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Survival of infliximab and adalimumab biosimilar therapy in patients with Crohn's disease

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ABSTRACT *AIM: to evaluate the two-year survival of therapy with biosimilars of infliximab and adalimumab in patients with Crohn's disease (CD).*

PATIENTS AND METHODS: survival was assessed by primary medical records (electronic medical records) of patients with CD who started on adalimumab or infliximab therapy in 2017–2019. Forty-nine patients who received infliximab therapy and 39 patients who received adalimumab therapy were included in the study. The main clinical and demographic data, laboratory tests (hemoglobin, leukocyte, platelet, albumin, C-reactive protein and fibrinogen levels) and instrumental checkup (ileocolonoscopy, intestinal ultrasound, CT enterography or MR enterography) at the time of therapy initiation and for 2 years were estimated. In addition, the need for therapy optimization during this period, the frequency and reasons for therapy discontinuation are assessed. In the context of the retrospective analysis, the "number of involved segments" (NIS) index was included. By this index, we meant the number of anatomical segments of the intestine to which the active inflammatory process was determined (duodenum, jejunum, ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum).

RESULTS: in patients with infliximab for 2 years, the intensity of the inflammatory process significantly decreased. The number of intestinal segments involved in the inflammatory process and endoscopic activity significantly decreased during all 2 years of therapy ($p < 0.001$ for both indices), the level of hemoglobin and plasma albumin significantly increased ($p = 0.004$ and $p = 0.025$, respectively). The median survival of therapy was 19 (9;24) months and the treatment continued for more than 2 years in 44.9% of patients. During adalimumab therapy of patients with CD, a significant decrease in all parameters of the inflammatory process activity was detected, the number of inflamed intestinal segments ($p < 0.001$), intestinal wall thickness ($p < 0.001$), C-reactive protein ($p < 0.001$). The median survival of therapy was 24 (12; 24) months, 55.1% of patients continued to receive adalimumab for more than 2 years. At the same time, during infliximab and adalimumab therapy, the frequency of complications of CD increased ($p < 0.001$) due to strictures ($p < 0.001$). This is probably explained by the healing of transmural ulcerative defects with the formation of cicatricial deformation of the intestine.

CONCLUSION: the study of predictors of high survival of biotherapy in patients with IBD is quite promising. Based on the results of retrospective analysis, several promising areas for prospective studies have been identified.

KEYWORDS: *Crohn's disease, therapy survival, GERD, infliximab, adalimumab*

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INTRODUCTION

Recently, genetically engineered biological drugs (GEBD) are actively used in the treatment of moderate and severe forms of inflammatory bowel diseases (IBD). The modern concept postulates the need to achieve and maintain a stable remission of the inflammatory process, and in such patients, this can be achieved only by prescribing permanent anti-recurrence therapy [1]. Accordingly, patients with indications for GEBD therapy should receive these drugs for a long time. Of course, in such conditions, the first question is not only about safety, but also about the survival of the

therapy. The survival rate of GEBD therapy refers to the time from prescribing the drug to its withdrawal for any reason [2].

About a third of patients with Crohn's disease (CD) need to intensify therapy with TNF inhibitors during the first 14 months of treatment due to the ebbing effect [3]. This is especially true for infliximab. Kim, N.H. et al. assessed the therapy survival in patients with CD, with and without previous experience of biological therapy. The 5-year survival rate of the therapy in this study was 44.8% and 58.7%, respectively [4]. Recently, biosimilars of adalimumab and infliximab have been actively used in domestic and foreign clinical practice. And while there is a lot of data on the comparable effectiveness of biosimilars with the original drug both in the world and in Russia [5–7], there are still few publications on the survival of the therapy, especially those describing the survival rate in the Russian population of patients with CD [8].

In connection with all of the above, we have undertaken a retrospective analysis of the survival of the therapy with Russian biosimilars infliximab and adalimumab in patients with CD.

AIM

The aim of the study was to evaluate the two-year survival of treatment with domestic biosimilars infliximab and adalimumab in patients with CD.

PATIENTS AND METHODS

Survival was assessed by analyzing the primary medical records (electronic medical records) of patients with CD who had started therapy with adalimumab or infliximab in the gastroenterology department in the period between 2017 and 2019. A total of 49 patients treated with infliximab and 39 patients treated with adalimumab were included in the analysis.

In all cases, the patients underwent a comprehensive laboratory and instrumental diagnostics, which specified the indications for starting therapy with infliximab or adalimumab. Regular monitoring of the effectiveness and tolerability of the therapy was also carried out.

The main clinical and demographic data, laboratory results (hemoglobin, leukocytes, platelets, albumin, C-reactive protein and fibrinogen levels) and instrumental studies (ileocolonoscopy, ultrasound of the intestine, CT enterography or MR enterography) at the time of initiation of the therapy and for 2 years against the background of its continuation were analyzed. In addition, the need to optimize the therapy during this period, the rate and reasons for discontinuation of the therapy were analyzed. As part of the retrospective study, we introduced the "number of involved segments" (NIS) indicator. By this indicator, we meant the number of anatomical segments of the intestine in which the active inflammatory process was detected (duodenum, jejunum, ileum, cecum, ascending intestine, transverse colon, descending intestine, sigmoid colon, rectum).

Considering that one of the significant drawbacks of our retrospective analysis was the inability to track the changes of the patient's condition according to strict control points, the following follow-up intervals were adopted: 6–12 months, 12–24 months and 24–36 months.

Statistical Analysis

The indicators of descriptive statistics were analyzed using the StatTech v. 4.6.1 program (developed by Stattech LLC, Russia). Quantitative indicators were evaluated for compliance with the normal distribution using Shapiro-Wilk's test.

Quantitative indicators with a normal distribution were described using arithmetic averages (M) and standard deviations (SD), the limit of the 95% coincidence interval (95% CI). In the absence of a normal distribution, quantitative data were described using the median (Me), and the lower and upper quartiles (Q1;Q3). Categorical data was described with absolute values and percentages. To compare three or more related groups according to a normally distributed quantitative feature, a univariate analysis of variance with repeated measurements was used. The statistical significance

of the changes in the dynamics of the indicator was assessed using Fischer's F test. A posteriori analysis was performed using a paired Student's t-test with Holm's correction. When comparing three or more dependent totalities whose distribution differed from the normal one, the nonparametric Friedman's test was used with posteriori comparisons using Conover-Iman's test with Holm's correction. The differences were considered statistically significant at $p < 0.05$.

The second part of the statistical data processing was performed in RStudio (R v. 4.4.1 (R Core Team, Vienna, Austria)) using the libraries dplyr, gtsummary, survival, survminer.. In order to estimate the probability of maintaining therapy by months, Kaplan-Meyer's curves were constructed (the fact of drug withdrawal was taken as the outcome). To find the risk factors associated with drug withdrawal, Cox regression analysis was performed with the calculation of the risk ratio (HR) and its 95% CI. The indicators were considered to be associated with the fact of discontinuation of therapy at $p < 0.05$.

RESULTS

Infliximab for Crohn's Disease

During this period, 49 patients with CD received infliximab. The median age of disease onset was 20 (17; 29) years; there were 26 (53.1%) women and 23 (46.9%) men. Infliximab was the second GEBD in most cases. These were mainly patients with mild CD attack (the median score as per Harvey-Bradshaw's index was 5 (2; 9)), with the ineffectiveness of basic therapy or after surgery for complications of CD as an anti-recurrence treatment. The clinical and demographic characteristics are presented in more detail in Table 1.

According to the location of the lesion, the patients were distributed as follows: terminal ileitis — 14 (28.6%) patients, CD in the form of colitis — 12 (24.5%), ileocolitis — 23 (46.9%). The majority of patients in the group had luminal inflammation — 31 (63.3%) patients, the stricturing phenotype was observed in 10 (20.4%), the penetrating form — in 8 (16.3%).

At the time of initiation of infliximab therapy, 27 (55.1%) patients were receiving steroids, while 6 (12.2%) of them were receiving topical budesonide therapy, 12 (24.5%) were receiving systemic steroids at the rate of 1 mg/kg in terms

Table 1. *Clinical and demographic data of CD patients on infliximab therapy*

Indicators	Infliximab for CD, N = 49
Age of onset of the disease, years, Me (Q1; Q3)	20 (17;29)
Gender, *n* (%) Male Female	 23 (46.9) 26 (53.1)
Duration of the disease before the start of therapy, months, Me (Q1; Q3)	66 (35;115)
Harvey-Bradshaw's Index, Me (Q1; Q3)	5 (2; 9)
Steroid addiction, *n* (%)	7 (14.3)
Steroid resistance, *n* (%)	3 (6.1)
History of resections, (%)	14 (28.6)
Surgeries for perianal manifestations in the anamnesis, *n* (%)	24 (49.0)
Ineffectiveness of azathioprine, *n* (%)	6 (12.2)
Ineffectiveness of methotrexate, *n* (%)	4 (8.2)
GEBD in the anamnesis, *n* (%)	24 (49.0)
Ineffectiveness of adalimumab, *n* (%)	15 (30.6)
Ineffectiveness of certolizumab pegol, *n* (%)	6 (12.2)
Ineffectiveness of vedolizumab, *n* (%)	3 (6.1)
Ineffectiveness of ustekinumab, *n* (%)	1 (2.0)
Smoking, *n* (%)	10 (20.4)
Lesion in the upper gastrointestinal tract, *n* (%)	1 (2.0)
Perianal manifestations, *n* (%)	32 (65.3)
Extra-intestinal manifestations, *n* (%)	10 (20.4)
Concomitant non-immune diseases, *n* (%)	10 (20.4)

Table 2. *Concomitant therapy in patients with CD treated with infliximab*

Drugs	Infliximab for CD, N = 49
Concomitant administration of glucocorticosteroids, *n* (%)	27 (55.1)
Concomitant administration of antibacterial drugs, *n* (%)	25 (51)
Combination with thiopurines, *n* (%)	32 (65.3)

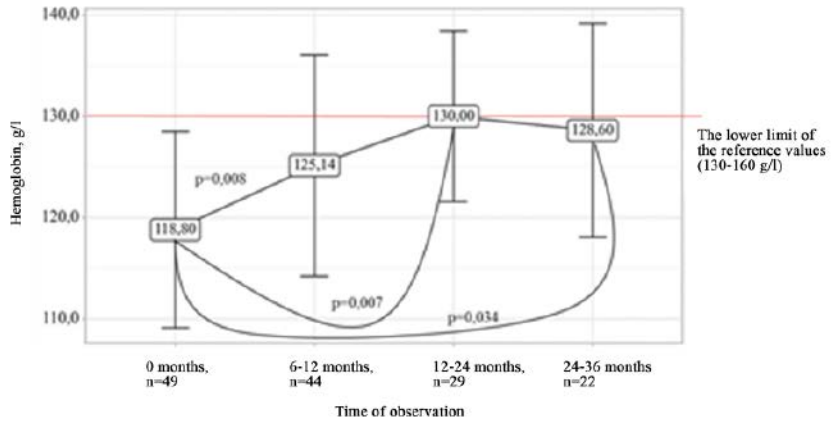

Figure 1. *Dynamics of hemoglobin level changes (in g/l) during infliximab therapy*

of prednisone, and 9 (18.4%) were receiving 2 mg/kg. 25 (51.0%) patients received antibiotic therapy, and in 32 (65.3%) cases, infliximab was administered in combination with thiopurines (Table 2). Laboratory data was analyzed as part of monitoring the effectiveness of the therapy. The average hemoglobin level at the start of treatment was 118.8 (95% CI: 109–128) g/l, which corresponded to mild anemia. During the year of infliximab therapy, there was a significant increase in this indicator to 130 (95% CI 123 -138) g/l (p = 0.004). It is worth noting that the median hemoglobin index reached the lower limit of normal values only by the second year of the therapy, remaining subnormal throughout the entire follow-up period (Fig. 1).

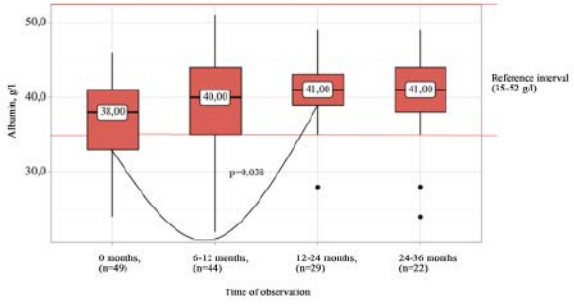

Figure 2. *Dynamics of changes in albumin levels (in g/l) during infliximab therapy*

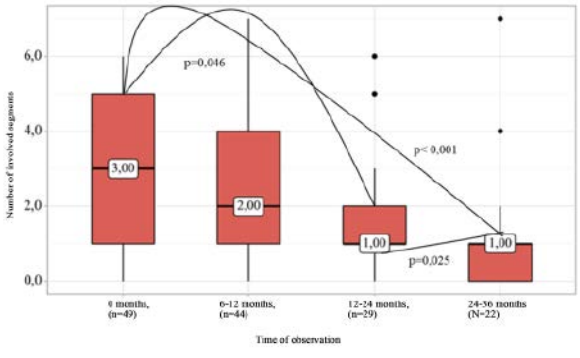

Figure 3. *Dynamics of changes in the number of involved intestinal segments during infliximab therapy*

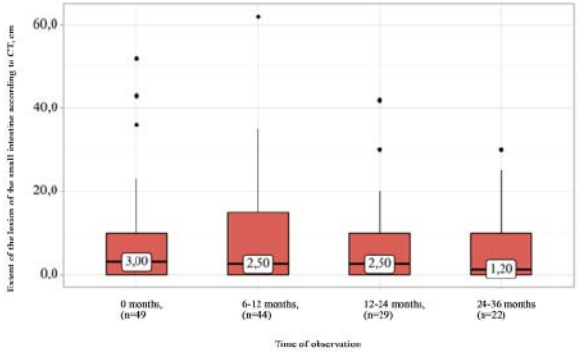

Figure 4. *Dynamics of changes in the extent of small intestine lesion (in cm) during infliximab therapy*

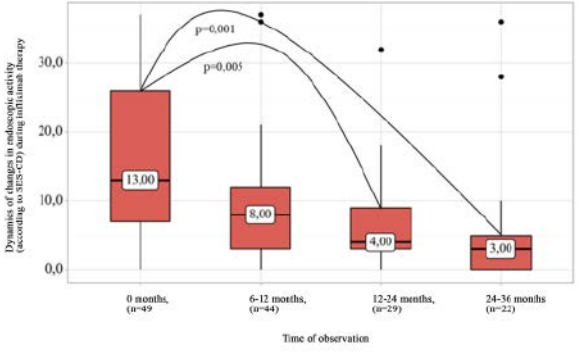

Figure 5. *Dynamics of changes in endoscopic activity (according to SES-CD) during infliximab therapy*

Table 3. *Outcomes of infliximab therapy in patients with CD*

Therapy outcomes	Infliximab for CD, N = 49
Any surgical treatment during the period from 6 to 12 months of therapy, *n* (%), of them:	5 (11.4)
Intestinal resection in the period from 6 to 12 months, *n* (%)	0
Surgical treatment for perianal manifestations in the period from 6 to 12 months, *n* (%)	5 (11.4)
Any surgical treatment between 12 and 24 months, *n* (%), of them:	3 (10.3)
Intestinal resection in the period from 12 to 24 months, *n* (%)	1 (3.4)
Surgical treatment for perianal manifestations in the period from 12 to 24 months, *n* (%)	2 (6.9)
Surgical treatment for any reason in the period from 24 to 36 months, *n* (%), of them:	1 (4.8)
Intestinal resection in the period from 24 to 36 months, *n* (%)	1 (4.8)
Surgical treatment for perianal manifestations in the period from 24 to 36 months, *n* (%)	0
The need to optimize therapy, *n* (%)	18 (36.7)
Primary ineffectiveness, *n* (%)	18 (36.7)
Loss of response, *n* (%)	5 (10.2)
Adverse events, *n* (%)	5 (10.2)

It is also important to note that the assessment of albumin levels showed a significant increase during the treatment (p = 0.025). In addition, starting from the second year of observation, all values, except for emissions, were within the reference range. As for the remaining laboratory parameters, which were determined routinely in patients with CD, as well as markers of inflammation (CRP and ESR), there were no significant deviations from normal values at baseline, as well as during the follow-up period during therapy for 2 years.

An assessment of the NIS changes during the observation period was carried out. At the beginning of the therapy, the median number of involved segments was 3 (1.5;4.5), significantly decreasing to 1 involved segment by the second year, p = 0.001 (Fig. 3).

We also assessed the changes in the extent of the lesion of the small intestine according to CT enterography. In the presence of several sites of the inflammatory process in the small intestine, their total length was taken into account (Fig. 4). There was no significant change in the extent of the inflammatory process in the small intestine during the therapy (p = 0.8).

Figure 5 shows changes in endoscopic activity during infliximab treatment. The median SES-CD at the start of the treatment was 13 (8; 26) points, decreasing to 3 (0;4) points by the beginning of the third year of the follow-up (p < 0.001).

Against the background of the therapy, there was a slight decrease in the thickness of the intestinal wall, p = 0.6 (Fig. 6), while it is noteworthy that it became close to the normal value (2–3 mm) only by the third year of the therapy. The median survival of infliximab therapy was 19 (9; 24) months (Fig. 13), while 22 (44.9%) patients continued therapy for more than 2 years. The treatment outcomes are presented in Table 3.

During the factor analysis, the following predictors of low survival of infliximab therapy were established:

1. Administration of infliximab after previously established ineffectiveness of certolizumab pegol (HR = 14.9; 95%CI 1.63–136, p = 0.017);

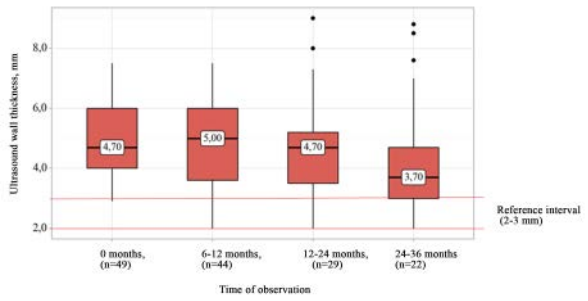

Figure 6. *Dynamics of changes in intestinal wall thickness (in mm) during infliximab therapy*

Table 4. *Clinical and demographic data of patients with CD treated with adalimumab*

Indicators	Adalimumab for CD,N = 39
Median age of debut, years (Q1; Q3)	23 (21;26)
Median duration of the disease before the start of therapy, months (Q1; Q3)	106 (49;157.5)
Gender, *n* (%) Male Female	22 (56.4) 17 (43.6)
Median of Harvey-Bradshaw's index, points (Q1; Q3)	5 (2;9)
Steroid addiction, *n* (%)	2 (5.1)
Steroid resistance, *n* (%)	2 (5.1)
History of resections, *n* (%)	17 (43.6)
Surgeries for perianal manifestations in the anamnesis, *n* (%)	17 (43.6)
Ineffectiveness of azathioprine, *n* (%)	24 (61.5)
Intolerance to azathioprine, *n* (%)	6 (15.4)
Ineffectiveness of methotrexate, *n* (%)	1 (2.6)
GEBD in the anamnesis, *n* (%)	15 (38.5)
Ineffectiveness of infliximab, *n* (%)	9 (23.1)
Ineffectiveness of certolizumab pegol, *n* (%)	6 (15.4)
Ineffectiveness of vedolizumab, *n* (%)	2 (6.1)
Smoking, *n* (%)	8 (5.1)
Lesion in the upper gastrointestinal tract, *n* (%)	8 (20.5)
Perianal manifestations, *n* (%)	24 (61.5)
Extra-intestinal manifestations, *n* (%)	5 (12.8)
Concomitant non-immune diseases, *n* (%)	9 (23.1)

Table 5. *Concomitant therapy in patients with CD treated with adalimumab*

Drug	Adalimumab for CD,N = 39
Concomitant therapy with glucocorticosteroids, *n* (%)	17 (43.6)
Concomitant therapy with antibacterial drugs, *n* (%)	16 (41.0)
Combination with thiopurines, *n* (%)	21 (53.8)

2. Large thickness of the intestinal wall during transabdominal ultrasound examination (HR = 1.31; 95%CI 1.03–1.66, $p = 0.029$).

Adalimumab for Crohn's Disease

Adalimumab was started in 39 patients with CD. The median age of onset of the disease in this group was 23 (21;26) years, as a rule, these were biosimilar patients with mild CD attack (the median of Harvey-Bradshaw's index was 5 (2;9)). The gender distribution in the group was almost equal: 17 (43.6%) women and 22 (56.4%) men.

The analysis included 39 patients with CD, whose main clinical and demographic characteristics are presented in Table 4.

In the adalimumab group, 18 (46.2%) patients had terminal ileitis, 4 (10.3%) had colitis, and 17 (43.6%) had ileocolitis. Luminal inflammation was found in 17 (43.6%) patients, the stricturing form was observed in 12 (30.8%) cases, and the penetrating form in 10 (25.6%).

The clinical and demographic characteristics are presented in more detail in Table 4.

Seventeen (43.6%) patients received glucocorticoid therapy, with 7 (17.9%) patients receiving topical budesonide, 7 (17.9%) patients receiving

prednisone at the rate of 1 mg/kg, and 3 (7.7%) ones receiving 2 mg/kg. 16 (41.0%) patients received antibacterial drugs. Twenty-one (53.8%) patients were treated with adalimumab in combination with thiopurines (Table 5).

The changes of the NIS during the observation was analyzed (Fig. 7). The median NIS was 1 (0; 5), and it significantly decreased to 0 (0; 1) by the beginning of the third year of the follow-up ($p < 0.001$).

The analysis assessed the change in the extent of the lesion of the small intestine according to CT enterography (Fig. 8). Against the background of adalimumab therapy, no significant changes in the extent of the lesion of the small intestine were noted ($p = 0.866$).

According to the endoscopy, no significant changes in inflammatory activity were noted during the treatment, $p = 0.6$ (Fig. 9). By the time of the start of the treatment, the SES-CD was 3 (0; 9) points, maintaining close values at all stages of the follow-up. By the time of the end of the observation, it had reached 6 (2; 8) points.

Against the background of adalimumab therapy, there was no significant decrease in the thickness of the intestinal wall, $p = 0.9$ (Fig. 10).

An assessment of the laboratory data showed that the albumin level increased significantly during the treatment ($p < 0.001$) (Fig. 11), while at all stages of the follow-up, the albumin level was within the reference range (35–52 g/l).

There was a significant decrease in the level of C-reactive protein during the treatment with its normalization by the 2nd year of the therapy ($p < 0.001$) (Fig. 12).

The median survival of adalimumab therapy was 24 (12; 24) months (Fig. 13), while 22 (56.4%)

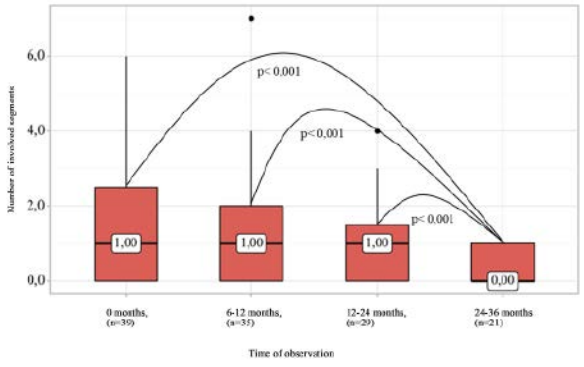

Figure 7. *Dynamics of changes in the number of involved intestinal segments during adalimumab therapy*

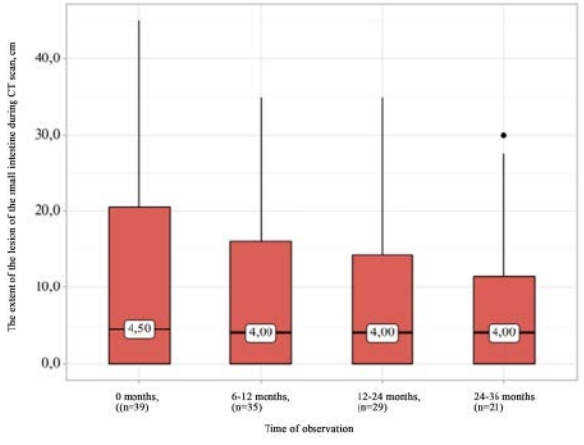

Figure 8. *Dynamics of the extent of small intestine lesion (in cm) during adalimumab therapy according to CT enterography*

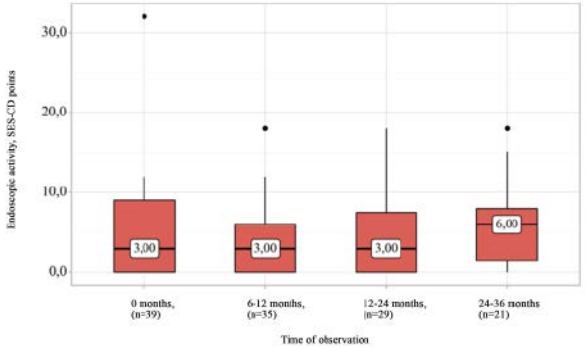

Figure 9. *Dynamics of changes in endoscopic activity (according to SES-CD) during adalimumab therapy*

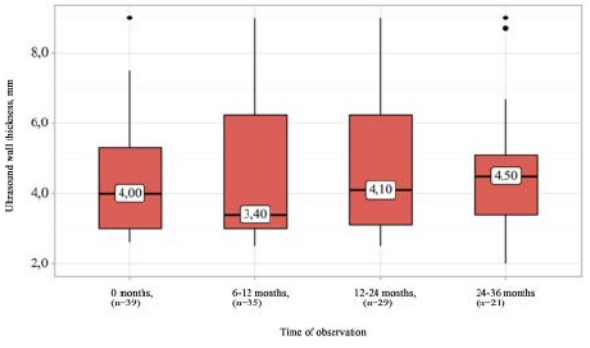

Figure 10. *Dynamics of changes in intestinal wall thickness (in mm) during transabdominal ultrasound of the intestine during adalimumab therapy*

Table 6. *Outcomes of adalimumab therapy in patients with CD*

Therapy outcomes	Adalimumab for CD, N = 39
Any surgical treatment in the period between 6 and 12 months of therapy, *n* (%)	6 (17.1)
Intestinal resection in the period between 6 and 12 months, *n* (%)	1 (2.9)
Surgical treatment for perianal manifestations in the period between 6 and 12 months, *n* (%)	5 (14.3)
Any surgical treatment between 12 and 24 months, *n* (%)	0
Surgical treatment for any reason in the period between 24 and 36 months, *n* (%)	1 (5.3)
Intestinal resection in the period between 24 and 36 months *n* (%)	1 (5.3)
The need to optimize therapy, *n* (%)	6 (15.4)
Primary ineffectiveness, *n* (%)	13 (33.3)
Loss of response, *n* (%)	1 (2.6)
Adverse events, *n* (%)	3 (7.7)

patients continued the therapy for over 2 years. The treatment outcomes are presented in Table 6.

The following predictors of survival of adalimumab therapy were established during the factor analysis:

1. A history of intestinal resections proved to be a factor positively influencing the survival of the therapy (HR = 0.12, 95% CI 0.03–0.52);

2. A factor reducing the survival of the therapy was the combined administration of systemic glucocorticosteroids with adalimumab induction (HR = 6.1, 95% CI 2.19–17.0), systemic antibiotics (HR = 3.54, 95% CI 1.3–9.63) in combination with a more severe course of the disease: a greater number of intestinal segments involved in the inflammatory process (HR = 1.5, 95% CI 1.23–1.83), greater endoscopic activity (HR = 1.06, 95% CI 1.02–1.09), higher score as per Harvey-Bradshaw's index (HR = 1.12, 95% CI 1.02–1.23).

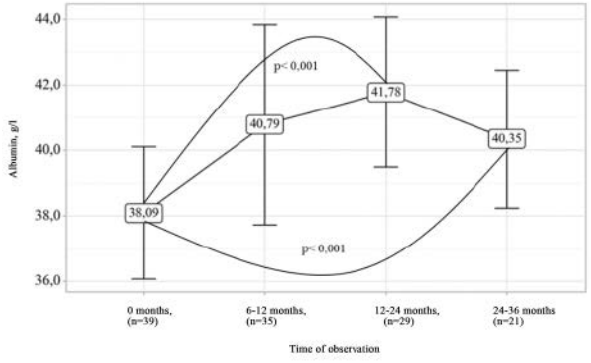

Figure 11. *Dynamics of changes in albumin levels (g/l) during adalimumab therapy*

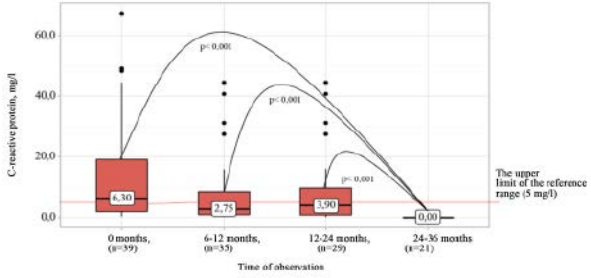

Figure 12. *Dynamics of changes in the level of C-reactive protein (in mg/l) during adalimumab therapy*

DISCUSSION

From the point of view of current trends, the survival rate of GEBD therapy is of fundamental importance. It is important not only to select

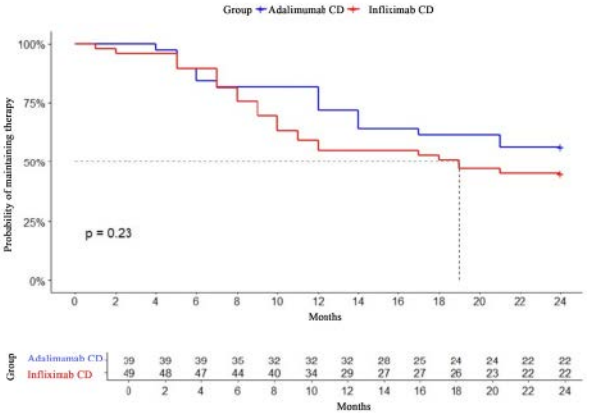

Figure 13. *Two-year survival schedule for infliximab and adalimumab therapy in CD*

a drug that effectively induces remission of the disease, but will also be able to maintain remission for as long a period of time as possible. In this regard, it is extremely important to determine the likely survival of therapy with various drugs, as well as to identify the factors influencing it. Our retrospective analysis of our own experience in managing CD patients undergoing therapy with various GEBD has, of course, a number of limitations, just like any other retrospective study. Such limitations include, first of all, the "blurriness" in the time of control points for examining patients, the lack of clear criteria for optimizing therapy or changing it. However, this study allowed us to identify a number of promising clinical and anamnestic indicators for further study, possibly relevant in reducing the survival of therapy, as well as to identify groups of patients for whom infliximab or adalimumab therapy is likely to be the best treatment option. Naturally, all the conclusions of this analysis should be confirmed by future well-planned prospective studies.

When assessing the outcomes in patients with CD who were on infliximab therapy for 2 years, the intensity of the inflammatory process significantly decreased. The number of intestinal segments involved in the inflammatory process and endoscopic activity significantly decreased during all 2 years of therapy ($p < 0.001$ for both indicators), plasma hemoglobin and albumin levels increased significantly ($p = 0.004$ and $p = 0.025$, respectively). The median survival of therapy was 19 (9; 24) months and the drug administration was continued for more than 2 years in 44.9% of patients. Of the factors contributing to a decrease in the survival rate of therapy, we identified the following:

1. Administration of infliximab after finding the ineffectiveness of certolizumab pegol (HR = 14.9; 95% CI 1.63–136);
2. Large thickness of the intestinal wall during transabdominal ultrasound examination (HR = 1.31; 95% CI 1.03–1.66).

The first point remains unclear to us, because when analyzing previous therapy with another TNF inhibitor, adalimumab, we did not record a similar trend. Most likely, this effect is associated with a decrease in the effectiveness of TNF inhibitor therapy in non-bionaive patients, which has been the subject of a number of studies [9]. The second judgment requires an additional prospective study to clarify the specific reference values of intestinal wall thickness, followed by the development of a prognostic model of the effectiveness of therapy.

Against the background of adalimumab therapy in patients with CD, a significant decrease in all indicators of inflammatory process activity was noted, namely the number of inflamed intestinal segments ($p < 0.001$), intestinal wall thickness ($p < 0.001$), C-reactive protein ($p < 0.001$). At the same time, as with infliximab therapy, the incidence of CD complications increased ($p < 0.001$) due to strictures ($p < 0.001$). This is probably due to the same healing of transmural ulcerative defects with the formation of cicatricial deformity of the intestine. The median survival of therapy was 24 (12; 24) months, 55.1% of patients continued to receive adalimumab therapy for over 2 years.

Factors affecting the survival of adalimumab therapy in patients with CD:

1. A history of intestinal resection proved to be a factor positively influencing the survival of therapy (HR = 0.12, 95% CI 0.03–0.52). The presence of intestinal resection indicates the use of adalimumab as a postoperative prevention of CD recurrence after surgical induction of remission.
2. A factor reducing the survival of therapy was the combined administration of systemic glucocorticosteroids with adalimumab induction (HR = 6.1, 95% CI 2.19–17.0), systemic antibiotics (HR = 3.54, 95%CI 1.3–9.63) in combination with a more severe course of the disease: a greater number of intestinal segments involved in the inflammatory process (HR = 1.5, 95% CI 1.23–1.83), more pronounced endoscopic

activity (HR = 1.06, 95% CI 1.02–1.09), higher Harvey-Bradshaw's index score (HR = 1.12, 95% CI 1.02–1.23).

In addition, the survival rate of adalimumab therapy is higher in patients with milder CD. However, these theses should be confirmed by further prospective studies.

CONCLUSION

The study of predictors of high survival of GEBD in patients with IBD is quite promising. Based on the results of our retrospective analysis, several promising areas for prospective research have been identified.

Promising areas:

1. Assessment of the survival of therapy in patients with CD, taking into account previous GEBD therapy;
2. Assessment of changes in intestinal wall thickness as a promising prognostic marker for patients with CD against the background of GEBD;
3. Assessment of the survival of adalimumab therapy in patients with varying degrees of CD severity and in different clinical situations.

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REFERENCES

1. 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. doi: 10.1053/j.gastro.2020.12.031

2. Reinisch W, Gecse K, Halfvarson J, et al. Clinical Practice of Adalimumab and Infliximab Biosimilar Treatment in Adult Patients With Crohn's Disease. *Inflamm Bowel Dis*. 2021 Jan 1;27(1):106–122. doi: 10.1093/ibd/izaa078

3. Bastida G, Marín-Jiménez I, et al. Treatment patterns and intensification within 5 year of follow-up of the first-line anti-TNFα used for the treatment of IBD: Results from the VERNE study. *Dig Liver Dis*. 2022 Jan;54(1):76–83. doi: 10.1016/j.dld.2021.06.005

4. Kim NH, Lee JH, Hong SN, et al. Long-term efficacy and safety of CT-P13, a biosimilar of infliximab, in patients with inflammatory bowel disease: A retrospective multicenter study. *J Gastroenterol Hepatol*. 2019 Sep;34(9):1523–1532. doi: 10.1111/jgh.14645

5. Cohen HP, Blauvelt A, Rifkin RM, et al. Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes. *Drugs*. 2018;78(4):463–478. doi: 10.1007/s40265-018-0881-y

6. Peda E.S., Alexandrov T.L., Baranova T.A., et al. The effectiveness and safety of switching from therapy with original drugs to biosimilars in the treatment of inflammatory bowel diseases. *Experimental and clinical gastroenterology*. 2021;195(11):35–41. (in Russ.). doi: 10.31146/1682-8658-ecg195-11-35-41

7. Ye BD, Pesegova M, Alexeeva O, et al. Efficacy and safety of biosimilar CT-P13 compared with originator infliximab in patients with active Crohn's disease: an international, randomised, double-blind, phase 3 non-inferiority study. *Lancet*. 2019;393(10182):1699–1707. doi: 10.1016/S0140-6736(18)32196-2

8. Knyazev O.V., Zvyaglova M.Yu., Kagramanova A.V, et al. Loss of response and frequency of adverse events in patients with ulcerative colitis and Crohn's disease during the transition from the original drug infliximab to its biosimilars. *Therapeutic Archive*. 2021;93(2):150–

157. (in Russ.). doi: 10.26442/00403660.2021.02.200624

9. Singh S, Murad MH, Fumery M, et al. First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis. *Clin Gastroenterol Hepatol.* 2020 Sep;18(10):2179–2191.e6. doi: 10.1016/j.cgh.2020.01.008 Epub 2020 Jan 13. PMID: 31945470; PMCID: PMC8022894.