NERIMAN TSINTSADZE [1,2,3], LIA SAGINADZE [3], NATO KAKABADZE [1,2], IA KAKHIDZE [3], RUSUDAN VADATCHKORIA [1,2], MIKHEIL ARTMELADZE [1]

PATIENTS TREATING WITH RHEUMATOID ARTHRITIS IN ADJARA REGION: WHY BIOLOGICAL THERAPY?

[1]Avicenna - Batumi Medical University; [2]Batumi Shota Rustaveli State; [3]"SoloMed" Clinic, Batumi, Georgia

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ნერიმან ცინცაძე [1,2,3], ლია საგინაძე [3], ნატო კაკაბაძე [1,2], ია კახიძე [3], რუსუდან ვადაჭკორია [1,2], მიხეილ არტმელაძე [1]

რევმატოიდული ართრიტით დაავადებული პაციენტების მკურნალობა აჭარის რეგიონში: რატომ ბიოლოგიური თერაპია?

[1] ავიცენა - ბათუმის სამედიცინო უნივერსიტეტი; [2] ბათუმის შოთა რუსთაველის სახელმწიფო უნივერსიტეტი; [3] კლინიკა „სოლომედი", ბათუმი, საქართველო

რეზიუმე

შესავალი. რევმატოიდული ართრიტი (RA) სახსრების ქრონიკული, სისტემური ანთებითი დაავადებაა, რომელიც მოსახლეობის დაახლოებით 1%-ს აღენიშნება. უფრო ხშირად ვლინდება 30-დან 60 წლამდე ასაკის ქალებში და ხასიათდება ხრტილისა და ძვლების პროგრესირებადი დაზიანებით, რაც იწვევს ინვალიდობის განვითარებას. მიუხედავად იმისა, რომ ზუსტი მიზეზი უცნობია, ცნობილია, რომ გენეტიკური და გარემო ფაქტორები მნიშვნელოვან როლს თამაშობს დაავადების განვითარებაში. მკურნალობის ბოლო მიღწევებმა, განსაკუთრებით დაავადების მამოდიფიცირებელი ბიოლოგიური ანტირევმატული მედიკამენტების (bDMARDs) გამოყენებამ, მნიშვნელოვნად გააუმჯობესა შედეგები, მაგრამ განკურნება კვლავ რჩება მიუღწეველი. ტოცილიზუმაბი, IL-6 რეცეპტორების ინჰიბიტორი, წარმოადგენს RA-ის სამკურნალოდ ბიოლოგიურ თერაპიას, განსაკუთრებით იმ პაციენტებისთვის, რომლებიც არ რეაგირებენ ჩვეულებრივ სინთეზურ DMARD-ებზე (csDMARDs). მიუხედავად პრეპარატის ეფექტურობისა, გამოვლენილი გვერდითი მოვლენების გამო, მისი გამიყენება საჭიროებს სიფრთხილეს და რეგულარულ მონიტორინგს.

მიზანი. კვლევა მიზნად ისახავს აჭარის რეგიონის პაციენტებში რევმატოიდული ართრიტის სამკურნალოდ გამოყენებული აქტემრას (ტოცილიზუმაბი) ეფექტურობისა და უსაფრთხოების შეფასებას, მდგრადი რემისიის ან დაავადების დაბალი აქტივობის მიღწევას, და ამავდროულად გამოვლენილი გვერდითი მოვლენების შეფასებას.

მასალები და მეთოდები. ჩვენ შევისწავლეთ რევმატოიდული ართრიტის მქონე 26 პაციენტი (22 ქალი, 4 მამაკაცი) 28-დან 68 წლამდე ასაკის, რომლებიც იღებდნენ 162 მგ ტოცილიზუმაბის კანქვეშა ინექციას კვირაში ერთხელ. კლინიკური პარამეტრები, მათ შორის ტკივილის ინტენსივობა, C-რეაქტიული ცილა და ერითროციტების დალექვის სიჩქარე, შეფასდა 3, 6 და 12 თვის მკურნალობის შემდეგ. მკურნალობის ინტერვალები განისაზღვრა მკურნალობაზე პაციენტის პასუხის მიხედვით.

შედეგები. ტოცილიზუმაბით მკურნალობამ მნიშვნელოვნად გააუმჯობესა პაციენტების მდგომარეობა ანთების, ტკივილისა და დილის შებოჭილობის სწრაფი შემცირებით, ფიზიკური ფუნქციის გაუმჯობესებით და გრძელვადიანი გართულებების შემცირებით. C-რეაქტიული ცილის (CRP) და ერითროციტების დალექვის სიჩქარის (ESR) დონე მნიშვნელოვნად შემცირდა 3 თვის შემდეგ და კიდევ უფრო მეტად 12 თვის შემდეგ. 12 თვის შემდეგ პაციენტების უმეტესობას აღენიშნებოდა მსუბუქი ტკივილის ინტენსივობა და არავის არ აღენიშნებოდა ძლიერი ტკივილი. 12 თვის შემდეგ პაციენტების 27%-ს ჰქონდა მომატებული CRP (მამაკაცების 0%, ქალების 27%) და პაციენტების 73%-ს ჰქონდა ნორმალური CRP. 12 თვის შემდეგ პაციენტების მხოლოდ 11%-ს (მამაკაცების 0%, ქალების 11%) ჰქონდა მაღალი ერითროციტების დალექვის სიჩქარე.

დასკვნა. ბიოლოგიურმა თერაპიამ ტოცილიზუმაბით აჩვენა მნიშვნელოვანი ეფექტურობა ანთების დონის შემცირებაში, სახსრების ფუნქციის გაუმჯობესებასა და რევმატოიდული ართრიტის

მქონე პაციენტებში მდგრადი რემისიის ან დაავადების დაბალი აქტივობის მიღწევაში. მიუხედავად იმისა, რომ დაავადების მართვაში გვერდითი მოვლენები მოითხოვს სიფრთხილეს, ბიოლოგიური თერაპია გვთავაზობს მნიშვნელოვან გაუმჯობესებას რევმატოიდული ართრიტის პერსონალიზებულ მართვაში, განსაკუთრებით იმ შემთხვევებში, როდესაც ცუდია პროგნოზი ან სინთეზური დაავადების მამოდიფიცირებელი მედიკამენტები csDMARD-ები არაეფექტურია.

BACKGROUND. Rheumatoid arthritis (RA) is a common chronic, symmetrical, inflammatory, systemic autoimmune disease, that requires early diagnosis and treatment to prevent the progression of joint damage. The disease is associated with a major impact on the patient, their environment, and the healthcare system [1,20,18,19]. Affecting initially the small and progressively involves larger joints, potentially affecting the skin, eyes, heart, kidneys, and lungs with varying severity [12,9,22]. Although RA is heterogeneous, immune-mediated, and dynamic, it can lead to progressive disability if not treated promptly and effectively. Studies have identified several baseline factors associated with worse prognoses, such as higher disease activity and radiographic image damage [1,17,23].

Furthermore, in recent years it has become increasingly clear that RA is a highly heterogeneous disease and that there are likely to be distinct patient subgroups and disease sub-phenotypes. RA's heterogeneity, including distinct subgroups and sub-phenotypes, adds complexity to its management [3,17,24,25].

Rheumatoid arthritis is estimated to affect up to 1% of the adult population. Using the 2010 criteria applied to the Norfolk Arthritis Cohort, the incidence of rheumatoid arthritis in the UK was estimated to be 54/100,000 women and 25/100,000 men from 1990-1995. A 2023 publication using UK general practice data estimated the incidence of rheumatoid arthritis to be 58/100,000 person-years between 2000 and 2002, although the incidence increased with age, peaking in the sixth and seventh decades of life. Globally, the incidence of rheumatoid arthritis is increasing [4].

The etiology of RA is still largely unknown, and there is still a lack of bio- markers for the prediction of response to individual drugs [17,26]. In this scenario, the choice of the drugs to be used in the individual patient is still mainly left to the expertise of the rheumatologist and to a trial-and-error approach [27,17]. Risk factors for RA include age, gender, genetics, and environmental exposures like smoking and air pollution.

Rheumatoid arthritis (RA) is closely associated with permanent disability. The Pan American Health Organization estimates that 34 million people suffer from it, with a direct impact on work ability and functional performance. Complications can involve permanent joint damage requiring arthroplasty, rheumatoid vasculitis, and Felty syndrome, requiring splenectomy if it remains unaddressed [12]. Therefore, early diagnosis and timely treatment are essential pillars to improve disease prognosis and reduce severity [5].

Auto antibodies are detected in 50-60% of newly diagnosed patients, rising to 80% of patients with longstanding/active disease; potentially reflecting increased remission rates in seronegative disease. Anti-citrullinated peptide antibodies (ACP As) - Present in 60-80% of patients with rheumatoid arthritis. Other anti-modified protein autoantibodies (AMP As) Aside from ACP As, autoantibodies to carbamylated and acetylated protein antibodies are well described and associated with rheumatoid arthritis; being unlikely to add diagnostic value, they are not routinely tested for, but remain of pathophysiological interest [4].

Patients with RA should work closely with their healthcare providers to develop a personalized treatment plan that addresses their specific needs [3]. Two parallel developments of recent decades underlie advances in rheumatoid arthritis treatment. Firstly, an expanding armamentarium of targeted treatments has been driven by improved knowledge of the disease's pathobiology, coupled with

biotechnology developments. Secondly, the realization that early and effective control of inflammation improves outcomes has heralded formalized disease activity targets against which to titrate treatments: this is called the treat-to-target strategy. (T2T) [4].

Rheumatoid arthritis (RA) treatment strategies primarily focus on managing symptoms, reducing inflammation, preventing joint and organ damage, improving physical function, and overall quality of life. The most common treatments for RA are disease-modifying anti rheumatic drugs (DMARDs), which are divided into conventional synthetic DMARDs, biologic DMARDs, and targeted synthetic DMARDs [3].

RA treatment focuses on preventing joint deformities, functional impairment, and disability through early and effective intervention. Disease-modifying antirheumatic drugs (DMARDs) play a central role in reducing disease activity and achieving remission [8,28,29]. The treat-to-target strategy—a systematic approach to meeting specific disease activity goals—has significantly advanced RA management [4,17]. As there is no cure for RA [12], various therapeutic options, including conventional synthetic DMARDs (csDMARDs), Biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs), are available. According to the 2019 recommendations of the European Alliance of Associations for Rheumatology (EULAR), methotrexate (MTX) or another csDMARD, often combined with low-dose corticosteroids, is recommended as first-line treatment. If first-line therapy fails, bDMARDs or tsDMARDs should be introduced [30,7,17].

Treatment options for rheumatoid arthritis (RA) have progressed over the past two decades. Have significantly improved disease activity, functional disability, and joint prognosis of RA patients [6,22]. Therapy with DMARDs should be started as soon as the diagnosis of RA is made [2]. It can be said that biologics have improved the life quality of these patients by improving body mobilization. If the treatment target is not achieved with the first csDMARD strategy, when poor prognostic factors are present, a bDMARD should be added [2].

The bDMARDs approved to date for the therapy of RA include five TNFis (Infliximab, Adalimumab, Golimumab, Certolizumab Pegol and Etanercept), two IL6 inhibitors (Tocilizumab and Sarilumab), a monoclonal anti-B-cell CD20 antibody (Rituximab) and a T-lymphocyte co-stimulation inhibitor (Abatacept). They are all monoclonal antibodies, with the exception of Abatacept and Etanercept, which are fusion proteins. Their key feature is their therapeutic target selectivity [17].

Also, Pivotal studies on bDMARD showed their efficacy and safety for patients with RA refractory to csDMARD [1,2,31]. Subsequent publications have presented the results of post hoc analyses and studies specifically designed to analyze bDMARD as the initial treatment for RA (csDMARD-naive patients) [32,33]. However, the guidelines of national and international scientific societies still recommend using csDMARD, particularly MTX, as the initial treatment for RA. These guidelines highlight the high cost of many bDMARDs as a limitation to their wider use [1,34,35].

From 2012 to 2021, b/tsDMARD use increased while glucocorticoid use decreased. Functional disability and disease activity measures improved over time, with TNFi showed better short-term improvements in b/tsDMARD-naive patients, while IL6Ri demonstrated significant long-term benefits. IL6Ri had better retention rates in switched patients. After adjustment for patient characteristics, the annual change of RA disease activity and functional disability fared significantly better from 2012 to 2021 [6].

The primary goals of RA treatment are to reduce joint inflammation and pain, maximize joint function, and prevent joint destruction and deformity. Treatment regimens are tailored to individual patient characteristics, combinations of pharmaceuticals, weight-bearing exercise, educating patients about the disease, and rest, overall health, and lifestyle factors [12,3,36]. Achieving sustained remission at

the lowest effective dose is a key management objective [16]. It is commonly recommended to wait for at least six months to one year of sustained remission or LDA before considering tapering DMARDs [37,38,16]. RA management can be carried out with multiple care interventions diseases modifying anti-rheumatic drugs or biologics, according to the treating clinical specialist criteria [5,39,40].

To support high-quality clinical care, in 2021, American College of Rheumatology developed Guideline for the Treatment of Rheumatoid Arthritis. The guideline addresses treatment with disease-modifying antirheumatic drugs (DMARDs), including conventional synthetic DMARDs, biologic DMARDs, and targeted synthetic DMARDs, use of glucocorticoids, and use of DMARDs in certain high-risk populations (i.e., those with liver disease, heart failure, lymphoproliferative disorders, previous serious infections, and nontuberculous mycobacterial lung disease). The guideline includes 44 recommendations (7 strong and 37 conditional) [7,2].

In 2010, the EULAR has developed recommendations for the management of rheumatoid arthritis (RA) with disease-modifying antirheumatic drugs (DMARDs). To provide an update of the EULAR rheumatoid arthritis (RA) management recommendations addressing the most recent developments in the field [2]. The task force agreed on 5 overarching principles and 11 recommendations concerning use of conventional synthetic (cs) DMARDs (methotrexate (MTX), Leflunomide, sulfasalazine); GCs; biological (b)DMARDs (tumor necrosis factor inhibitors (Adalimumab, Certolizumab Pegol, Etanercept, Golimumab, Infliximab including biosimilars), Abatacept, Rituximab, Tocilizumab, Sarilumab and targeted synthetic (ts)DMARDs, namely the Janus kinase inhibitors Tofacitinib, Baricitinib, Filgotinib, Upadacitinib. Guidance on monotherapy, combination therapy, treatment strategies (treat-to-target) and tapering in sustained clinical remission is provided [2].

These updated EULAR recommendations provide consensus on RA management including safety, effectiveness and cost [2].

This clinical practice guideline is intended to serve as a tool to support clinician and patient decision-making. Recommendations are not prescriptive, and individual treatment decisions should be made through a shared decision-making process based on patients' values, goals, preferences, and comorbidity [7,2]. These recommendations are the following [2]:

1. Therapy with DMARDs should be started as soon as the diagnosis of RA is made.
2. Treatment should be aimed at reaching a target of sustained remission or low disease activity in every patient.
3. Monitoring should be frequent in active disease (every 1–3 months); if there is no improvement by at most 3 months after the start of treatment or the target has not been reached by 6 months, therapy should be adjusted.
4. MTX should be part of the first treatment strategy. recommendation (to prescribe leflunomide or sulfasalazine when MTX is contraindicated).
5. In patients with a contraindication to MTX (or early intolerance), Leflunomide or Sulfasalazine should be considered as part of the (first) treatment strategy.
6. Short-term GCs should be considered when initiating or changing csDMARDs, in different dose regimens and routes of administration, but should be tapered and discontinued as rapidly as clinically feasible.
7. If the treatment target is not achieved with the first csDMARD strategy, in the absence of poor prognostic factors, other csDMARDs should be considered.
8. If the treatment target is not achieved with the first csDMARD strategy, when poor prognostic factors are present, a bDMARD should be added.

9. bDMARDs and tsDMARDs* should be combined with a csDMARD; in patients who cannot use csDMARDs as comedication, IL-6 pathway inhibitors and tsDMARDs* may have some advantages compared with other bDMARDs.
10. If a bDMARD or tsDMARD* has failed, treatment with another bDMARD or a tsDMARD* should be considered.
11. After GCs have been discontinued and a patient is in sustained remission, dose reduction of DMARDs (bDMARDs/tsDMARDs and/or csDMARDs) may be considered.

Healthy lifestyle is also very important. Lifestyle changes can also contribute to managing RA symptoms and improving quality of life. Regular exercise can help keep joints flexible, while maintaining a healthy weight can reduce stress on the joints. Smoking cessation is particularly important, as smoking can increase the severity of RA and reduce the activeness of some treatments.

In cases where medications do not prevent or slow joint damage, surgical treatment might be necessary to restore function to a damaged joint. Surgeries can include synovectomy (removal of the inflamed lining of the joint), tendon repair, joint fusion, or total joint replacement [3]. Non-pharmacologic treatments, including physical and occupational therapy, are integral to comprehensive care. Low-impact exercises like swimming, yoga, and tai chi are particularly beneficial.

There is a consensus that csDMARDs are the mainstay of RA treatment, and the 2019 update of the EULAR recommendations supported the use of methotrexate as the first-line DMARD. If there is insufficient response to the initial csDMARD or if the patient is not suitable for these medications, bDMARDs or tsDMARDs should be considered [13].

Different biologics target different parts of the immune system that fuel inflammation. Tumor necrosis factor (TNF) inhibitors, for example, block an inflammatory protein called TNF [11]. Other biologic work by inhibiting different cytokines or cells in the immune system; these include Abatacept, Rituximab, Tocilizumab, and Sarilumab, while other drugs block pro-inflammatory B cells or T cells [3].

Targeted synthetic DMARDs are a newer class of medications that selectively inhibit specific pathways involved in the immune response. Tofacitinib (Xeljanz), baricitinib (Olumiant), and upadacitinib (Rinvoq) are Janus kinase (JAK) inhibitors that have been approved for the treatment of RA [3].

Whilst anti-TNF drugs are the most frequently used first-line bDMARDs, the response can decline over time in some patients, necessitating the switch to another biologic [42,43,2]. Data from real-life settings show that as many as 40–50% of patients stop their first anti-TNF treatment due to loss of therapeutic effectiveness; this is typically seen after a good initial response or due to adverse events (AEs) [14,44,45].

Even with several options, drug selection can be difficult because inflammatory diseases are often driven by many factors. That's why one biologic may work well for some people but not for others [14].

Tocilizumab is a humanized monoclonal antibody targeting the IL-6 receptor that was approved by the FDA in 2010 as an intravenous formulation for the treatment of RA. Tocilizumab is indicated for adult patients with moderately to severely active RA who have had an inadequate response to a csDMARD. It can be given in combination with a csDMARD or as monotherapy [13].

Tocilizumab provided statistically significant DAS28 improvement at 2 years, compared to Infliximab and Abatacept. As of bDMARD initiation, lower values of clinical parameters (numbers of tender and swollen joints, pain/disease VAS) used in daily practice were obtained [9]. Regarding drug persistence, IL6Ri had a better drug retention rate in the KURAMA cohort [6]. Another factor that could

account for the annual decline in disease activity and functional disability is the encouragement of exercise or physical therapy [6,47].

Tocilizumab efficacy was described previously. The Japanese ROSE study [47], a 24-week multicenter phase IIIb clinical trial, compared double-blind Tocilizumab ($n = 412$) to placebo ($n = 207$) for patients whose RA had not responded adequately to conventional synthetic DMARDs (csDMARDs). Tocilizumab obtained significant early responses vs. placebo for global VAS, pain VAS, and DAS28, and CRP and ESR levels improved as early as day 7. As of week 4, mean CRP levels were significantly lower for Tocilizumab recipients and remained significantly lower throughout follow-up [9].

Several lines of evidence suggest that women tend to respond less to bDMARDs than men do, despite similar baseline disease activity between the sexes [47,48]. Response was lower in women than in men in each treatment arm, particularly in the Tocilizumab group [50,17]. Unlike randomized studies - considered the "gold standard" to establish treatment efficacy - real-life observational studies such as ours provide better representation of patients seen in daily practice, along with their long-term follow-up data. They are therefore important to evaluate a drug's efficacy and safety [9].

Other Therapies. It has been found that, in contrast to suggestions in the past, there are no specific foods that patients with RA should avoid. The idea that diet can "aggravate" symptoms is no longer accepted as true [48]. Fish oils and omega-3 fatty acid supplements are beneficial for the short-term symptoms of RA. Cumin has been shown to have anti- inflammatory effects in patients with this disease. Calcium and vitamin D supplementation can be helpful in preventing osteoporosis [12]. A comprehensive strategy including also non-pharmacological treatments like physical exercise pro-grams should be implemented in the management [16,51].

Non-Pharmacologic Treatments. Non-pharmacologic interventions, including physical therapy, occupational therapy, and lifestyle modifications such as exercise and smoking cessation, are integral to the comprehensive management of RA. Movement exercises that are less traumatic for joints but good for muscle strength include swimming, yoga, and tai chi [12]. Patient education and support groups are also beneficial for coping with the disease [52,53,54,10].

Considerations and Monitoring. All treatments for RA come with potential risks and side effects, which must be carefully weighed against the benefits. Regular monitoring for drug efficacy and adverse effects is essential. This typically includes blood tests to check for signs of toxicity or infection, as well as regular assessments of joint function and pain.

Patients should discuss the risks and benefits of each treatment option with their healthcare provider to determine the most appropriate therapy for their condition. It is also crucial for patients to inform their healthcare providers of any other medications they are taking to avoid drug interactions.

The current study aimed to evaluate the efficacy and safety of Actemra (Tocilizumab) managing RA in patients from the Adjara region, aiming to achieve sustained remission or low disease activity while assessing adverse drug reactions.

MATERIAL AND METHODS. The 26 patients with moderate or severe manifestations of Rheumatoid arthritis in the Adjara region were taken under follow-up. This observational study was conducted at the Rheumatology Department of Clinic "SoloMed" on patients who in 2024, received Tocilizumab to treat moderate-to-severe active RA.

The patients were aged 28 to 68 years and had a confirmed diagnosis of rheumatoid arthritis (RA) according to the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) criteria. Active RA was defined by elevated C-reactive protein (CRP > 5)

and high erythrocyte sedimentation rate (ESR), with contraindications to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).

Among these patients, 22 were women (age group from 28 year to 68 year) and 4 were men (age group from 45 year to 48 year). Of these, 24 patients were with positive Anticcp and 2 patients-with negative.

Before starting Actemra (Tocilizumab), patients were assessed at baseline. The presence of infections and contraindications to medication were excluded. Also, they all were tested for Tuberculosis before starting Tocilizumab monotherapy. These patients met the inclusion criteria for biological therapy. We started treating patients with Tocilizumab 162 mg weekly for the first 6 months. We checked the laboratory parameters and evaluated the condition, the intensity of the pain, levels of CRP and ESR.

ACR Recommendations for tapering/discontinuing DMARDs- the recommendations specify that patients be at target (low disease activity or remission) for at least 6 months prior to tapering. Patients in remission for <6 months should not routinely be considered for dose reduction or withdrawal. Although the optimal time at target prior to tapering has not been established, the voting panel considered 6 months to be a reasonable minimal length of time to ensure stable disease control. “Dose reduction” refers to lowering the dose or increasing the dosing interval of a DMARD. “Gradual discontinuation” denotes gradually lowering the dose of a DMARD and subsequently stopping it [7].

RESULTS. Initial treatment with biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) is effective and has an acceptable safety profile [1]. Patient-reported outcomes indicated that Biologic therapy with Tocilizumab has demonstrated significant clinical improvement, including rapid reduction of inflammation, pain, and morning stiffness, as well as improved physical function, decreased functional disability after 3 months, and enhanced overall well-being, with a reduction in long-term complications. Significant decreases in C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were observed after 3 months of therapy, with further significant reductions after 12 months.

Pain intensity decreased in both women and men, from severe to light gradually (Table 1). Before the start of biological therapy, the majority of patients had a rather severe pain intensity 61.53%, moderate pain had 38.47%. Pain intensity was significantly reduced after 3 months, and the majority of patients had moderate pain or light pain. After 6 months, the condition improved significantly, none of the patients had severe pain, and the majority of patients already had moderate pain. After 12 months, most of the patients had light pain intensity and no one had severe pain.

Table 1. Pain intensity in patients

Course of Therapy	Light Pain				Moderate Pain						Severe Pain							
	Male		Female		Total		Male		Female		Total		Male		Female		Total	
	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n
At the Beginning	0	0	0	0	0	0	3.84	1	19.24	5	23.08	6	11.53	3	65.39	17	76.92	20
After 3 months	7.7	1	3.9	2	11.54	3	13.26	3	75.20	20	88.46	23	0	0	0	0	0	0
After 6 months	7.7	2	30.8	8	38.47	10	7.69	2	53.84	14	61.53	16	0	0	0	0	0	0
After 12 months	15.4	4	65.36	17	80.75	21	0	0	19.23	5	19.23	5	0	0	0	0	0	0

The observation also showed a decrease in C-reactive protein shortly after the start of treatment, and then in some patients we reached up the norm (Table 2). At the beginning 100% of patients had an increased CRP. After 3 months, 89% of patients (7% males, 81% females) had still high number, but reduced CRP. After 6 months, 54% of patients had high CRP (0% of male, 54% of female). Only 46% had normal CRP. After 12 months 27% of patients had an increased CRP (0% of male, 27% of female), and 73% of patients had normal CRP.

Table 2. Increased C-Reactive Protein Levels

Course of therapy	Male		Female		Total	
	n	%	n	%	n	%
At the Beginning	4	15	22	85	26	100
After 3 months	2	7	21	81	23	89
After 6 months	0	0	14	54	14	54
After 12 months	0	0	7	27	7	27
n = number of patients; % = percentage of patients						

Shortly after the initiation of biologic therapy, erythrocyte sedimentation rate (ESR) levels began to decrease (Table 3). At baseline, 100% of patients had elevated ESR. After 3 months of treatment, elevated ESR was observed in 65% of patients (0% of males and 65% of females). After 6 months, only 19% of patients (0% males and 19% females) had elevated ESR. After 12 months, elevated ESR persisted in only 11% of patients (0% males and 11% females).

Table 3. Levels of erythrocyte sedimentation rate (ESR) (>22mm/hr)

Course of therapy	Male		Female		Total	
	n	%	n	%	n	%
At the Beginning	4	15	22	85	26	100
After 3 months	0	0	17	65	17	65
After 6 months	0	0	5	19	5	19
After 12 months	0	0	3	11	3	11
n = number of patients % = percentage of patients						

After receiving Tocilizumab, five patients experienced episodes of acute rhinitis within several months; two patients reported mild sneezing lasting one month as a side effect; and five patients experienced transient general weakness immediately after injection. Three patients developed urinary tract infections lasting approximately one month as a complication. No serious adverse events were observed.

DISCUSSION. Parameters of function of liver, kidney (Alanine Transaminase (ALT), Aspartate aminotransferase (AST), creatinine, peripheral blood analysis and urine analysis) were without significant changes. The study highlighted Tocilizumab's effectiveness as a biologic therapy for moderate-to-severe RA, particularly in patients unable to tolerate csDMARDs. The findings align with global evidence supporting IL-6 inhibitors for long-term disease control and functional improvement. However, individual responses to biologics can vary, necessitating personalized treatment plans and regular monitoring.

CONCLUSION. Biologic therapies, including Tocilizumab, represent significant advancements in the management of rheumatoid arthritis (RA), particularly for patients with poor prognostic factors, inadequate response to previous DMARD therapy, or intolerance to conventional synthetic DMARDs (csDMARDs). Our data demonstrated that Tocilizumab, an anti-IL-6R monoclonal antibody, provides early and sustained efficacy in RA patients.

Early diagnosis and adherence to a treat-to-target strategy remain pivotal for achieving optimal outcomes, with the once aspirational goals of disease prevention and sustained drug-free remission becoming attainable for a subset of patients. Treatment approaches are expected to continue evolving, resulting in substantial improvements in RA management.

Interdisciplinary teamwork among healthcare professionals is essential to ensure patient safety, effective disease monitoring, achievement of disease control, and prevention of joint damage and disability.

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NERIMAN TSINTSADZE [1,2,3], LIA SAGINADZE [3], NATO KAKABADZE [1,2], IA KAKHIDZE [3], RUSUDAN VADATCHKORIA [1,2], MIKHEIL ARTMELADZE [1]

PATIENTS TREATING WITH RHEUMATOID ARTHRITIS IN ADJARA REGION: WHY BIOLOGICAL THERAPY?

[1]Avicenna - Batumi Medical University; [2]Batumi Shota Rustaveli State; [3]"SoloMed" Clinic, Batumi, Georgia

SUMMARY

Background. Rheumatoid arthritis (RA) is a chronic systemic inflammatory joint disease of autoimmune origin, affecting approximately 1% of the population. It primarily impacts women aged 30 to 60 and is characterized by progressive cartilage and bone damage, leading to significant disability. While the exact cause is unknown, genetic and environmental factors are implicated. Advances in treatment, particularly with biologic disease-modifying anti-rheumatic drugs (bDMARDs) have improved outcomes, but a cure remains elusive. Tocilizumab, an IL-6 receptor inhibitor, represents a promising biologic therapy for RA, especially for patients unresponsive to conventional synthetic DMARDs (csDMARDs), despite its efficacy, adverse reactions necessitate careful monitoring.

Aim of Study Was to evaluate the efficacy and safety of Actemra (Tocilizumab) managing RA in patients from the Adjara region, aiming to achieve sustained remission or low disease activity while assessing adverse drug reactions.

Materials and Methods. We observed 26 RA patients (22 females, 4 males) aged 28 to 68 years treated with weekly subcutaneous injections of 162 mg Tocilizumab. Clinical parameters, including pain intensity, CRP, and ESR levels, were assessed at 3, 6, and 12 months. Treatment intervals were adjusted based on patient response.

Results. Biologic therapy with Tocilizumab significantly improves patients' conditions by rapidly reducing inflammation, pain, and morning stiffness, enhancing physical function, and lowering long-term complications. CRP and ESR levels drop notably after 3 months and even more after 12 months. After 12 months, most of the patients had light pain intensity and no one had severe pain. After 12 months 27 % of patients had an increased CRP (0% of male, 27% of female), and 73% of patients had normal CRP. After 12 months, just 11% of patients (0% males, 11% females) had high ESR.

Conclusion. Biological treatment demonstrated significant efficacy in reducing inflammation, improving joint function, and achieving sustained remission or low disease activity in RA patients. While adverse events require vigilance, this therapy offers a valuable option for personalized RA management, particularly in cases with poor prognostic factors or csDMARDs failure.

Keywords: Rheumatoid arthritis, biological therapy, Actemra (Tocilizumab)