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REAL-LIFE DATA IN RHEUMATOID ARTHRITIS PATIENTS USING BARICITINIB AT A SINGLE CENTER

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Abstract

Aim: Rheumatoid arthritis (RA) poses a significant health challenge and is characterized by chronic immune-mediated inflammation and potential joint damage. This study explores the real-life effectiveness of baricitinib, a Janus kinase inhibitor, in treating patients with RA. The goal of this study was to assess its impact on disease activity and factors influencing treatment outcomes.

Material and Methods: Ninety patients with RA diagnosed between September 2021 and 2023 at Necmettin Erbakan University Meram Medical Faculty Hospital were retrospectively analyzed. Baricitinib, prescribed during this period, was evaluated for its impact on C-reactive protein (CRP), Disease Activity Score-28 with CRP (DAS28/CRP), and overall treatment continuation rates. Demographic and clinical data, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) markers, were collected.

Results: Significant reductions in CRP and DAS28/CRP levels were observed over a 12-week follow-up after baricitinib use. Positive detection rates for RF and anti-CCP were 60% and 57.8%, respectively. Baricitinib demonstrated a high continuation rate (82%) at an average of 9.37 months. No significant differences were found in the continuation rates based on the prior use of conventional or biological disease-modifying anti-rheumatic drugs (DMARDs).

Conclusion: Comparisons with existing studies support the efficacy of baricitinib in improving disease activity. Our findings align with the literature, emphasizing positive outcomes in patients with prior DMARD experience. Unlike some studies reporting higher discontinuation risks, our results highlight a favorable safety profile. The study's limitations include a short follow-up period, which warrants further investigation with larger cohorts. In conclusion, baricitinib exhibits promising real-life effectiveness in RA treatment, emphasizing its role as a valuable therapeutic option.

Keywords: Real-life experience, baricitinib, rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, multisystemic, immune-mediated disease that can lead to progressive joint damage. Left untreated, RA may result in loss of physical function. In addition, specific comorbidities such as nodules, interstitial lung disease, fatigue, depression, and cardiovascular disease may develop, contributing to increased mortality.

The goal of treatment is to achieve and maintain remission or low disease activity by initiating early disease-modifying anti-rheumatic drug (DMARD) therapy during the course of the disease. Traditional synthetic DMARDs (csDMARDs), primarily methotrexate (MTX), with or without low-dose glucocorticoids, have long been the cornerstone of treatment. Updated management guidelines from the European League Against

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Rheumatism (EULAR) recommend the addition of biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) to csDMARD therapy (1).

Janus kinases (JAKs) are key enzymes in the signaling pathways of numerous surface cytokine receptors, including those involved in inflammatory physiology. Janus kinase inhibitors (JAKi), a novel class of drugs, are small molecules designed for targeted therapy with rapid onset of action. Baricitinib, an oral selective inhibitor within the JAK family of protein tyrosine kinases, exhibits high potency and selectivity for JAK1 and JAK2. JAK enzymes phosphorylate and activate signal transducers and transcription activators (STATs) within the cell, modulating gene expression. Baricitinib acts by blocking cytokine signaling associated with RA through the JAK-STAT pathway, thereby reducing inflammation, cellular activation, and proliferation of key immune cells (2). Baricitinib is the first drug approved for treating RA in the JAKi class. As a selective inhibitor of JAK1 and JAK2, it modulates the signaling of various cytokines involved in the immune-inflammatory response. It has been approved for the treatment of moderately to severely active RA in adults in more than 40 countries, including European countries and the United States. Baricitinib has demonstrated efficacy in clinical trials encompassing all clinically relevant RA patient populations: those not using MTX, inadequate responders to MTX (MTX-IR), and inadequate responders to bDMARDs (3).

The primary objective of this study was to evaluate the real-life effectiveness of baricitinib treatment in patients with RA. Secondary objectives include assessing the impact of gender and positivity for markers such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), as well as evaluating the influence of concomitant use of DMARDs on drug persistence.

MATERIAL AND METHODS

Study Population

Between September 01, 2021, and September 01, 2023, patients diagnosed with RA who sought treatment at the Rheumatology Outpatient Clinic of Necmettin Erbakan University Meram Medical Faculty Hospital and were prescribed baricitinib were retrospectively screened. Ninety patients aged 18 years or older were included in the study. Participants had a history of prior treatment with cDMARDs and/or bDMARDs. Patients with additional inflammatory diseases, liver diseases, end-stage kidney disease, diabetic nephropathy, other autoimmune diseases, active infections, recent blood transfusions, or a history of anemia were excluded from the study. The study was approved by the Pharmaceutical and Non-Medical Device Research Ethics Committee (2023/4583).

Demographics and Clinical Data

Patients were diagnosed with RA on the basis of the 2010 American College of Rheumatology/EULAR criteria. The RF and anti-CCP results for all patients are available in the system. Initial and 12-week post-treatment C-reactive protein (CRP) values, as well as Disease Activity Score with 28 Joint Counts (DAS-28)/CRP values, were extracted by reviewing the records. These parameters were systematically analyzed to assess the inflammatory response and disease activity in patients with RA before and after a 12-week treatment period.

Statistical Analysis

Data analysis was performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). A p value <0.05 was considered statistically significant. The Kolmogorov-Smirnov test was used to assess the normality of the variables. All continuous data showed a nonnormal distribution. Results were expressed as mean (standard deviation) for continuous variables and as numbers and percentages for categorical variables. Pearson's chi-square test, Fisher's exact test, and Mann-Whitney U test were used for the comparison of findings between the two groups. Intra-group assessments were conducted using the Wilcoxon signed-rank test.

RESULTS

Ninety patients diagnosed with RA using baricitinib were included in the study. The demographic data of the patients are presented in Table 1. The rates of positive detection of RF and anti-CCP in our patients were 54 (60%) and 52 (57.8%), respectively.

A significant difference was found between the initial CRP values and the CRP values in the 12th week after the use of baricitinib in the patients included in the study ($p<0.01$). Additionally, the DAS-28/CRP values, which were 4.71 at the beginning, were found to be 2.42 at the end of the 12-week follow-up ($p<0.01$).

Table 1. Demographic data of patients treated with baricitinib

Variables	Values
Age (year old)	47.1 (±8.8)
Female gender, n (%)	95 (94.0)
RF, n (%) Negative Positive	 36 (40) 54 (60)
Anti-CCP, n (%) Negative Positive	 26 (28.9) 52 (57.8)

RF: Rheumatoid factor, Anti-CCP: Anti-cyclic citrullinated peptide

Out of the 90 patients who initiated baricitinib, treatment is ongoing for 74, while 16 have undergone a medication change due to ineffectiveness; no side effects necessitating discontinuation were observed. At the end of the 9.37-month duration of baricitinib use, the medication continuation rate was 82%.

When comparing patients using only conventional synthetic DMARDs (csDMARDs) and those using both bDMARDs and csDMARDs regarding medication continuation, no significant difference was found (p=0.951). Furthermore, when comparing patients based on the positivity or negativity of RF and anti-CCP for medication continuation, no significant difference was observed (p=0.564). See Table 2 for details.

DISCUSSION

In our study, we observed a significant reduction in CRP and DAS-28 levels in patients using baricitinib during the 12-week follow-up. Our retrospective study revealed that patients had prior experience with csDMARDs or bDMARDs. When comparing patients who had previously used both bDMARDs and csDMARDs with those who had only used csDMARDs, we did not find a significant difference in the continuation rates of baricitinib treatment.

Upon reviewing the literature, we encountered a study conducted by Yang et al. (2) in China, which included 231 patients with a mean age of 48.2 years, all of whom had previously used csDMARDs. This study focused on patients with moderate to severe active RA who showed resistance to MTX treatment. The DAS28-hsCRP values from baseline to weeks 12 and 24 demonstrated significant improvement with baricitinib treatment compared with the placebo group (2). In Takahashi et al. (4) involving 113 patients, a substantial decrease in the mean DAS28-CRP values was observed. Additionally, in the study conducted by Wu et al. (5), it was observed that 52.4% of patients achieved DAS28-CRP remission at 24 weeks. The results regarding the efficacy of baricitinib in these studies were similar to our findings.

In comparison with previous studies, Takahashi et al. (4) and Baldi et al. (6) reported continuation rates for baricitinib over 24 weeks as 86.5% and 69.3%, respectively (4,5). Additionally, Alten et al. (7) esreported a medication continuation rate of 87.6% during the 24-week follow-up, while Takagi et al. (8) and co-authors reported it as 73.35%, and Deprez et al. (9) and the team documented a baricitinib retention rate of 67% over the course of 54 weeks. In our study, the continuation rate for baricitinib use after an average of 9.37 months was found to be 82%. This rate is notably consistent with findings from other studies.

Upon reviewing the literature, Baldi et al. (6) conducted a study where they found no significant difference in the continuation of baricitinib treatment based on RF and/or anti-CCP positivity or negativity. Similarly, in our study, there was no significant relationship between the continuation of treatment and the seropositivity or seronegativity of patients, aligning with the findings of Baldi et al. (6).

In the study conducted by Baldi et al. (6), they observed that while the improvement in disease activity was greater in the group that had previously used only conventional csDMARDs, baricitinib was still effective in patients who had previously used bDMARDs. However, the analyses revealed that in patients with a history of bDMARD treatment, this situation was associated with a higher risk of treatment discontinuation (9). In contrast, our study did not reveal any significant differences.

Given the potential increased risk of serious cardiac events (e.g., myocardial infarction, stroke, venous thromboembolism, pulmonary embolism) associated with baricitinib, the Food and Drug Administration recommends conducting a thorough risk-benefit assessment for patients before initiating or continuing treatment (9). Similarly, the European Medicines Agency advises against the use of JAK inhibitors in patients with a high risk of major cardiovascular problems or those with a history of significant tobacco use unless there are suitable alternative treatments available (6).

Table 2. Factors affecting the continuation of baricitinib treatment

Variables	Medication usage continues	Medication has been changed	p
Previously administered medications Using csDMARD Using bDMARDs and/or csDMARDs	 41 (%55.4) 33 (44.6)	 9 (%56.3) 7 (%43.8)	**0.951***
Serology positivity Serology negativity	48 (%64.9) 26 (%35.1)	12 (75.0) 4 (25.0)	**0.564****

*Pearson chi-square, **Fisher's exact test, csDMARD: Conventional synthetic disease-modifying antirheumatic drug, bDMARD: Biologic disease-modifying antirheumatic drug

In our study, the average age of patients was 47.18 years,reflecting a preference for treatment in younger patients due to the increased risk of cardiovascular diseases and thromboembolism in older individuals. The limited number of patients and the retrospective nature of the study with an average follow-up of 9.37 months may have contributed to the absence of observed side effects necessitating the discontinuation of baricitinib. Treatment changes in our study were primarily driven by ineffectiveness rather than safety concerns. In our study, 82% of patients treated with baricitinib continued the treatment, indicating that eighteen percent of patients did not continue with the treatment. In the study conducted by Alten et al. (7), the discontinuation rate of baricitinib due to inadequate efficacy at 6 months was 12.4%. Similarly, in Takagi et al. (8), this rate was 10.10%, aligning with our findings.

Study Limitations

A significant limitation of our study is the short follow-up period, which consequently resulted in a limited number of patients. However, the study's major strength lies in presenting the efficacy of baricitinib treatment based on real-life data. This provides valuable insights into the clinical applicability and effectiveness of the treatment.

Although the efficacy of baricitinib has been demonstrated in patients who have previously used csDMARDs and/or bDMARDs, further research with additional analyses and larger patient groups is required to comprehensively assess side effects.

CONCLUSION

As a conclusion, this study underscores that the utilization of baricitinib constitutes an efficacious and secure alternative in the management of rheumatoid arthritis.

Ethics

Ethics Committee Approval: The study was approved by the Pharmaceutical and Non-Medical Device Research Ethics Committee (2023/4583).

Informed Consent: Retrospective study.

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