Revista Română de Reumatologie
Romanian Journal of Rheumatology

ORIGINAL PAPER

Treatment of Axial Spondyloarthritis Patients with Biologic and Targeted Disease-Modifying Anti-Rheumatic Drugs in 2024 - Data from the Romanian Registry of Rheumatic Diseases

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Abstract

Objective: to describe the demographic, clinical, and treatment characteristics, as well as short-term outcomes, of patients with axial spondyloarthritis (axSpA) receiving biologic or targeted synthetic DMARDs (b/tsDMARDs) in Romania during 2024, using data from the Romanian Registry of Rheumatic Diseases (RRBR).

Methods. We performed a cross-sectional analysis of RRBR data from January to December 2024, including all patients with finalized visits. Demographics, disease phenotype, comorbidities, treatment patterns, and disease activity measures (BASDAI, ASDAS) were described. Outcomes at 6 months were evaluated for treatment initiations, continuations, and switches.

Results. Of 5,055 patients (73.5% male; mean age 49.2 years; 89.2% HLA-B27 positive), 11.8% had non-radiographic axSpA. Comorbidities were common, including hypertension (22.5%) and obesity (23.6%). TNF inhibitors predominated as first-line agents (85%), with IL-17 and JAK inhibitors more frequent in later lines. Biosimilars accounted for the majority of adalimumab, etanercept, and infliximab use; 173 non-medical switches occurred. Tapered dosing was reported in 9% of patients. At 6 months, initiations showed marked improvement (ΔBASDAI = -5.04; ΔASDAS = -2.55), while continuations and switches had smaller gains. Non-smokers and patients with ≤ 1 comorbidity had significantly lower ASDAS values. Radiographic axSpA was associated with older age, male predominance, longer disease duration, higher HLA-B27 frequency, and slightly higher CRP, but similar current ASDAS.

Conclusions. In Romanian clinical practice, TNF inhibitors remain the dominant first-line b/tsDMARDs, with increasing IL-17 and JAK inhibitor use in later lines. High biosimilar uptake and frequent switching are observed. Most patients achieve low disease activity, with lifestyle factors and comorbidity burden influencing outcomes.

Keywords:. axial spondyloarthritis; biologic DMARDs (bDMARDs); targeted synthetic DMARDs (tsDMARDs); real-world registry data Romania; Rheumatic diseases registry outcomes.

Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic condition predominantly affecting the spine and sacroiliac joints, typically manifesting as chronic back pain before the age of 45 years. The disease encompasses both non-radiographic axSpA and ankylosing spondylitis (AS), and is frequently accompanied by enthesitis, dactylitis, uveitis, psoriasis, and inflammatory bowel disease.

Across Europe, several national registries systematically collect longitudinal data on patients with axSpA receiving advanced therapies [1], such as such as the German RABBIT-SpA, the Danish DANBIO, the Swedish ARTIS, the Spanish BIOBADASER, and the British BSRBR-RA/BSRBR-AS. These registries serve as invaluable tools for real-world evidence generation, enabling monitoring of treatment effectiveness, safety, and persistence, as well as evaluation of comorbidities and healthcare resource use. They also facilitate comparative effectiveness studies across biologic and targeted synthetic disease-modifying anti-rheumatic drugs (bDMARDs and tsDMARDs), support pharmacovigilance, and inform updates to clinical guidelines and reimbursement policies. Looking forward, the integration of registry data with electronic health records, patient-reported outcomes, and genomic or imaging datasets is expected to expand

their scope, enhance predictive modelling, and enable personalized treatment strategies in axSpA.

To better understand real-world treatment patterns, safety, and outcomes in Romania, the Romanian Registry of Rheumatic Diseases (RRBR) was established. Originally launched in 2013 for rheumatoid arthritis, the registry expanded in 2015 to include patients with axSpA treated with reimbursed bDMARDs. RRBR mandates routine data collection (every six months) on demographics, clinical features, treatment regimens, efficacy, and adverse events, thereby offering a national prospective observational cohort. Analyses of earlier RRBR data from 2022 revealed important trends [2]: most patients (88%) were treated with tumor necrosis factor inhibitors (TNFi), usually in monotherapy; the most frequently prescribed bDMARDs were adalimumab (36%), etanercept (32%) and secukinumab (12%); the uptake of biosimilars reached one third of patients on molecules with available biosimilars. However, since this earlier report, the therapeutic landscape has evolved. The integration of newer b/tsDMARDs, as well as the adaptation of reimbursement protocols, may have shifted prescribing trends, treatment efficacy, and safety profiles. Despite these anticipated changes, updated data on axSpA management in Romania has not yet been published.

In this context, this article aims to bridge that gap by presenting the latest evidence from RRBR on the real-world use of bDMARDs and tsDMARDs in Romanian axSpA patients during 2024, ultimately seeking to enhance understanding of current clinical practice and inform future management approaches in axSpA care across Romania.

Methods

RRBR structure

RRBR functions as a secure, online platform accessible to rheumatologists nationwide. Participating physicians enter patient information at baseline (treatment initiation) and at mandatory follow-up visits every 6 months. The recorded variables include: demographics (age, sex, residence, education level), disease characteristics (onset, diagnosis, disease duration), laboratory parameters (CRP - C-reactive protein; erythrocyte sedimentation rate - ESR; HLA-B27 status); imaging findings (X-ray; magnetic resonance imaging - MRI), comorbidities (chronic infections, tuberculosis, hypertension, ischemic heart disease, chronic heart failure, diabetes mellitus, dyslipidemia, peripheral vascular diseases, stroke, Parkinson's disease, demyelinating diseases, epilepsy, gastroduodenal ulcer, liver disease, inflammatory bowel disease, psoriasis, kidney disease, neoplasia, hematological disorders, osteoporosis, fibromyalgia, mental illness, thyroid dysfunction, alcoholism), current and prior treatments (conventional synthetic DMARDs; b/tsDMARDs; glucocorticoids; nonsteroidal anti-inflammatory drugs - NSAIDs), efficacy measures (activity scores such as BASDAI, ASDAS) and safety data (adverse events). RRBR is overseen by the Romanian Society of Rheumatology and complies with national data protection regulations. Data entry is mandatory for all patients receiving reimbursed advanced therapies, ensuring near-complete national coverage. In 2024, patients fulfilling the initiation criteria could have received any of the following: adalimumab (original and biosimilar), certolizumab, etanercept (original and biosimilar), golimumab, infliximab (original and biosimilar), secukinumab, ixekizumab and upadacitinib.

RRBR criteria for inclusion and exclusion

RRBR encompasses all patients with axSpA or AS who are initiated on reimbursed b/tsDMARDs because of persistent active disease despite traditional therapies, or who continue b/tsDMARD treatment which was initiated from a non-reimbursed source (e.g. clinical study, initiation in a different healthcare system). Case definition relies on the axSpA classification criteria [3] or AS modified New York classification criteria [4]. Active disease is defined by two criteria: the first, BASDAI of 6 or above on two successive assessments separated by at least 4 weeks or ASDAS of 2.1 or above; the second, the presence of objective signs of inflammation, meaning either ESR above 28 mm/h or CRP above 3 times the upper limit of normal or sacroiliac MRI with bone edema. This current severity criterion allows therefore inclusion of patients with normal CRP and MRI-defined sacroiliac edema, which was not possible in 2022. The presence of hip joint damage and extra-articular manifestations are additional severity factors that allow b/tsDMARD initiation at lower disease activity scores (BASDAI above 4 or ASDAS above 1.3). Failure of traditional therapies is defined by three criteria: first, the use of at least two NSAIDs administered continuously, with a total duration of at least 4 weeks, at maximum recommended or tolerated doses; second, failure of sulfasalazine for peripheral manifestations (administration for at least 4 months of maximum/tolerated doses, usually 2-3 g/day); third, ineffective response to at least one administration of glucocorticoid injection at the affected site in peripheral arthritis and/or active enthesitis, if indicated. Exclusion criteria rely on b/tsDMARD contraindications as per summary of product characteristics, withdrawal of the patient's informed consent or loss of insured status.

RRBR treatment decisions

The therapeutic target is ASDAS < 2.1, or, if this is not achievable, the secondary goal is to maintain the lowest possible disease activity to prevent structural damage, preserve function, and maintain quality of life [5]. Treatment is continued if the patient is a responder, registering a reduction in the ASDAS score

≥ 1.1 compared to the initial evaluation. If there is no such therapeutic response, a switch of b/tsDMARD is recommended. Patients with severe disease (presence of structural changes, ossification or involvement of the hip joints or extra-articular manifestations) may continue treatment even if the ASDAS is above 2.1, provided that they have shown a reduction in the ASDAS score ≥ 1.1 compared to the initial assessment. Patients who have shown a therapeutic response but subsequently register an increase in disease activity, exceeding the ASDAS threshold of 2.1, but not more than 2.5, can continue the treatment for another 24 weeks with subsequent reassessment and reclassification in the responder or non-responder state. Patients who do not meet these efficacy criteria and patients experiencing adverse events are switched on to any other b/tsDMARD, original or biosimilar. It is recommended that, in patients with persistent inactive disease, with an ASDAS of 1.3 or bellow and with normal ESR and CRP values at two successive evaluations at least 6 months apart, b/tsDMARDs should be gradually tapered by increasing the time interval between administrations. Returning at any time to the initial regimen in the event of a flare of the disease is possible.

Statistics

Data distribution normality was assessed using descriptive statistics, normality, stem-and-leaf plots, and the Lilliefors corrected Kolmogorov-Smirnov tests. Continuous variables are reported as "mean ± standard deviation (SD)" if normally distributed, or as "median (first quartile - third quartile)" if non-normally distributed. Nominal variables are reported as "percentage of sub/group". The differences of continuous variable averages among categories of nominal variables were evaluated with t tests for dichotomous groups and with one-way ANOVA for multiple groups. The associations between categorical variables were studied using $\chi 2$ tests. The statistical tests were considered significant if $p < 0.05$. For the purpose of graphic representation, outliers were identified using boxplot criteria and extreme outliers (values outside 3 times the interquartile range) were excluded from the plotted dataset by filtering, without altering the underlying analytical dataset. The statistical analysis was performed using IBM SPSS Statistics version 25.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Demographics

Between 2022 and 2024, the number of patients with finalized visits rose from 4,315 to 5,055, representing a 17.1% increase. The study population was predominantly male (73.5%), with a mean age of 49.2 ± 12.2 years. Most participants resided in urban areas (68.5%), and 34.4% had completed college education. At the time of data collection, 69.0% were employed. Current smoking was reported by 14.6% of patients, and the mean body mass index was 27.0 ± 4.9 kg/m².

Disease phenotype and clinical characteristics

Regarding disease phenotype, non-radiographic axSpA accounted for 11.8% of cases. The mean disease duration to 2024 was 13.5 ± 9.6 years, with a median time from diagnosis to b/tsDMARD initiation of 3.0 (1.0-10.0) years. HLA-B27 presence was observed in 89.2% of patients. Extra-articular manifestations included eye involvement in 19.5%, pulmonary in 4.5%, gastrointestinal in 3.3%, psoriasis in 2.7%, and cardiac in 1.7% of cases.

Comorbidities were frequent in the study population, with arterial hypertension reported in 22.5%, other cardiovascular disease in 10.9%, dyslipidemia in 16.4%, and obesity in 23.6% of patients. Liver disease was present in 11.4%, kidney disease in 5.9%, and hematologic disease in 5.8%. Diabetes mellitus affected 7.6%, osteoporosis 4.9%, and thyroid disease 3.6% of cases. Inflammatory bowel disease was documented in 2.0%, and other gastrointestinal diseases in 10.9%. Cancer was reported in 0.9% of cases. Infectious risk screening revealed a positive QuantiFERON test in 26.3%, HBs antigen positivity in 2.1%, and anti-HCV antibodies in 1.0%. Vaccination coverage was 28.4% for anti-SARS-CoV-2, 4.3% for influenza, 1.4% for hepatitis B, 0.3% for pneumococcus, and 0% for herpes zoster.

Treatment outline and patterns

Most patients (79.5%) received b/tsDMARD monotherapy. Among the 1,034 patients on combination therapy with a csDMARDs, sulfasalazine was used in 86.7% of cases, methotrexate in 16.8%, and the combination of sulfasalazine and methotrexate in 3.5%. Oral glucocorticoids were administered in 0.9% of patients, while local glucocorticoid injections were reported in 7.1%.

Regarding molecule prevalence in the whole sample (n = 5055), the most frequently used agent was adalimumab (37.9% of patients), with biosimilars accounting for 59.5% of adalimumab use. Etanercept was used by 27.6% of patients, 49.1% of whom received a biosimilar, while infliximab was used by 5.2% of patients, with biosimilars representing 85.5% of infliximab indications. Other treatments included golimumab (4.8%), certolizumab (4.9%), secukinumab (13.2%), ixekizumab (2.7%), and upadacitinib (3.5%). Only 0.2% of patients were not receiving any b/tsDMARD therapy. In terms of treatment exposure, 54.5% of patients had received only one b/tsDMARD, 27.5% had been treated with two, 11.3% with three, 3.8% with four, 1.5% with five, and 1.3% with more than five different b/tsDMARDs during their treatment history.

In 2024, there were 593 treatment initiations on b/tsDMARDs, representing 11.7% of all patients with finalized visits. The most frequently initiated therapy

was adalimumab (51.8% of initiations), with only 3.9% of these on the originator product. Other agents included etanercept (14.5%; 9.3% originator), secukinumab (14.2%), upadacitinib (7.3%), ixekizumab (5.1%), certolizumab (4.7%), infliximab (2.4%; all biosimilar), and golimumab (0.2%). Of all initiations, 37.8% were based on the updated protocol criterion of sacroiliac joint bone marrow edema on MRI in the context of low/normal acute-phase reactants.

There were 3,690 treatment continuations recorded in 2024. The most common ongoing therapy was adalimumab (37.9% of continuations), with 52.5% of these on the originator product. Etanercept accounted for 31.5% of continuations (58.3% originator), followed by secukinumab (13.4%), golimumab (6.0%), certolizumab (5.0%), infliximab (4.2%; 23.9% originator), ixekizumab (1.2%), and upadacitinib (0.8%).

In total, 687 simple treatment switches were recorded, representing 13.6% of all visits. The main reasons for switching were primary non-response (15%), secondary non-response (38%), adverse events (8%), and other causes (40%). In addition, there were 73 multiple switches and 173 non-medical switches from originator products to biosimilars.

Across all treatment lines, TNF inhibitors remained the predominant therapeutic class, accounting for 85% of first-line, 81% of second-line, 66% of third-line, 64% of fourth-line, 53% of fifth-line, and 93% of sixth-line regimens. IL-17 inhibitors were the next most frequently used (13%, 17%, 26%, 27%, 25%, and 21% across the respective lines), followed by JAK inhibitors (2%, 1%, 7%, 11%, 22%, and 21% respectively).

On January 1st 2024, 474 patients (9.4% of sample) were on a tapered treatment regimen. Among them, etanercept accounted for 44.7% of patients, adalimumab for 42.4%, infliximab for 7.8%, golimumab for 2.5%, certolizumab for 1.7%, and secukinumab for 0.8%. By December 31st 2024, 459 patients (9.1%) remained on tapered exposure: etanercept in 48.1% of cases, adalimumab in 38.8%, infliximab in 5.0%, golimumab and certolizumab in 3.1% each, and secukinumab in 2.0% of cases). During 2024, 23 patients reverted from a tapered regimen to standard dosing of their bDMARD.

Treatment efficacy

Among 180 treatment initiations with complete data at the 6-month visit and without treatment switch, the mean BASDAI decreased from 7.14 at initiation to 2.10 at 6 months (Δ = –5.04), while the mean ASDAS declined from 4.46 to 1.91 (Δ = –2.55).

For the 3,690 treatment continuations, mean BASDAI changed minimally from 1.49 at the preceding 6-month visit to 1.40 at the current visit, and mean ASDAS from 1.54 to 1.51. Among these continuations, 51.5% of patients had BASDAI ≤ 1, 38.9% had BASDAI between > 1 and ≤ 3, 4.9% between > 3 and ≤ 4, and 4.7% > 4. For ASDAS, 46.1% had values < 1.3, 38.2% between 1.3 and < 2.1, 14.0% between 2.1 and < 3.5, and 1.7% ≥ 3.5. Patients with more than five previous b/tsDMARD had significantly higher mean ASDAS values (Figure 1). Non-smokers had a lower mean ASDAS than smokers (1.50 ± 0.70 vs 1.58 ± 0.70, p = 0.022; Figure 2). Patients with one or no comorbidities had lower mean ASDAS (1.47 ± 0.46 vs 1.59 ± 0.67, p < 0.001) and BASDAI (1.38 ± 1.35 vs 1.48 ± 1.30, p = 0.035) compared with those with two or more comorbidities (Figure 3). There were no significant differences of activity scores (ASDAS, BASDAI) and sex, BMI, age, disease duration and HLA-B27 presence.

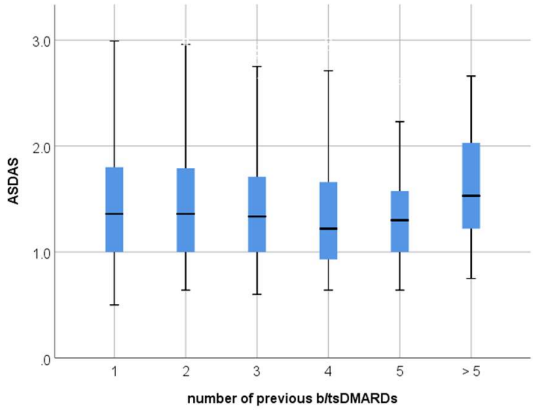

Figure 1. *Mean values of ASDAS according to the number of previous b/tsDMARD among patients continuing their treatment (n = 3690; ANOVA; p = 0.046)*

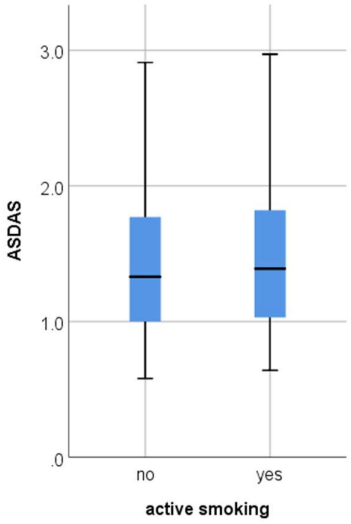

Figure 2. *Mean values of ASDAS among active smokers and non-smokers in patients continuing their treatment (n = 3690; t test; p = 0.022).*

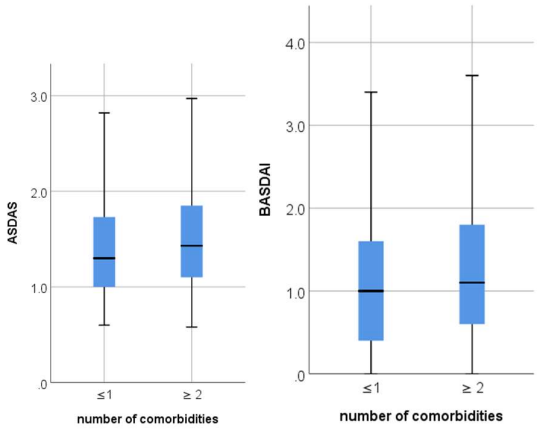

Figure 3. *Mean values of ASDAS (left) and BASDAI (right) among patients with up to one comorbidity and patients with 2 and more comorbidities in patients continuing their treatment (n = 3690; t test; p < 0.001 for ASDAS and p = 0.035 for BASDAI).*

Among the 273 switch cases with complete data at 6 months, the mean BASDAI decreased from 3.65 at the time of switch to 1.84 at 6 months (Δ = –1.81), while the mean ASDAS decreased from 2.68 to 1.78 (Δ = –0.90).

Radiographic versus non-radiographic axSpA

Compared with patients with radiographic axSpA (Table 1), those with non-radiographic axSpA were younger (42.8 vs 49.9 years, p < 0.001), less frequently male (62.7% vs 75.0%, p < 0.001), and had a lower BMI (26.3 vs 27.3 kg/m², p < 0.001). Disease duration was significantly shorter in nr-axSpA, both from diagnosis to 2024 (7.7 vs 14.2 years, p < 0.001) and from diagnosis to b/tsDMARD initiation (3.6 vs 7.4 years, p < 0.001). HLA-B27 was more frequent in r-axSpA (90.3% vs 81.4%, p < 0.001). Baseline disease activity scores were slightly higher in r-axSpA for BASDAI (7.1 vs 7.0, p = 0.032) and ASDAS (4.6 vs 4.4, p < 0.001). Current BASDAI remained higher in nr-axSpA (2.8 vs 2.4, p = 0.013), while current ASDAS was similar between groups (p = 0.735). CRP was modestly higher in r-axSpA (9.4 vs 8.4 mg/L, p = 0.008), with no difference in ESR (p = 0.120).

Table 1. Comparison of demographics and efficacy measures between nr-axSpA and r-axSpA.

	nr-axSpA (n = 595)	**r-axSpA** (n = 4460)	p
men	62.7%	75.0%	< 0.001
smoking	16.6%	19.6%	0.050
age (y)	42.8 ± 11.9	49.9 ± 11.8	< 0.001
BMI (kg/m^2)	26.3 ± 4.7	27.3 ± 5.0	< 0.001
axSpA duration up to 2024 (y)	7.7 ± 6.0	14.2 ± 9.2	< 0.001
axSpA duration until initiation (y)	3.6 ± 1.0	7.4 ± 4.0	< 0.001
HLA-B27	81.4%	90.3%	< 0.001
initial BASDAI	7.0 ± 1.1	7.1 ± 1.2	0.032
current BASDAI	2.8 ± 2.5	2.4 ± 2.0	0.013
initial ASDAS	4.4 ± 0.7	4.6 ± 0.7	< 0.001
current ASDAS	2.1 ± 1.3	2.0 ± 1.2	0.735
ESR (mm/h)	20 ± 19	20 ± 18	0.120
CRP (mg/L)	8.4 ± 3.0	9.4 ± 4.0	0.008

ASDAS – Ankylosing Spondylitis Disease Activity Score; axSpA – axial spondyloarthritis; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; BMI – body mass index; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; HLA – human leukocyte antigen; n/r-axSpA – non/radiographic axSpA; y – years.

Discussions

In summary, analysis of 5,055 patients from RRBR with axSpA revealed a predominantly male cohort, with middle-aged, urban, and HLA-B27-positive patients, with substantial comorbidity burden. TNF inhibitors remained the most common therapy across all treatment lines, though IL-17 and JAK inhibitors gained use in later lines. Most patients achieved and maintained low disease activity, with greater improvements observed in treatment initiations than continuations or switches. Lower ASDAS values were associated with non-smoking status and fewer comorbidities. Compared with radiographic axSpA, non-radiographic cases were younger, had shorter disease duration, less frequent HLA-B27 positivity, and higher current BASDAI despite similar ASDAS.

In Romania, b/tsDMARD access for axSpA requires BASDAI ≥ 6 on two occasions or ASDAS ≥ 2.1 plus objective inflammation (elevated ESR, CRP > 3× ULN, or MRI bone marrow edema), with limited exceptions for hip damage or extra-articular disease. This is more restrictive than ASAS-EULAR 2023 recommendations [5], which permit escalation at ASDAS ≥ 2.1 after NSAID failure, typically without repeat measurements or uniformly mandatory biomarkers. Guidelines in the UK, Spain, Italy, and Germany generally align with ASAS–EULAR, using BASDAI ≥ 4 or ASDAS thresholds, recommending but not always requiring objective inflammation, and accepting single-timepoint assessments. These frameworks are thus more permissive, potentially

enabling earlier biologic initiation. The Romanian approach may improve specificity and stewardship of reimbursement resources but risks delaying therapy for patients with high symptomatic burden yet fluctuating inflammatory markers. Harmonizing thresholds toward ASDAS-based high disease activity could align Romania with prevailing European practice while retaining evidence-based control.

In the RRBR, TNF inhibitors remained the predominant choice for first-line b/tsDMARD therapy, despite the availability of IL-17 and JAK inhibitors. This pattern aligns with European real-world data, where TNF inhibitors have historically dominated first-line use due to established efficacy, safety and clinician familiarity [6]. The increasing share of IL-17 inhibitors and, to a lesser extent, JAK inhibitors, in later treatment lines in our cohort is consistent with treatment-sequencing trends reported across European registries: secukinumab shows robust effectiveness and persistence, particularly when used earlier, and is frequently introduced after TNF inhibitor failure or intolerance [6-8]. Biosimilar uptake was high, mirroring the cost-driven adoption seen across Europe and supported by evidence that non-medical switches from originators to biosimilars maintain effectiveness and retention (e.g., national switch programs) [9-11]. Tapered dosing was documented in approximately 9% at the start and end of 2024, predominantly with TNF inhibitors, with a small proportion reverting to standard dosing; similar de-escalation strategies and outcomes have been reported in axSpA routine care [12, 13].

In our cohort, non-smokers and patients with fewer comorbidities had significantly lower current ASDAS values, which aligns with existing evidence. Studies confirmed that smoking is independently associated with higher disease activity in axSpA, even after adjusting for confounders such as age and sex [14], although conflicting reports exist [15]. Longitudinal cohort data also suggest that smoking correlates with earlier onset of inflammatory back pain, greater axial inflammation on MRI, and more severe disease activity, traits which diminish responsiveness to biologic therapies [16]. Regarding comorbidities, analysis of the BSRBR-AS registry showed that each additional comorbidity was associated with an increased ASDAS and a larger effect on patient-reported activity scores like BASDAI, though the absolute effect on ASDAS was modest [17]. More recent reports also found that multimorbidity correlates with higher BASDAI and functional impairment in axSpA populations, underscoring the broader influence of overall health burden on disease experience [18]. These observations were confirmed by systematic review and meta-analysis, which demonstrated the negative effect of overall comorbidity burden in axSpA [19]. Our findings thus reinforce the incremental negative impact of smoking and comorbidities on inflammatory activity, even when objective measures like ASDAS are relatively tightly controlled, highlighting the importance of lifestyle modification and comorbidity management within treat-to-target frameworks.

Our r-axSpA versus nr-axSpA differences mirror much of the literature. Like multiple cohorts, r-axSpA patients in RRBR were older, more often male, and had longer disease duration, while nr-axSpA skewed younger with shorter time to b/tsDMARD initiation, patterns also reported by Wallman *et al.* [20]. HLA-B27 was more frequent in r-axSpA in our data (90.3% versus 81.4%), aligning with reports that radiographic disease clusters with classical SpA features and higher objective inflammation [21, 22]. For disease activity, our current ASDAS was similar between groups while current BASDAI was slightly higher in nr-axSpA, a nuance consistent with reviews showing broadly comparable disease burden despite imaging differences and with cohort studies where group differences in activity narrow over time under treatment [23, 24]. CRP was modestly higher in r-axSpA in our registry, again in line with prior observations that radiographic disease tends to show greater inflammatory burden [20-22, 25]. Overall, RRBR findings reinforce that phenotype (radiographic vs non-radiographic) chiefly reflects age/sex and structural-damage trajectory, while on-treatment activity levels converge, supporting similar treat-to-target strategies across subtypes.

This study has several limitations. First, its observational, non-randomized design precludes establishing causal relationships between treatment and outcomes, and confounding by indication may be present. Second, the RRBR includes only patients meeting Romanian reimbursement criteria for b/tsDMARDs, which are more restrictive than in many other European countries, potentially limiting generalizability to the broader axSpA population. Laboratory and imaging assessments were performed according to local practice without central standardization. In addition, some patients began b/tsDMARD therapy outside the RRBR, introducing heterogeneity in prior treatment exposure. Finally, efficacy analyses reflect short-term outcomes, and differences in healthcare systems and treatment protocols may limit extrapolation of these findings to other settings.

Conclusions

In this national, real-world analysis from the Romanian Registry of Rheumatic Diseases (RRBR), patients with axSpA initiating or continuing b/tsDMARD therapy in 2024 achieved and maintained low disease activity in the majority of cases, with the largest improvements observed in initiations. TNF inhibitors remained the predominant first-line agents despite the availability of IL-17 and JAK inhibitors, which were more frequently prescribed in later treatment lines. Biosimilar uptake was high, and non-medical switching was common, with a small proportion of patients undergoing tapered dosing regimens. Non-smoking status and fewer

comorbidities were independently associated with lower disease activity scores, highlighting the importance of lifestyle and comorbidity management alongside pharmacologic treatment. Differences between radiographic and non-radiographic axSpA were consistent with international findings, with the groups converging in on-treatment ASDAS values. These results provide a comprehensive national benchmark for axSpA management under Romania's current therapeutic protocols and support alignment with treat-to-target strategies observed across Europe.

Conflicts of Interest: The authors declare no conflicts of interest.

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Received: 27.04.2025

Accepted: 22.06.2025