EDITORIAL

The news is clear: real-life studies show the actual effectiveness of treatment

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by Batko et al

Rheumatoid arthritis (RA) is a chronic rheumatic disease that affects approximately 0.5%–1% of the adult population. It leads to functional disability, affects many organs, worsens the quality of life, and increases the risk of premature death.[1] The disease and its treatment are associated with high medical and social costs. So far, the etiopathogenesis of RA has not been fully elucidated[2] and a complete cure of the disease is still not achievable.[3]

However, significant progress has been made in pharmacological treatment. A number of potent biological disease-modifying antirheumatic drugs (bDMARDs), mainly cytokine blockers, have been introduced in addition to conventional disease-modifying drugs (csDMARDs), such as methotrexate (Mtx), leflunomide, sulfosalazine, or hydroxychloroquine. Furthermore, in the last 5 years targeted synthetic DMARDs (tsDMARDs) that are Janus kinase inhibitors have become available.[3,4] Glucocorticosteroids and symptomatic drugs, mainly non-steroidal anti-inflammatory drugs, are used frequently all the time. The current management recommendations reflect the balance of clinical efficacy, safety, and costs of treatment, and indicate remission or low disease activity as the treatment target (treat to target strategy [T2T]).[5,6] So far, this has not been an easy goal to achieve. Moreover, the remission in RA can be defined in various ways.[7] In daily routine, remissions are usually defined by disease activity scores, such as disease activity score using 28 joint count (DAS 28), Clinical Disease Activity Index (CDAI), Simple Disease Activity Index, and less frequently by the Boolean-based European League Against Rheumatism / American College of Rheumatology criteria.[5,7] The most beneficial and difficult to achieve is sustained drug-free remission, lasting at least 6 months without progressive joint destruction.[8]

We currently use a group of drugs with different mechanisms of action and follow the evidence-based recommendations for therapeutic management,[5,6] but do we achieve the assumed therapeutic goals in everyday practice in a given country?

Randomized clinical trials (RCTs) of consecutive bDMARDs and tsDMARDs with Mtx as a comparator, conducted in carefully selected groups of RA patients indicated the possibility of achieving remission in the Mtx monotherapy group in an average of about 28% (7.6%–50%) of patients after 24–26 weeks, while bDMARDs and tsDMARDs induced the remission in about 40% to 60% of patients.[9] Patient selection criteria, concomitant medication, remission definitions (DAS 28 ≤2.6, CDAI ≤2.8, etc.), and other factors in RCTs are different and the comparison of results is often questionable. A better analysis of the effectiveness and safety of treatment is provided by large, comprehensive national registers,[4,8] which mainly concern groups of patients receiving second-line therapies with expensive bDMARDs and tsDMARDs, while data on the effectiveness of treatment of most RA patients with commonly used csDMARDs in the real world are rather limited or derived from older studies.[9-11]

In this issue of *Polish Archives of Internal Medicine*, Batko et al[12] present a prospective observational study evaluating the actual effectiveness of treatment with csDMARDs in routine RA care conducted by 82 rheumatologists in Poland. The rates of low disease activity and remission achieved at 3 and 6 months in a cohort of 780 outpatients with RA were assessed. The authors, however, did not investigate the efficacy of individual DMARDs. Their aim was to identify potential clinical and demographic predictors conducive to achieving the therapeutic target, that is, DAS 28 below or equal to 3.2. It turned out that after 3 months of treatment, 9% of the patients achieved remission or low disease activity, and

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after 6 months either of these were achieved in 35% of patients. Compared with other reports, the rate of adequate disease control was shown to be low.[12]

The negative effects of undoubtedly important factors reported by Batko et al,[12] such as smoking or BMI above 25 kg/m^2 on achieving the therapeutic target do not appear to sufficiently explain why 65% of the patients did not achieve the T2T goals. When delving into the analysis of the causes of the treatment failure, it seems most desirable to investigate the impact of the missing factors, such as the dosage and route of Mtx administration (because underuse of Mtx at doses below 15 mg/week is quite common)[13], and the dosing of other csDMARDs, presence of early erosions, comedication, and comorbidities, that is, an important factor in daily practice, almost eliminated in drug RCTs.[14,15] It is also unclear if any treatment-naive patients were enrolled by Batko et al.[12] It could have mattered because "a percentage of patients fails one or more DMARDs, before achieving remission."[3] It would also be worth answering the question whether all of the 82 rheumatologists participating in the study followed the current recommendations and the T2T strategy,[5] and whether the patient compliance was sufficient. Finding the right answers to these questions is essential, because in many countries, as in Poland, the overwhelming majority of RA patients are treated with csDMARDs only, and access to bDMARDs and tsDMARDs is very limited.

Real-life studies assessing the effectiveness of treatment of this chronic rheumatic disease are highly desirable, and the work of Batko et al[12] provides valuable information and corroborates investigations seeking ways to definitely improve the outcomes of our current therapy for RA. Undoubtedly, the implementation of the T2T strategy in daily care is crucial. There is also a hope that much better access to bDMARDs and tsDMARDs for RA patients, the adoption of personalized medicine principles in our daily routine, and possibly the implementation of machine learning prediction models in the future may change our treatment outcomes.[3]

ARTICLE INFORMATION

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REFERENCES

1 Uhlig T, Moe RH, Kvien TK. The burden of disease in rheumatoid arthritis. Pharmacoeconomics. 2014; 32: 841-851.

2 McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011; 365: 2205-2219.

3 Graffoni C, Adinolfi A, Bortoluzzi A, et al. Novel insights into the management of rheumatoid arthritis: one year in review 2022. Clin Exp Rheumatol. 2022; 40: 1247-1257.

4 Lauper K, Iudici M, Mongin D. Effectiveness of TNF-inhibitors, abatacept, IL6-inhibitors and JAK-inhibitors in 31 846 patients with rheumatoid arthritis in 19 registers from the JAK-pot collaboration. Ann Rheum Dis. 2022 Jun 15. [Epub ahead of print]

5 Smolen JS, Landewé RBM, Bijlsma JWJ, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis. 2020; 79: 685-699.

6 Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2021; 73: 924-939.

7 Felson DT, Smolen JS, Wells G. et al. American College of Rheumatology/European League Against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. Arthritis Rheum. 2011; 63: 573-586.

8 Einarsson JT, Minna Willim M, Ernestam S, et al. Prevalence of sustained remission in rheumatoid arthritis: impact of criteria sets and disease duration, a nationwide study in Sweden. Rheumatology (Oxford). 2019; 58: 227-236.

9 Chatzidionysiou K, Sfikakis PP. Low rates of remission with methotrexate monotherapy in rheumatoid arthritis: review of randomised controlled trials could point towards a paradigm shift. RMD Open. 2019; 5: e000993.

10 Emery P, Breedveld FC, Lemmel EM, et al. A comparison of the efficacy and safety of leflunomide and methotrexate for the treatment of rheumatoid arthritis. Rheumatology (Oxford). 2000; 39: 655-665.

11 Braun J, Kastner P, Flaxenberg P, et al. Comparison of the clinical efficacy and safety of subcutaneous versus oral administration of methotrexate in patients with active rheumatoid arthritis: results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. Arthritis Rheum. 2008; 58: 73-81

12 Batko B, Jeka S, Wiland P, et al. Deep dive into achieving the therapeutic target: results from a prospective, 6-month, observational study nested in routine rheumatoid arthritis care. Pol Arch Intern Med. 2022; 132: 16244.

13 Rohr MK, Mikuls TR, Cohen SB, et al. Underuse of methotrexate in the treatment of rheumatoid arthritis: a national analysis of prescribing practices in the US. Arthritis Care Res (Hoboken). 2017; 69: 794-800.

14 Aletaha D, Dörner T. Considering comorbidity in managing rheumatic diseases: going where trials cannot go. Arthritis Res Ther. 2011; 13: 116.

15 Thomas K, Lazarini A, Kaltsonoudis E. Treatment patterns and achievement of the treat-to-target goals in a real-life rheumatoid arthritis patient cohort: data from 1317 patients. Ther Adv Musculosceletal Dis. 2020; 12: 1759720X20937132.