects are similar to those typical of anti-TNF drugs. Among the drug's advantages is its low immunogenicity, which may prove effective in patients who are intolerant to other anti-TNF drugs or who develop antibodies against them [101]. Certolizumab pegol is approved for the treatment of Crohn's disease in some countries, including the United States. However, it is not approved for the treatment of inflammatory bowel disease in the European Union [93,102]. Certolizumab pegol is a recombinant, humanized Fab fragment of a monoclonal antibody against TNF-alpha, conjugated to polyethylglycol, therefore its action profile is slightly different than the previously mentioned drugs [103].

Vedolizumab is a gut-selective anti-integrin monoclonal antibody that blocks leukocyte trafficking to the intestinal mucosa by targeting the α4β7 integrin. Its selective action minimizes systemic immunosuppression and contributes to a favorable safety profile. Clinical studies have demonstrated its effectiveness in inducing and maintaining remission in patients with moderate-to-severe Crohn's disease and ulcerative colitis, including those who failed conventional or anti-TNF therapy [101,104]. Ustekinumab, another biologic drug approved for the treatment of moderate to severe Crohn's disease and ulcerative colitis in adult patients, is an antibody against the p40 subunit, a component of interleukins 12 and 23. By blocking their activity, the drug suppresses the immune system, thereby reducing disease symptoms. Like vedolizumab, ustekinumab has a high safety profile and low immunogenicity. Furthermore, studies have not found an increased risk of cancer with either drug [49,82,105]. Currently, both vedolizumab and ustekinumab, both in Crohn's disease and ulcerative colitis, may be the first-line drugs in adults if biological treatment is necessary [49,82]. In both cases, the benefits of treatment with vedolizumab and ustekinumab in combination with immunomodulators have not been described so far [49].

The next group are interleukin-23 inhibitors (including mirikizumab, risankizumab, guselkumab, and brazikumab). These represent the latest and most promising discovery in the

treatment of IBD. They have been shown to be effective for both Crohn's disease and ulcerative colitis. They selectively inhibit the p19 subunit of interleukin-23, thus having no effect on interleukin-12. IL-12 participates in the body's normal immune response, while IL-23 is responsible for maintaining chronic inflammation and tissue damage. Understanding the distinct functions of these cytokines has enabled the development of selective IL-23 inhibitors, which limit the inflammatory process while maintaining normal immunity. Moreover, they appear to be a better choice than TNF-alpha inhibitors in immunocompromised patients susceptible to infections [106]. Previous meta-analyses indicate that selective IL-23p19 inhibitors are among the most effective therapies for the treatment of moderate to severe inflammatory bowel disease, demonstrating high efficacy with a favorable safety profile. Although JAK inhibitors sometimes achieve better results, IL-23p19 agents often surpass or equal the efficacy of anti-TNF therapies, vedolizumab, and ustekinumab, particularly in patients with Crohn's disease [106,107].

Janus kinase inhibitors (JAK inhibitors) are a unique group of small-molecule drugs. These drugs include tofacitinib, filgotinib, and upadacitinib. The former two are currently approved for ulcerative colitis, while the latter is approved for both IBDs. Among the advantages of this group are oral administration and lack of antigenicity [108-111]. Janus kinases are enzymes involved in the transduction of signals triggered by many cytokines involved in the development and maintenance of inflammation in IBD. Through phosphorylation, JAK kinases activate STAT proteins, where they control the expression of genes responsible for the development and maintenance of the inflammatory response. Inhibiting the JAK-STAT pathway therefore limits the activation of immune cells, leading to a reduction in disease activity [108,112]. Among the JAK kinase isoforms, JAK1 is considered the most important in the pathogenesis of IBD. Of these drugs, upadacitinib is the most selective for JAK1 [44], which is why its approval also covers Crohn's disease [108]. Available reports also indicate it as potentially the most effective JAK inhibitor in the treatment of IBD, characterized by high effectiveness in inducing rapid and strong induction and maintenance of remission, while maintaining a high safety profile [108,112]. Common side effects include pneumonia, opportunistic infections (including, in particular, shingles), lymphopenia, hypertension and hypertransaminasemia [82,109-111].

The last drug described in this group is ozanimod - sphingosine-1-phosphate receptor modulator, registered for the treatment of moderate to severe ulcerative colitis, for patients for whom conventional or biological therapy is contraindicated, has been ineffective, or has lost a sufficient response. Ozanimod inhibits the movement of lymphocytes from the lymph nodes

into the circulatory system and intestinal mucosa, thereby limiting the damage caused by the overreaction of the immune system, slowing the progression of ulcerative colitis [82,113]. *True Notch* studies have demonstrated its effectiveness in both treatment phases (induction and maintenance) and its high safety profile [46]. Infections and hypertransaminasemia have been reported as the most common side effects. The advantage is oral administration [113,114]. Studies have also shown its effectiveness in Crohn's disease, but the drug has not yet been registered for this indication [114].

5.4. Antibiotics in IBD

Current reports indicate that antibiotics should be used in IBD with concomitant infections and purulent and septic complications. In Crohn's disease, the main indication for their use is perianal tissue infection (not as monotherapy, but as a combination therapy with surgery or biological treatment). Among the antibiotics with the highest degree of proven effectiveness are metronidazole and ciprofloxacin. Antibiotics can also support the treatment of fistulas. In ulcerative colitis, antibiotics should be used for J-pouch infections (created during proctocolectomy); ciprofloxacin (first-line drug) or metronidazole are also indicated. In cases of antibiotic-dependent pouchitis (when recurrence occurs more than four times a year, we can speak of antibiotic-dependent inflammation), extended (four weeks) combined antibiotic therapy can be used. Rifaximin has been shown to be effective in maintenance therapy. Rifaximin has also been shown to be effective in inducing and maintaining remission in Crohn's disease [49,82,115,116].

5.5. Other drugs

In Crohn's disease, which can affect the entire gastrointestinal tract, upper gastrointestinal lesions should be treated with proton pump inhibitors as first-line medications. In moderate to severe disease, they should not be used as monotherapy but only as a combination therapy with anti-inflammatory, immunosuppressive, or biological therapy [49].

5.6. Surgical treatment

Indications for surgical treatment of ulcerative colitis may be elective, urgent, or emergency. In cases of massive hemorrhage with hemodynamic complications, intestinal perforation, or toxic colonic distension with signs of sepsis, surgical treatment should be initiated immediately, on an emergency basis. In emergency cases, a Hartmann colectomy should be the preferred surgical procedure, especially in debilitated patients who have been exposed to long-term steroid therapy [33,82].

Indications for elective surgery in ulcerative colitis include, among others, the lack of full efficacy and/or adverse effects of the pharmacotherapy previously used in a patient with severe

or moderately severe IBD (but who do not meet the criteria for ASUC), the presence of precancerous lesions or colorectal cancer, or the presence of chronic colonic stricture (especially symptomatic) of an unclear and difficult-to-determine nature (inflammatory or neoplastic stricture). The most commonly performed procedure is proctocolectomy with creation of an intestinal reservoir, which can be performed using either the laparoscopic or open approach. In exceptional cases, a colectomy with preservation of the rectum and ileorectal anastomosis may be performed. Indications for this type of surgery include: minimal inflammatory changes in the rectum and women planning to become pregnant in the future. On the one hand, this type of procedure is associated with better functional outcomes (fewer bowel movements per day), but it carries an increased risk of colorectal cancer. In addition, a proctocolectomy with creation of a terminal stoma on the ileum is sometimes performed [33,117,118,119].

Surgical treatment should be considered at every stage of ChLC therapy, especially in cases where the lesions are confined to a short segment of the intestine and/or complications (fistulas, strictures, abscesses) have developed. Surgical treatment is the best option in cases of intra-abdominal abscesses and conditions involving recurrent obstruction and/or subobstruction [49]. Endoscopic balloon dilation of the esophagus, stomach, and duodenum is an important surgical procedure, as strictures are a common complication in patients with Crohn's disease. Typically, several dilation sessions are required to achieve full clinical efficacy. Other methods for treating strictures include stricturoplasty and bypass anastomoses (gastrojejunostomy, jejunojejunostomy) [120-122].

The first step in treating perianal conditions (fistulas, abscesses) should be local treatment involving incision and drainage of the abscess, placement of a seton, fistulotomy, fistulectomy, the Hippocrates procedure, intersphincteric ligation of the fistula tract, endoscopic techniques, negative pressure therapy, adhesives, or plugs. The optimal surgical treatment method is selected by the surgeon depending on the type of fistula, the presence and course of its branches, the internal and external openings, the condition of the anal sphincters, or the presence of a concomitant abscess [33,123].

The latest and most promising treatment for perianal fistulas at ChLC is the use of allogeneic (donor-derived) or autologous (patient-derived) stem cells administered locally to the area of the internal opening and along the fistula tract following surgical preparation. A study involving 212 participants (ADMIRE CD) showed that, one year after surgical repair of the fistula and administration of stem cells, remission was observed in 56.3% of the treated (treatment group) compared to 38.6% of participants who underwent fistula repair but did not receive stem cells

(control group) [124,125].

If pharmacotherapy and/or local surgical treatment are ineffective, a temporary stoma should be created to allow perianal lesions to heal by eliminating or reducing mechanical irritation caused by fecal matter. A 2015 meta-analysis showed that a clinical response was observed in 63.8% of patients, but gastrointestinal continuity was successfully restored in only 16.6% of patients, and 41.6% of patients required proctectomy due to a lack of clinical response following the creation of a temporary stoma or a recurrence of symptoms after restoration of gastrointestinal continuity [33,120,126,127].

6. Discussion

The therapeutic approach to inflammatory bowel disease (IBD) has changed considerably over the past two decades. This review demonstrates that treatment options have expanded beyond conventional anti-inflammatory and immunosuppressive therapies to include a broad range of biologic agents and targeted small molecules. These advances reflect a better understanding of the mechanisms underlying Crohn's disease and ulcerative colitis and have enabled a more individualized approach to treatment.

Conventional therapies continue to play an important role in IBD management. Corticosteroids remain highly effective for inducing remission but should not be used for maintenance therapy because of their well-established adverse effects. Thiopurines and methotrexate remain valuable maintenance options in selected patients despite their delayed onset of action and potential toxicity. Mesalazine continues to be a cornerstone of ulcerative colitis treatment, whereas its role in Crohn's disease remains limited.

The introduction of anti-TNF agents marked a major milestone in IBD treatment. Infliximab and adalimumab have consistently demonstrated efficacy in inducing and maintaining remission, promoting mucosal healing, and reducing corticosteroid use and the need for surgery. Combination therapy with thiopurines has shown superior efficacy in selected patients, although immunogenicity, loss of response, and an increased risk of infections remain important limitations.

The availability of biologics targeting alternative inflammatory pathways has further broadened therapeutic options. Vedolizumab and ustekinumab have demonstrated favorable efficacy and safety profiles, while selective IL-23 inhibitors represent a promising treatment option with encouraging results in both Crohn's disease and ulcerative colitis. Similarly, small-molecule therapies, including Janus kinase inhibitors and ozanimod, provide effective oral treatment options, although careful monitoring for adverse effects remains necessary.

Current treatment strategies increasingly emphasize deep remission, including normalization of

inflammatory biomarkers, mucosal healing, and prevention of long-term bowel damage, rather than symptom control alone. Consequently, treatment decisions should consider disease severity, prognostic factors, previous treatment exposure, disease phenotype, comorbidities, and patient preferences.

Despite the growing number of available therapies, several challenges remain. Direct comparisons between treatment strategies are still limited, recommendations regarding treatment sequencing differ between guidelines, and reliable predictive biomarkers are still lacking. In addition, long-term comparative safety data for recently introduced therapies remain limited, while unequal access to advanced treatments continues to affect patient outcomes.

This review has several limitations. As a narrative review, it does not provide a quantitative synthesis of the available evidence. The included studies differ in design, patient populations, study endpoints, and follow-up duration, limiting direct comparisons between therapeutic approaches. Furthermore, the rapidly evolving therapeutic landscape means that some recommendations may require updating as new evidence emerges.

Overall, the available literature indicates that IBD management is becoming increasingly personalized, with a growing number of therapeutic options allowing treatment to be adapted to individual patient characteristics. Future research should focus on optimizing treatment sequencing, identifying predictive biomarkers, evaluating long-term safety, and improving access to advanced therapies to further improve outcomes and quality of life for patients with IBD.

7. Conclusions

Inflammatory bowel disease remains a major therapeutic challenge because of its chronic, relapsing course and heterogeneous clinical presentation. Advances in understanding disease pathogenesis have expanded the range of available treatment options and enabled a more individualized approach to therapy. Conventional therapies, including aminosalicylates, corticosteroids, and immunosuppressive agents, continue to play an important role in selected patient populations, while biologic agents and targeted small-molecule therapies have substantially improved clinical remission, mucosal healing, steroid-free remission, and patients' quality of life.

The growing number of therapies targeting different inflammatory pathways has broadened therapeutic possibilities and allows treatment to be tailored according to disease phenotype, severity, previous treatment exposure, and individual patient characteristics. Despite these advances, further research is needed to optimize treatment sequencing, identify reliable biomarkers predicting treatment response, evaluate the long-term safety of newer therapies, and

further improve personalized treatment strategies and long-term outcomes for patients with inflammatory bowel disease.

Disclosure

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REFERENCES

1. Holko P, Kawalec P, Stawowczyk E. Prevalence and drug treatment practices of inflammatory bowel diseases in Poland in the years 2012-2014. Eur J Gastroenterol Hepatol. 2018;30(4):456-464. https://doi.org/10.1097/meg.0000000000001047

2. Baldassano RN, Piccoli DA. Inflammatory bowel disease in pediatric and adolescent patients. Gastroenterol Clin North Am. 1999;28(2):445-458. https://doi.org/10.1016/S0889-8553(05)70064-9 PMID: 10372276.

3. Tysk C, Lindberg E, Järnerot G, Flodérus-Myrhed B. Ulcerative colitis and Crohn's disease in an unselected population of monozygotic and dizygotic twins: a study of heritability and the influence of smoking. Gut. 1988;29(7):990-996. https://doi.org/10.1136/gut.29.7.990

4. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. Gastroenterology. 2004;126(6):1504-1517. https://doi.org/10.1053/j.gastro.2004.01.063

5. Bager P, Simonsen J, Nielsen NM, Frisch M. Cesarean section and offspring's risk of inflammatory bowel disease: a national cohort study. Inflamm Bowel Dis. 2012;18(5):857-862. https://doi.org/10.1002/ibd.21805

6. Klement E, Cohen RV, Boxman J, Joseph A, Reif S. Breastfeeding and risk of inflammatory bowel disease: a systematic review with meta-analysis. Am J Clin Nutr. 2004;80(5):1342-1352. https://doi.org/10.1093/ajcn/80.5.1342

7. Hou JK, Abraham B, El-Serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. Am J Gastroenterol. 2011;106(4):563-573. https://doi.org/10.1038/ajg.2011.44

8. Shaw SY, Blanchard JF, Bernstein CN. Association between the use of antibiotics in the first year of life and pediatric inflammatory bowel disease. Am J Gastroenterol. 2010;105(12):2687-2692. https://doi.org/10.1038/ajg.2010.398

9. Knights D, Lassen KG, Xavier RJ. Advances in inflammatory bowel disease pathogenesis: linking host genetics and the microbiome. Gut. 2013;62(10):1505-1510. https://doi.org/10.1136/gutjnl-2012-303954

10. Gevers D, Kugathasan S, Denson LA, et al. The treatment-naive microbiome in new-onset Crohn's disease. Cell Host Microbe. 2014;15(3):382-392. https://doi.org/10.1016/j.chom.2014.02.005

11. Rosen MJ, Dhawan A, Saeed SA. Inflammatory bowel disease in children and adolescents. JAMA Pediatr. 2015;169(11):1053-1060. https://doi.org/10.1001/jamapediatrics.2015.1982

12. Bousvaros A, Antonioli DA, Colletti RB, et al. Differentiating ulcerative colitis from Crohn disease in children and young adults: report of a Working Group of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America. J Pediatr Gastroenterol Nutr. 2007;44(5):653-674. . https://doi.org/10.1097/mpg.0b013e31805563f3

13. Kugathasan S, Judd RH, Hoffmann RG, et al.; Wisconsin Pediatric Inflammatory Bowel Disease Alliance. Epidemiologic and clinical characteristics of children with newly diagnosed inflammatory bowel disease in Wisconsin: a statewide population-based study. J Pediatr. 2003;143(4):525-531. https://doi.org/10.1067/S0022-3476(03)00444-X

14. Nahon S, Lahmek P, Lesgourgues B, et al. Diagnostic delay in a French cohort of Crohn's disease patients. J Crohns Colitis. 2014;8(9):964-969. https://doi.org/10.1016/j.crohns.2014.01.023

15.Schoepfer AM, Dehlavi MA, Fournier N, et al. Diagnostic delay in Crohn's disease is associated with a complicated disease course and increased operation rate. Am J Gastroenterol. 2013;108(11):1744-1753. https://doi.org/10.1038/ajg.2013.248

16. Thia KT, Sandborn WJ, Harmsen WS, et al. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. Gastroenterology. 2010;139(4):1147-1155. https://doi:10.1053/j.gastro.2010.06.070

17. Vavricka SR, Spigaglia SM, Rogler G, et al. Systematic evaluation of risk factors for diagnostic delay in inflammatory bowel disease. Inflamm Bowel Dis. 2012;18(3):496-505. https://doi:10.1002/ibd.21719

18. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting therapeutic targets in inflammatory bowel disease (STRIDE): determining therapeutic goals for treat-to-target. Am J Gastroenterol. 2015;110(9):1324-1338. https://doi.org/10.1038/ajg.2015.233

19. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterology. 2021;160(5):1570-1583. https://doi.org/10.1053/j.gastro.2020.12.031

20. Schoepfer AM, Beglinger C, Straumann A, et al. Fecal calprotectin correlates more closely with the Simple Endoscopic Score for Crohn's disease (SES-CD) than CRP, blood leukocytes, and the CDAI. Am J Gastroenterol. 2010;105(1):162-169. https://doi:10.1038/ajg.2009.545

21. Boschetti G, Laidet M, Moussata D, et al. Levels of fecal calprotectin are associated with the severity of postoperative endoscopic recurrence in asymptomatic patients with Crohn's disease. Am J Gastroenterol. 2015;110(6):865-872. https://doi.org/10.1038/ajg.2015.30

22. Klimczak K, Lykowska-Szuber L, Eder P, et al. The diagnostic usefulness of fecal lactoferrin in the assessment of Crohn's disease activity. Eur J Intern Med. 2015;26(8):623-627. https://doi.org/10.1016/j.ejim.2015.06.015

23. Wright EK, Kamm MA, De Cruz P, et al. Measurement of fecal calprotectin improves monitoring and detection of recurrence of Crohn's disease after surgery. Gastroenterology.

2015;148(5):938-947.e1. https://doi:10.1053/j.gastro.2015.01.026

24. Ferrante M, Colombel JF, Sandborn WJ, et al. Validation of endoscopic activity scores in patients with Crohn's disease based on a post hoc analysis of data from SONIC. Gastroenterology.2013;145(5):978-986.e5. https://doi.org/10.1053/j.gastro.2013.08.010

25. Khanna R, Bressler B, Levesque BG, et al. Early combined immunosuppression for the management of Crohn's disease (REACT): a cluster randomised controlled trial. Lancet.2015;386(10006):1825-1834. https://doi.org/10.1016/s0140-6736(15)00068-9

26. Colombel JF, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. Lancet. 2017;390(10114):2779-2789. https://doi.org/10.1016/s0140-6736(17)32641-7

27. Maaser C, Sturm A, Vavricka SR, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. J Crohns Colitis. 2019;13(2):144-164. https://doi.org/10.1093/ecco-jcc/jjy113

28. Sandborn WJ, Hanauer S, Van Assche G, et al. Treating beyond symptoms with a view to improving patient outcomes in inflammatory bowel diseases. J Crohns Colitis. 2014;8(9):927-935. https://doi.org/10.1016/j.crohns.2014.02.021

29. Zallot C, Peyrin-Biroulet L. Deep remission in inflammatory bowel disease: looking beyond symptoms. Curr Gastroenterol Rep. 2013;15(3):315. https://doi.org/10.1007/s11894-013-0315-7

30. Baert F, Moortgat L, Van Assche G, et al. Mucosal healing predicts sustained clinical remission in patients with early-stage Crohn's disease. Gastroenterology. 2010;138(2):463-468.e5. https://doi.org/10.1053/j.gastro.2009.09.056

31. Frøslie KF, Jahnsen J, Moum BA, Vatn MH; IBSEN Group. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. Gastroenterology. 2007;133(2):412-422. https://doi.org/10.1053/j.gastro.2007.05.051

32. Nuti F, Civitelli F, Bloise S, et al. Prospective evaluation of the achievement of mucosal healing with anti-TNF-α therapy in a paediatric Crohn's disease cohort. J Crohns Colitis. 2016;10(1):5-12. https://doi.org/10.1093/ecco-jcc/jjv126

33. Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019;68(Suppl 3):s1-s106. https://doi.org/10.1136/gutjnl-2019-318484

34. Rodemann JF, Dubberke ER, Reske KA, et al. Incidence of Clostridium difficile infection in inflammatory bowel disease. Clin Gastroenterol Hepatol. 2007;5(3):339-344. https://doi.org/10.1016/j.cgh.2006.12.027

35. Monaghan TM, Cockayne A, Mahida YR. Pathogenesis of Clostridium difficile infection and its potential role in inflammatory bowel disease. Inflamm Bowel Dis. 2015;21(8):1957-1966. https://doi.org/10.1097/mib.0000000000000461

36. Pascual V, Dieli-Crimi R, López-Palacios N, et al. Inflammatory bowel disease and celiac disease: overlaps and differences. World J Gastroenterol. 2014;20(17):4846-4856. https://doi.org/10.3748/wjg.v20.i17.4846

37. Bar Yehuda S, Axelrod R, Toker O, et al. The association of inflammatory bowel diseases with autoimmune disorders: a report from the epi-IIRN. J Crohns Colitis. 2019;13(3):324-329.https://doi.org/10.1093/ecco-jcc/jjy166

38. Le Baut G, O'Brien C, Pavli P, et al. Prevalence of Yersinia species in the ileum of Crohn's disease patients and controls. Front Cell Infect Microbiol. 2018;8:336. https://doi.org/10.3389/fcimb.2018.00336

39. Hanada Y, Khanna S, Loftus EV Jr, et al. Non-Clostridium difficile bacterial infections are rare in patients with flares of inflammatory bowel disease. Clin Gastroenterol Hepatol. 2018;16(4):528-533. https://doi.org/10.1016/j.cgh.2017.10.008

40. Limsrivilai J, Lee CK, Prueksapanich P, et al. Validation of models using basic parameters to differentiate intestinal tuberculosis from Crohn's disease: a multicenter study from Asia. PLoS One. 2020;15(11):e0242879. https://doi.org/10.1371/journal.pone.0242879

41. Dyson JK, Rutter MD. Colorectal cancer in inflammatory bowel disease: what is the real magnitude of the risk? World J Gastroenterol. 2012;18(29):3839-3848. https://doi.org/10.3748/wjg.v18.i29.3839

42. Benchimol EI, Seow CH, Steinhart AH, Griffiths AM. Traditional corticosteroids for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2008;(2):CD006792. https://doi.org/10.1002/14651858.cd006792.pub2

43. Summers RW, Switz DM, Sessions JT Jr, et al. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979;77(4 Pt 2):847-869. Available from: https://pubmed.ncbi.nlm.nih.gov/38176/

44. Malchow H, Ewe K, Brandes JW, et al. European Cooperative Crohn's Disease Study (ECCDS): results of drug treatment. Gastroenterology. 1984;86(2):249-266. Available from: https://pubmed.ncbi.nlm.nih.gov/6140202/

45. Adamed Pharma SA. Encorton 1 mg, 5 mg, 10 mg, 20 mg tablets. Summary of Product Characteristics [Internet]. Pieńków (Poland): Adamed Pharma SA; [cited 2026 Jul 18]. Available from: https://leki.urpl.gov.pl/files/42_Encorton.pdf

46. Chande N, Townsend CM, Parker CE, MacDonald JK. Azathioprine or 6-mercaptopurine

for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2016;(10):CD000545. https://doi.org/10.1002/14651858.cd000545.pub5

47. Feagan BG, Rochon J, Fedorak RN, et al. Methotrexate for the treatment of Crohn's disease. The North American Crohn's Study Group Investigators. N Engl J Med. 1995;332(5):292-297. https://doi.org/10.1056/nejm199502023320503

48.. McDonald JWD, Wang Y, Tsoulis DJ, MacDonald JK, Feagan BG. Methotrexate for induction of remission in refractory Crohn's disease. Cochrane Database Syst Rev. 2014;(8):CD003459. doi:10.1002/14651858.CD003459.pub3

49. Łodyga M, Eder P, Gawron-Kiszka M, et al. Guidelines for the management of patients with Crohn's disease. Recommendations of the Polish Society of Gastroenterology and the Polish National Consultant in Gastroenterology. Gastroenterol Rev. 2021;16(4):257-296. https://doi.org/10.5114/pg.2021.110914

50. Chhaya V, Saxena S, Cecil E, et al. Steroid dependency and trends in prescribing for inflammatory bowel disease: a 20-year national population-based study. Aliment Pharmacol Ther. 2016;44(5):482-494.https://doi.org/10.1111/apt.13700

51. Schoepfer AM, Bortolotti M, Pittet V, et al. The gap between scientific evidence and clinical practice: 5-aminosalicylates are frequently used for the treatment of Crohn's disease. Aliment Pharmacol Ther. 2014;40(8):930-937. https://doi.org/10.1111/apt.12929

52. Ford AC, Kane SV, Khan KJ, et al. Efficacy of 5-aminosalicylates in Crohn's disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):617-629. https://doi.org/10.1038/ajg.2011.71

53. Rasmussen SN, Lauritsen K, Tage-Jensen U, et al. 5-Aminosalicylic acid in the treatment of Crohn's disease: a 16-week double-blind, placebo-controlled, multicentre study with Pentasa. Scand J Gastroenterol. 1987;22(7):877-883. https://doi.org/10.3109/00365528708991929

54. Singleton JW, Hanauer SB, Gitnick GL, et al. Mesalamine capsules for the treatment of active Crohn's disease: results of a 16-week trial. Pentasa Crohn's Disease Study Group. Gastroenterology. 1993;104(5):1293-1301. https://doi.org/10.1016/0016-5085(93)90337-c

55. Tremaine WJ, Schroeder KW, Harrison JM, Zinsmeister AR. A randomized, double-blind, placebo-controlled trial of the oral mesalamine (5-ASA) preparation, Asacol, in the treatment of symptomatic Crohn's colitis and ileocolitis. J Clin Gastroenterol. 1994;19(4):278-282. https://doi.org/10.1097/00004836-199412000-00003

56. Ferring Pharmaceuticals. PEACE study: a study with Pentasa in patients with active Crohn's disease [Internet]. ClinicalTrials.gov identifier: NCT00862121. 2012 [cited 2026 Jul 17].

Available from: https://clinicaltrials.gov/ct2/show/NCT00862121

57. Moja L, Danese S, Fiorino G, et al. Systematic review with network meta-analysis: comparative efficacy and safety of budesonide and mesalazine (mesalamine) for Crohn's disease. Aliment Pharmacol Ther. 2015;41(11):1055-1065. https://doi.org/10.1111/apt.13190

58. Rezaie A, Kuenzig ME, Benchimol EI, et al. Budesonide for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2015;(6):CD000296. https://doi.org/10.1002/14651858.cd000296.pub4

59. Akobeng AK, Zhang D, Gordon M, MacDonald JK. Oral 5-aminosalicylic acid for maintenance of medically-induced remission in Crohn's disease. Cochrane Database Syst Rev. 2016;(9):CD003715. https://doi.org/10.1002/14651858.cd003715.pub3

60. Lim WC, Hanauer S. Aminosalicylates for induction of remission or response in Crohn's disease. Cochrane Database Syst Rev. 2010;(12):CD008870. https://doi.org/10.1002/14651858.cd008870

61. Lim WC, Wang Y, MacDonald JK, Hanauer S. Aminosalicylates for induction of remission or response in Crohn's disease. Cochrane Database Syst Rev. 2016;(7):CD008870. https://doi.org/10.1002/14651858.cd008870.pub2

62. Subramanian S, Ekbom A, Rhodes JM. Recent advances in clinical practice: a systematic review of isolated colonic Crohn's disease: the third IBD? Gut. 2017;66(2):362-381. https://doi.org/10.1136/gutjnl-2016-312673

63. Hanauer SB, Strömberg U. Oral Pentasa in the treatment of active Crohn's disease: a meta-analysis of double-blind, placebo-controlled trials. Clin Gastroenterol Hepatol. 2004;2(5):379-388. https://doi.org/10.1016/s1542-3565(04)00122-3

64. Coward S, Kuenzig ME, Hazlewood G, et al. Comparative effectiveness of mesalamine, sulfasalazine, corticosteroids, and budesonide for the induction of remission in Crohn's disease: a Bayesian network meta-analysis. Inflamm Bowel Dis. 2017;23(2):E26-E37. https://doi.org/10.1097/mib.0000000000001023

65. Stidham RW, Lee TC, Higgins PDR, et al. Systematic review with network meta-analysis: the efficacy of anti-TNF agents for the treatment of Crohn's disease. Aliment Pharmacol Ther. 2014;39(12):1349-1362. https://doi.org/10.1111/apt.12749

66. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711-721. doi:10.1056/NEJMoa1215739. https://doi.org/10.1056/nejmoa1215739

67. Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2016;375(20):1946-1960.

https://doi.org/10.1056/nejmoa1602773

68. Singh S, Fumery M, Sandborn WJ, Murad MH. Systematic review and network meta-analysis: first- and second-line biologic therapies for moderate-severe Crohn's disease. Aliment Pharmacol Ther. 2018;48(4):394-409. https://doi.org/10.1111/apt.14852

69. Raine T, Bonovas S, Burisch J, et al. ECCO guidelines on therapeutics in ulcerative colitis: medical treatment. J Crohns Colitis. 2022;16(1):2-17. https://doi.org/10.1093/ecco-jcc/jjab178

70. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020;158(5):1450-1461. https://doi.org/10.1053/j.gastro.2020.01.006

71. Harbord M, Eliakim R, Bettenworth D, et al. Third European Evidence-based Consensus on diagnosis and management of ulcerative colitis. Part 2: current management. J Crohns Colitis. 2017;11(7):769-784. https://doi.org/10.1093/ecco-jcc/jjx009

72. Sandborn WJ, Travis S, Moro L, et al. Once-daily budesonide MMX extended-release tablets induce remission in patients with mild to moderate ulcerative colitis: results from the CORE I study. Gastroenterology. 2012;143(5):1218-1226.e2. https://doi.org/10.1053/j.gastro.2012.08.003

73. Travis SP, Danese S, Kupcinskas L, et al. Once-daily budesonide MMX in active, mild-to-moderate ulcerative colitis: results from the randomised CORE II study. Gut. 2014;63(3):433-441. https://doi.org/10.1136/gutjnl-2012-304258

74. Rubin DT, Cohen RD, Sandborn WJ, et al. Budesonide multimatrix is efficacious for mesalamine-refractory, mild to moderate ulcerative colitis: a randomised, placebo-controlled trial. J Crohns Colitis. 2017;11(7):785-791. https://doi.org/10.1093/ecco-jcc/jjx032

75. Lennard-Jones JE, Longmore AJ, Newell AC, et al. An assessment of prednisone, salazopyrin, and topical hydrocortisone hemisuccinate used as out-patient treatment for ulcerative colitis. Gut. 1960;1:217-222. https://doi.org/10.1136/gut.1.3.217

76. Ford AC, Bernstein CN, Khan KJ, et al. Glucocorticosteroid therapy in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):590-599. https://doi.org/10.1038/ajg.2011.70

77. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019;114(3):384-413. https://doi.org/10.14309/ajg.0000000000000152

78. Dinesen LC, Walsh AJ, Protic MN, et al. The pattern and outcome of acute severe colitis. J Crohns Colitis. 2010;4(4):431-437. https://doi.org/10.1016/j.crohns.2010.02.001

79. Bojic D, Radojicic Z, Nedeljkovic-Protic M, et al. Long-term outcome after admission for acute severe ulcerative colitis in Oxford: the 1992-1993 cohort. Inflamm Bowel Dis. 2009;15(6):823-828. https://doi.org/10.1002/ibd.20843

80. Travis SP, Farrant JM, Ricketts C, et al. Predicting outcome in severe ulcerative colitis. Gut. 1996;38(6):905-910. https://doi.org/10.1136/gut.38.6.905

81. Dassopoulos T, Cohen RD, Scherl EJ, et al. Ulcerative colitis care pathway. Gastroenterology. 2015;149(1):238-245. https://doi.org/10.1053/j.gastro.2015.05.036

82. Eder P, Łodyga M, Gawron-Kiszka M, et al. Guidelines for the management of ulcerative colitis. Recommendations of the Polish Society of Gastroenterology and the Polish National Consultant in Gastroenterology. Gastroenterology Rev 2023; 18 (1): 1–42. DOI: https://doi.org/10.5114/pg.2023.125882

83. Borrelli O, Cordischi L, Cirulli M, et al. Polymeric diet alone versus corticosteroids in the treatment of active pediatric Crohn's disease: a randomized controlled open-label trial. Clin Gastroenterol Hepatol. 2006;4(6):744-753. https://doi.org/10.1016/j.cgh.2006.03.010

84. Critch J, Day AS, Otley A, et al. Use of enteral nutrition for the control of intestinal inflammation in pediatric Crohn disease. J Pediatr Gastroenterol Nutr. 2012;54(2):298-305. https://doi.org/10.1097/mpg.0b013e318235b397

85. Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2012;(10):CD000543. https://doi.org/10.1002/14651858.cd000543.pub3

86. Zeisler B, Lerer T, Markowitz J, et al. Outcome following aminosalicylate therapy in children newly diagnosed as having ulcerative colitis. J Pediatr Gastroenterol Nutr. 2013;56(1):12-18. https://doi.org/10.1097/mpg.0b013e31826ac41a

87. Astellas Pharma Sp. z o.o. Asamax 250 mg, Asamax 500 mg gastro-resistant tablets. Summary of Product Characteristics [Internet]. Warsaw (Poland): Astellas Pharma Sp. z o.o.; [cited 2026 Jul 18]. Available from: https://rejestrymedyczne.ezdrowie.gov.pl/api/rpl/medicinal-products/12779/characteristic

88. Markowitz J, Grancher K, Kohn N, Lesser M, Daum F. A multicenter trial of 6-mercaptopurine and prednisone in children with newly diagnosed Crohn's disease. Gastroenterology. 2000;119(4):895-902. https://doi.org/10.1053/gast.2000.18144

89. Dulai PS, Thompson KD, Blunt HB, Dubinsky MC, Siegel CA. Risks of serious infection or lymphoma with anti-tumor necrosis factor therapy for pediatric inflammatory bowel disease: a systematic review. Clin Gastroenterol Hepatol. 2014;12(9):1443-1451. https://doi.org/10.1016/j.cgh.2014.01.021

90. Turner D, Grossman AB, Rosh J, et al. Methotrexate following unsuccessful thiopurine therapy in pediatric Crohn's disease. Am J Gastroenterol. 2007;102(12):2804-2812. https://doi.org/10.1111/j.1572-0241.2007.01474.x

91. European Medicines Agency. Jylamvo (methotrexate): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/jylamvo

92. Selinger CP, Rosiou K, Lenti MV. Biological therapy for inflammatory bowel disease: cyclical rather than lifelong treatment? BMJ Open Gastroenterol. 2024;11(1):e001225. https://doi.org/10.1136/bmjgast-2023-001225

93. Vulliemoz M, Brand S, Juillerat P, Mottet C, Ben-Horin S, Michetti P; on on behalf of Swiss IBDnet, an official working group of the Swiss Society of Gastroenterology. TNF-alpha blockers in inflammatory bowel diseases: practical recommendations and a user's guide: an update. Digestion. 2020;101(Suppl 1):16-26. https://doi.org/10.1159/000506898

94. Verstockt B, Salas A, Sands BE, Abraham C, Leibovitzh H, Neurath MF, Vande Casteele N; Alimentiv Translational Research Consortium (ATRC). IL-12 and IL-23 pathway inhibition in inflammatory bowel disease. Nat Rev Gastroenterol Hepatol. 2023;20(7):433-446. https://doi.org/10.1038/s41575-023-00768-1

95. Colombel JF, Sandborn WJ, Reinisch W, et al.; SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010;362(15):1383-1395. https://doi.org/10.1056/NEJMoa0904492

96. Panaccione R, Ghosh S, Middleton S, et al. Combination therapy with infliximab and azathioprine is superior to monotherapy with either agent in ulcerative colitis. Gastroenterology. 2014;146(2):392-400.e3. https://doi.org/10.1053/j.gastro.2013.10.052

97. Ruder B, Atreya R, Becker C. Tumour necrosis factor alpha in intestinal homeostasis and gut related diseases. Int J Mol Sci. 2019;20(8):1887. https://doi.org/10.3390/ijms20081887

98. European Medicines Agency. Remicade (infliximab): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/remicade

99. European Medicines Agency. Humira (adalimumab): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/humira

100. European Medicines Agency. Simponi (golimumab): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from:

https://www.ema.europa.eu/en/medicines/human/EPAR/simponi

101. Łodyga M, Eder P, Bartnik W, et al. New pharmaceuticals in inflammatory bowel disease. Prz Gastroenterol. 2015;10(2):57-60. https://doi.org/10.5114/pg.2015.52702

102. European Medicines Agency. Cimzia (certolizumab pegol): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/cimzia-0

103. Yamazaki H, So R, Matsuoka K, et al. Certolizumab pegol for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2019;(8):CD012893. https://doi.org/10.1002/14651858.CD012893.pub2

104. European Medicines Agency. Entyvio (vedolizumab): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/cimzia-0

105. European Medicines Agency. Stelara (ustekinumab): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 12]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/stelara

106. Puca P, Parello S, Colantuono S, et al. Interleukin-23 inhibitors in inflammatory bowel disease. BioDrugs. 2026;40(3):479-492. https://doi.org/10.1007/s40259-026-00781-1

107. Pool IA, Otten AT, Kosterink JGW, Dijkstra G, Mian P, Bourgonje AR. Interleukin-23p19 inhibitors in inflammatory bowel disease: from current insights to future directions. J Pers Med. 2026;16(2):119. https://doi.org/10.3390/jpm16020119

108. Wu H, Zhou Y, Chen X, Wang L, Guo Y, Du X, Miao X. Safety and efficacy of different JAK inhibitors in the treatment of inflammatory bowel disease: a network meta-analysis. Front Pharmacol. 2026;16:1699928. https://doi.org/10.3389/fphar.2025.1699928

109. European Medicines Agency. Rinvog (upadacitinib): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 14]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/rinvoq

110. European Medicines Agency. Xeljanz (tofacitinib): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 14]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/xeljanz

111. European Medicines Agency. Jyseleca (filgotinib): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 14]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/jyseleca

112. Choi Y, Lee S, Kim HJ, Park T, Kwack WG, Yang S, Chung EK. State-of-the-art evidence for clinical outcomes and therapeutic implications of Janus kinase inhibitors in moderate-to-

severe ulcerative colitis: a narrative review. Pharmaceuticals (Basel). 2025;18(5):740. https://doi.org/10.3390/ph18050740

113. European Medicines Agency. Zeposia (ozanimod): summary of product characteristics [Internet]. 2026 [cited 2026 Jul 15]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/zeposia

114. Sandborn WJ, Feagan BG, D'Haens G, et al.; True North Study Group. Ozanimod as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2021;385(14):1280-1291. https://doi.org/10.1056/NEJMoa2033617

115. Nitzan O, Elias M, Peretz A, Saliba W. Role of antibiotics for treatment of inflammatory bowel disease. World J Gastroenterol. 2016;22(3):1078-1087. https://doi.org/10.3748/wjg.v22.i3.1078

116. Tocia C, Dumitru IM, Alexandrescu L, Petcu LC, Dumitru E. Does rifaximin offer any promise in Crohn's disease in remission and concurrent irritable bowel syndrome-like symptoms? Medicine (Baltimore). 2021;100(1):e24059. https://doi.org/10.1097/MD.0000000000024059

117. Spinelli A, Bonovas S, Burisch J, et al. ECCO guidelines on therapeutics in ulcerative colitis: surgical treatment. J Crohns Colitis. 2022;16(2):179-189. https://doi.org/10.1093/ecco-jcc/jjab177

118. Magro F, Gionchetti P, Eliakim R, et al. Third European Evidence-based Consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. J Crohns Colitis. 2017;11(6):649-670. https://doi.org/10.1093/ecco-jcc/jjx008

119. Tomasik M, Warzyszak P, Małek R, et al. Ulcerative colitis – recent and potential methods of treatment: review. J Educ Health Sport. 2023;13(3):65-73. https://doi.org/10.12775/JEHS.2023.13.03.009

120. Adamina M, Bonovas S, Raine T, et al. ECCO guidelines on therapeutics in Crohn’s disease: surgical treatment. J Crohns Colitis. 2020;14(2):155-168. https://doi.org/10.1093/ecco-jcc/jjz187

121. Navaneethan U, Lourdusamy V, Njei B, Shen B. Endoscopic balloon dilation in the management of strictures in Crohn’s disease: a systematic review and meta-analysis of non-randomized trials. Surg Endosc. 2016;30(12):5434-5443. https://doi.org/10.1007/s00464-016-4902-1

122. Yamamoto T, Fazio VW, Tekkis PP. Safety and efficacy of strictureplasty for Crohn’s disease: a systematic review and meta-analysis. Dis Colon Rectum. 2007;50(11):1968-1986.

https://doi.org/10.1007/s10350-007-0279-5

123. Torres J, Bonovas S, Doherty G, et al. ECCO guidelines on therapeutics in Crohn's disease: medical treatment. J Crohns Colitis. 2020;14(1):4-22. https://doi.org/10.1093/ecco-jcc/jjz180

124. Panés J, García-Olmo D, Van Assche G, et al. Long-term efficacy and safety of stem cell therapy (Cx601) for complex perianal fistulas in patients with Crohn's disease. Gastroenterology. 2018;154(5):1334-1342.e4. https://doi.org/10.1053/j.gastro.2017.12.020

125. Panés J, García-Olmo D, Van Assche G, et al. Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial. Lancet. 2016;388(10051):1281-1290. https://doi.org/10.1016/S0140-6736(16)31203-X

126. Van Assche G, Dignass A, Reinisch W, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: special situations. J Crohns Colitis. 2010;4(1):63-101. doi:10.1016/j.crohns.2009.09.009. https://doi.org/10.1016/j.crohns.2009.09.009

127. Gionchetti P, Dignass A, Danese S, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 2: Surgical Management and Special Situations. J Crohns Colitis. 2017;11(2):135-149. https://doi.org/10.1093/ecco-jcc/jjw169