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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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DUAL BIOLOGICAL THERAPY IN INFLAMMATORY BOWEL DISEASE

Aleksandra Karnas *(Corresponding Author, Email: aleksandrakarnas25@gmail.com)*
Rzeszów University, Tadeusza Rejtana 16C, 35-310 Rzeszów, Poland
ORCID ID: 0009-0005-9708-3467

Gabriela Majka
Rzeszów University, Tadeusza Rejtana 16C, 35-310 Rzeszów, Poland
ORCID ID: 0009-0002-7100-5119

Karol Bednarz
Clinical Provincial Hospital No. 2 in Rzeszów, Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0000-0001-9196-1621

Piotr Pitrus
Clinical Provincial Hospital No. 2 in Rzeszów, Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0009-0006-2168-9187

Anita Krowiak
Clinical Provincial Hospital No. 2 in Rzeszów, Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0009-0008-0077-0925

Magdalena Kowalczyk
Rzeszów University, Tadeusza Rejtana 16C, 35-310 Rzeszów, Poland
ORCID ID: 0009-0000-6786-8232

Karolina Krowiak
Clinical Provincial Hospital No. 2 in Rzeszów, Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0009-0001-6704-0838

Anita Warzocha
University Clinical Hospital F. Chopin in Rzeszów, Fryderyka Szopena 2, 35-055 Rzeszów, Poland
ORCID ID: 0009-0006-9845-4634

Wiktoria Hander
Rzeszów University, Tadeusza Rejtana 16C, 35-310 Rzeszów, Poland
ORCID ID: 0009-0002-3000-9703

Maria Jasiewicz
Rzeszów University, Tadeusza Rejtana 16C, 35-310 Rzeszów, Poland
ORCID ID: 0009-0008-0718-2528

ABSTRACT

Background: Inflammatory bowel diseases are increasingly common conditions occurring mainly in young people. The etiology of these diseases is not fully understood, so the treatment of choice is mainly conservative. The main target is to achieve and sustain clinical and endoscopic glucocorticosteroid-free remission.
Purpose: The purpose of this study is to describe the non-standard use of dual biological therapy in selected groups of patients who have lost secondary response to treatment.
Description: This article discusses two cases of patients suffering from ulcerative colitis and Crohn's disease. During standard therapy, disease exacerbations and secondary loss of response to biologic drugs were observed. The combination of two biologic drugs resulted in remission of the disease and improvement in the patient's clinical condition.
Conclusions: Dual biologic therapy may show promise in the treatment of inflammatory bowel disease in selected groups of patients. Combining different mechanisms of action of drugs allows for comprehensive control of inflammation, increasing the effectiveness of treatment.

KEYWORDS

Dual Biologic Therapy, Inflammatory Bowel Diseases

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Introduction

Ulcerative colitis (UC) and disease

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by recurrent inflammation of various sections of the gastrointestinal tract. UC mainly affects the large intestine and is superficial in nature, while CD involves full-thickness, segmental inflammatory lesions that can occur in any section of the gastrointestinal tract. [1]

Biologic therapy, including TNF-α inhibitors (e.g., infliximab, adalimumab), integrin inhibitors (e.g., vedolizumab) and interleukin inhibitors (e.g., ustekinumab), is the mainstay of therapy for advanced IBD, especially in patients refractory to conventional treatment. According to current guidelines, biologic therapy can be used both as monotherapy and in combination therapy with other drugs, such as immunosuppressants, to increase the effectiveness of therapy and reduce the risk of relapse. In addition, it is possible to use therapy with two biologic drugs simultaneously in selected cases of severe forms of IBD, which makes it possible to achieve better control of the disease in situations where monotherapy or combination therapy with immunosuppressants are not successful. This type of therapeutic approach, despite limited data, is becoming increasingly popular, especially in advanced and complicated cases of [2, 3]

The two clinical cases presented below demonstrate the use of combination therapy using two biologic drugs in patients with ulcerative colitis and Crohn's disease.

Case Descriptions

A 50-year-old patient with Ulcerative Colitis treated with biologics for 6 years.

In 2018, she was hospitalized in the Department of Gastroenterology for severe abdominal pain, chronic diarrhea and weight loss. Laboratory tests showed microcytic anemia and increased fecal calprotectin levels to 2478.5 µg/g. Ultrasound examination revealed swelling of the colon walls from the cecum to the rectum and smoothing of the ascending and sigmoid haustrations. After histopathological evaluation during sigmoidoscopy, Ulcerative Colitis was diagnosed. Mesalazine, glucocorticosteroids with dose reduction were started. During steroid withdrawal, an exacerbation of the disease-an increase in fecal calprotectin of 5007.5 µg/g was noted. Azathioprine was added and steroid-dependent disease was diagnosed. At the beginning of

2019, due to the severe course of the disease and steroid-dependence, the decision was made to treat with biologic vedolizumab with good tolerance. Disease activity in the modified MAYO Classification was assessed at 9 points. At the 3rd dose of vedolizumab, disease activity was reassessed on the modified Mayo Scale at 6 points. It was decided to discontinue azathioprine due to the resulting inflammatory changes in the lungs. During treatment, the patient was diagnosed with acute pancreatitis as a side effect of mesalazine use. The drug was discontinued. A secondary response to vedolizumab was recognized during treatment. The score on the Modified Mayo Scale was 8 points. Decisions were made to switch to infliximab. After 3 doses of the drug, there was an exacerbation of the disease and it was decided to shorten the drug interval to 4 weeks. Due to the lack of satisfactory effect of the applied therapy, it was decided to include the patient in the treatment program for Ulcerative Colitis with tofatinib in combination with the existing treatment with infliximab.

After the treatment, a follow-up sigmoidoscopy was performed and the disease activity was graded at 1 point based on the endoscopic picture on the Mayo scale. The patient remains under the control of the gastroenterology clinic.

Description

A 17-year-old patient was admitted to the Department of Gastroenterology (2007) for diagnosis of persistent abdominal pain, feverish conditions and weight loss progressing over several months. A colonoscopy performed revealed lesions in the form of afts, ulcers and pseudopolyps from the cecum to the rectum.

After taking specimens and histopathological evaluation, a diagnosis of Crohn's disease was made. Treatment with azathioprine (2x150mg) p.o., Encorton (3x3mg) p.o., Ortanol (1x20mg) p.o., Folic Acid (1x15mg) p.o. was started.

A patient with an exacerbation of the disease was brought (2010) to the Department of Gastroenterology for endoscopic re-evaluation and possible modification of treatment. Colonoscopy revealed new lesions - a single longitudinal ulceration and small ulcerations surrounded by normal mucosa. The ileocecal valve was visualized, which was swollen, friable with ulcerations present. Examination showed the cecum with a scarred deformity and the descending colon occupied by numerous small areas of mucosa with a reddened surface and small pseudopolyps. In the rectum, new sparse redness and just behind the anal canal, longitudinal ulcerations passing into the anal canal.

In 2011, there was a mucosal remission in the small intestine. It was decided to discontinue the corticosteroid and include mesalazine. The patient was admitted to the Gastroenterology Department in April 2014 with a recurrence of disease exacerbation, anemia and leukopenia. The use of mesalazine and azathioprine was considered the cause of the leukopenia, and it was decided to discontinue the therapy. At the same time, a decision was made to start biologic therapy-infliximab. Control biochemical tests showed almost complete normalization of blood morphotic values. The patient was discharged in good condition with recommendations to report every 4 weeks for further doses of infliximab. At the visit on 18.07, he received the first remission maintenance dose of Remicade, 500 mg i.v. Subsequent remission maintenance doses were administered approximately two months apart (12.09; 7.11). In addition, skin lesions appeared on the palms, soles of the feet and scalp-diagnosis of psoriasis. Metypred was applied.

On 01.02.2015. The patient presented to the hospital with purulent lesions in the axillary and interscapular regions. Another dose of infliximab was discontinued due to loss of response to this drug. The Quantiferon test performed was positive, indicating latent Mycobacterium tuberculosis infection. Due to the positive result, the patient was started on Rifamazid as part of chemoprophylaxis. In 2015. 1 dose of Humira-Adalimumab 4x4mg was administered in an induction cycle with good tolerance. The second dose of Adalimumab (80mg) was given after 2 weeks. The next 3rd, 4th, 5th and 6th doses (40 mg) were also given with a two-week interval between doses. After completing the treatment cycle with Humira on September 21, 2015, there was several months of remission of the disease. The patient reported good general well-being, no abdominal pain, bowel movements 1-2 per day, with no blood present. The patient reported to the Gastroenterology department again on 05.02.2016 with persistent diarrhea for 2 weeks-about 10 stools per day-in addition, in laboratory tests, iron deficiency anemia. Subsequent tests showed the presence of IgA class antibodies indicative of a newly diagnosed Yersinia enterocolitica infection. A decision was made to include Mercaptopurine (60mg), Asamax (500mg) and Metypred (16mg) as therapy. The patient was discharged from the hospital in good condition. In June of the same year, there was a worsening of his condition and clinical features of disease progression. The man reported abdominal pain, subfebrile states and multiple bowel movements (12 per day). Treatment with methotrexate 25 mg was started. In October, the patient continued to complain of multiple bowel movements (6-8 per day) and malaise. An induction dose of infliximab (Remsima)

was administered. Two more doses were administered one month apart with an allergic reaction following the third induction dose (with corhydron as a slow drip infusion of 450 mg).

After completion of infliximab treatment in the induction cycle, the decision was made to discontinue further therapy due to high levels of antibodies to the drug in the absence of reaching therapeutic concentrations of the drug and a previous allergic reaction to the drug.

After several months, the man reported a lack of appetite and numerous bowel movements of about 20 per day. The patient's clinical condition was re-evaluated and adalimumab 160 mg was started on 22.03.17. The second dose-80 mg-was administered after about 2 weeks with good results.

Magnetic resonance imaging (12.04) showed a perianal fistula with branching bilaterally and an inflammatory infiltrate around the hyoid bone with signs of healing. In January of the same year, a seton was placed into the fistula. Therapy at that time included mesalazine, mycophenolate mofetil and subsequent doses of adalimumab. Clinically, the patient showed hyperthermia, severe muscle pain, weakness, and hypotonia.

After withdrawal of mycophenolate mofetil, clinical improvement was achieved. Subsequently, methotrexate was started- 2 doses at weekly intervals- and a febrile state with flu-like symptoms was noted again. Suspecting IE, a cardiology consultation was ordered. ECHO studies performed showed no significant abnormalities or features of infective endocarditis. Due to the severity of the diarrhea, a microbiological re-diagnosis was performed, which confirmed Clostridium difficile infection, and vancomycin was started, achieving clinical improvement and a reduction in inflammatory indices. Subsequent abdominal ultrasound (March 15, 2018) showed progression of inflammatory changes in the colon and suspected intestinal fistula. Treatment with adalimumab was terminated on 22.03.2018. In August 2018, disease activity was assessed at 110.6 points on the CDAI scale. And on 14.08, 40 mg of Humira was administered without complications. Subsequent doses (40 mg) were administered every 2 weeks. Sigmoidoscopy examination on 28.02.2019. Showed new active inflammatory changes in the examined section of the intestine with numerous ulcerations. Then in December 2019. Colonoscopy revealed further inflammatory changes in the rectum, sigmoid colon and descending colon - flat, longitudinal ulcerations and manufacturing changes. For this reason, the man was qualified for a clinical program of Risankizumab treatment. During the course of the program, improvement was initially observed but worsening again after several months. The patient required systemic steroid therapy and intravenous antibiotic therapy(Ciprofloxacin, Metronidazole).

Laboratory tests showed calprotectin levels of 1621.2µg.

The patient qualified for vedolizumab biologic treatment on 18/06/20 with a CDAI score of 405. Treatment was started less than a month after qualification.

In August, he was admitted to the hospital for 3 doses of Entyvio-300 mg (shielded by 200mg of corhydron). Patient was additionally using 10mg Encorton in the morning due to passing 5-6 stools per day, lower abdominal pain (symptoms worsened when trying to reduce Encorton dose to 5mg per day). A follow-up appointment for Entyvio was set for 4 p.m. The patient presented with a recurrence of increased bowel movements after discontinuing Encorton and the appearance of condylomas of HPV 6 etiology.

In total, the man received 12 doses of Entyvio. Subsequent follow-up endoscopic examinations showed inflammatory changes in the sigmoid colon and rectum. It was decided to qualify for treatment with another biological drug- ustekinumab. On 28.04.2022r the drug Hyrimoz (4x40mg) was administered. Subsequently, with the approval of the bioethics committee, it was decided to double biological therapy with two preparations-Hyrimoz and Stellara.

Discussion

Novel biologic therapies target various specific immune pathways. Current treatment goals include rapid induction of clinical remission and its steroid-free maintenance. With biologic drugs, it is possible to rapidly improve the clinical condition of the intestine by healing active mucosal lesions. In addition, patients using biologic drugs are less likely to undergo less frequent gastrointestinal surgery. [4]

In the cases described, there was a secondary loss of response to biologic drugs. Secondary loss of response is defined as a relapse of disease activity during maintenance treatment after an adequate induction dose has been achieved.[4]

Although the use of drugs containing anti-TNF antibodies, which are effective in both induction and maintenance treatment of Crohn's disease and Ulcerative Colitis, there is sometimes a loss of efficacy during maintenance treatment. In such cases, it may be necessary to increase the dose or shorten the administration interval of the drug, which was applied to a patient suffering from UC. Studies have shown that up to 25-40% of patients who initially respond positively to maintenance treatment develop loss of effect or side effects.[5, 6, 7, 8, 9]

Loss of response to treatment may be associated with the presence of antibodies to biologic drugs. In a study conducted by A. Pękala et al, it was proven that measuring infliximab levels during the induction phase was useful, as up to 11.3% of patients had undetectable levels of the drug and the presence of antibodies to infliximab. [10]

A decrease in disease activity exponents (MAYO, CDAI) was observed after therapy with two biologic drugs. Administration of biologic drugs in monotherapy in the described patients was much less effective than using them together. The combination of drugs with different mechanisms of action allows for comprehensive control of inflammation, increasing the effectiveness of treatment. At the same time, biological therapy with two drugs has its limitations, such as the high cost of treatment, the difficulty of monitoring the side effects of a given drug (in which case it may be difficult to determine which drug is responsible for the lack of therapeutic response or the appearance of side effects), and availability.

Dual biological therapy carries the risk of increased side effects, as the patient is taking two different drugs at the same time, which can cause more serious side effects. This can include an increased risk of infection (due to) a weakened immune system), allergic reactions, organ dysfunction (e.g., liver, kidney), or other complications associated with biologic therapy.

Although dual biologic therapy may provide treatment benefits, long-term data on its safety and efficacy are still lacking. Further clinical trials are needed to more accurately assess the impact of long-term use of this therapy.

Conclusion

Dual biologic therapy for the treatment of inflammatory bowel disease (IBD) is an innovative approach, especially in advanced cases refractory to standard treatment. With the simultaneous use of two biologic drugs with different mechanisms of action, a more comprehensive control of the inflammatory process is possible. This therapy can lead to sustained clinical and endoscopic remission, reducing the risk of complications such as fistulas or the need for surgical interventions.

As the described cases indicate, dual biologic therapy is effective, especially in patients with secondary loss of response to previous treatment. Its use, however, requires an individualized approach and careful monitoring of the patient. Although there are risks of side effects, the benefits of better disease control often outweigh the potential risks.

In conclusion, dual biologic therapy is a promising therapeutic option in IBD, but one that requires further research into its safety and long-term efficacy. It may significantly improve the quality of life of patients with the most severe forms of the disease.

Conceptualization and methodology – Aleksandra Karnas
Check – Aleksandra Karnas**,** Gabriela Majka**,** Magdalena Kowalczyk
Form analysis – Anita Krowiak**,** Aleksandra Karnas
Investigation – Karolina Krowiak**,** Aleksandra Karnas
Resources – Gabriela Majka**,** Aleksandra Karnas
Data curation – Magdalena Kowalczyk**,** Karol Bednarz
Writing – rough preparation – Maria Jasiewicz**,** Aleksandra Karnas
Writing – review and editing – Wiktoria Hander**,** Aleksandra Karnas
Visualization – Aleksandra Karnas**,** Karol Bednarz
Supervision – Anita Warzocha**,** Aleksandra Karnas

All authors have read and agreed with the published version of the manuscript.

REFERENCES

1. Guo M, Wang X. Pathological mechanism and targeted drugs of ulcerative colitis: a review. Medicine (Baltimore). 2023 Sep 15;102(37):e35020. doi:10.1097/MD.0000000000035020. PMID: 37713856; PMCID: PMC10508406.
2. Łodyga M, Eder P, Gawron-Kiszka M, Dobrowolska A, Gonciarz M, Hartleb M, et al. Guidelines of the Polish Society of Gastroenterology and the National Consultant in Gastroenterology for the management of patients with Crohn's disease. Gastroenterol Rev. 2021;16(4):257-96.
3. Eder P, Łodyga M, Gawron-Kiszka M, Dobrowolska A, Gonciarz M, Hartleb M, et al. Guidelines of the Polish Society of Gastroenterology and the National Consultant in Gastroenterology on the management of patients with ulcerative colitis. Gastroenterol Rev. 2023;18(1):1-42.
4. Yanai H, Hanauer SB. Assessing response and loss of response to biological therapies in IBD. Am J Gastroenterol. 2011 Apr;106(4):685-98. doi:10.1038/ajg.2011.103. PMID: 21427713.
5. Lorinczy K, Miheller P, Kiss SL, Lakatos PL. A biológiai kezelés során bekövetkező hatásvesztés gyakorisága, okai és klinikai megközelítése gyulladásos bélbetegségek esetén [Epidemiology, predictors and clinical aspects of loss of response to biological therapy]. Orv Hetil. 2012 Feb 5;153(5):163-73. doi:10.1556/OH.2012.29294. PMID: 22275731. [Hungarian]
6. Colombel JF, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007 Jan;132(1):52-65.
7. Sands BE, Anderson FH, Bernstein CN, Chey WY, Feagan BG, Fedorak RN, et al. Infliximab maintenance therapy for fistulizing Crohn’s disease. N Engl J Med. 2004 Mar 4;350(9):876-85.
8. Schreiber S, Khaliq-Kareemi M, Lawrance IC, Thomsen OO, Hanauer SB, McColm J, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. N Engl J Med. 2007 Jul 5;357(3):239-50.
9. Baert F, Noman M, Vermeire S, Van Assche G, Gornet JM, Carbonez A, et al. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn’s disease. N Engl J Med. 2003 Feb 13;348(7):601-8.
10. Pękala A, Filip R, Aebisher D. Anti-drug antibodies in patients with inflammatory bowel diseases treated with biosimilar infliximab: a prospective cohort study. J Clin Med. 2021 Jun 16;10(12):2653. doi:10.3390/jcm10122653. PMID: 34208676; PMCID: PMC8235171.