Background: Patients with rheumatoid arthritis (RA) who have received multiple biologics or targeted therapies over time tend to have more refractory and more severe disease, which may lead to worse clinical response to treatment.

Objectives: We used data from the ACR RISE registry to assess whether disease severity was greater in those who received sarilumab shortly after its FDA approval (May 2017) than in subsequent time periods and to evaluate the effectiveness of sarilumab in populations with various degrees of disease severity.

Methods: Patients with RA who initiated sarilumab treatment in the period 2017-2020 were identified in the ACR RISE registry and divided into Cohort 1 (2017, year of the FDA approval) and the calendar year-based Cohorts 2-4 (2018-2020). Patient demographics, RA-related features, and comorbidities were determined using data prior to sarilumab initiation. The cohorts were compared using chi-square test (categorical variables) and a nonparametric test (continuous variables). Sarilumab effectiveness was assessed using 3 cohorts assembled based on progressively restrictive criteria: Active Disease cohort (Clinical Disease Activity Index [CDAI] >10 or Routine Assessment of Patient Index Data 3 [RAPID3] >6, and C-reactive protein, if measured, ≥ 8 mg/L), TARGET Eligibility cohort (patients who satisfied enrolment criteria for TARGET,¹ a Phase 3 sarilumab trial in patients with RA and an inadequate response to TNF inhibitors), and TARGET Baseline cohort (patients from TARGET Eligibility cohort with characteristics weighted to match those from the TARGET trial baseline,¹ using the matching-adjusted indirect comparison method²). In all 3 effectiveness cohorts, mean changes in CDAI and RAPID3 at 6 and 12 months post-initiation of sarilumab were evaluated using a model adjusted for baseline score, age, sex, race, calendar year, and seropositivity.

Results: A total of 2949 patients, treated by 585 rheumatologists, initiated sarilumab treatment in the period 2017–2020. The 4 yearly cohorts were relatively similar in terms of patients' age, sex, race, and most clinical characteristics. However, patients receiving sarilumab shortly after FDA approval (Cohort 1) had more ambulatory visits, a greater number of previously used non-TNFi biologics (particularly tocilizumab), and a higher comorbidity burden, and were more likely to be current users of glucocorticoids or opioids than sarilumab initiators in the subsequent 3 years. In the 3 cohorts used to assess sarilumab effectiveness, the greatest improvement was observed in the TARGET Baseline cohort, which also had the greatest mean baseline CDAI score (43), compared with the other two (24 both).

Conclusion: In this real-world cohort, we observed modest evidence for channeling of patients with greater RA severity and greater prior exposure to non-TNFi biologics to sarilumab shortly after its FDA approval. This cohort effect did not diminish the effectiveness of sarilumab. All cohorts showed improvement, with the greatest clinical improvement observed in the cohort with the highest baseline CDAI score who most closely resembled those enrolled in a phase 3 trial of patients with an inadequate response to TNF inhibitors.

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Figure 1. Adjusted improvements in CDAI and RAPID3

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POS0639

LONG-TERM EFFECTIVENESS OF THE RITUXIMAB HALF DOSE REGIMEN FOLLOWING A RESPONSE TO THE LICENSED DOSE IN RHEUMATOID ARTHRITIS

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Background: Following initial treatment with rituximab (RTX) full dose (2x1000mg), B-cell numbers are often lower than baseline. The half dose regime (2x500mg) has been reported to be similarly effective [1]; however, there is limited long-term data on the effectiveness of switching to RTX half-dose from the real-world perspective.

Objectives: To compare the 3-year RTX regime retention between patients receiving retreatment with half-dose and full-dose of RTX, and assess factors associated with maintenance of 2x500mg, with a view to establish an optimal long-term retreatment strategy in RA.

Methods: An observational study was conducted on 755 consecutive RTX-treated RA patients in a single centre for over 20 years. Of these, 165/755 (22%) received at least one cycle of 2x500mg. Long-term effectiveness was assessed using RTX retention rate. Drug survival of patients treated with 2x500mg was compared with 200 RA patients receiving 2x1000mg throughout the study, matched to the number of cycle when the 2x500mg regime was initiated.

Results: Of the 165 patients who received 2x500mg, 81.8% were female; mean age was 63.4 (26-91) years; mean disease duration 15.5 (2-53) years; 57 (34.5%) were bDMARDs-naïve; 121 (74%) were on concomitant DMARDs and mean DAS-28 was 3.9 (SD 1.29) at the half dose initiation. At 3 years, the retention rate was 38% for patients receiving 2x500mg compared to 87% for those on 2x1000mg; HR for half dose discontinuation was 6.17 [95%CI (3.91-12.27); p<0.001] (Figure 1A).

The main reasons for 2x500mg discontinuation were poor EULAR response (30%); moderate EULAR response (30%); shorter duration of response compared to the full dose (22%); and incomplete B-cell depletion (17%). The majority of these patients (87.9%) were switched back to 2x1000mg, 5.1% received other bDMARDs and 7.1% did not receive further DMARDs.

In multivariable analysis, previous TNFi use was associated with 3-year maintenance of the 2x500mg dose [OR 2.63 (1.12-6.10); p=0.024]; while higher plasmablasts at 2x500mg initiation was associated with shorter maintenance of this regime [OR 0.78 (0.67-0.97); p=0.028].

There were no significant differences in 5-year RTX retention rates between patients receiving 2x500mg and switched back to 2x1000mg vs those receiving 2x1000mg throughout the study (Log-Rank=0.186) (Figure 1B).

Conclusion: The use of RTX half-dose regimen was associated with poor retention at 3 years. Nevertheless, where loss of effectiveness occurs post-2x500mg initiation, switching back to 2x1000mg appears to be a pragmatic option. Patients with previous TNFi exposure and lower plasmablasts may be most suited to be commenced on the 2x500mg dose for long-term disease control.

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Figure 1A

Figure 1B

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POS0640

EFFECTIVENESS AND SAFETY OF ORIGINAL AND BIOSIMILAR ETANERCEPT IN bDMARD-NAÏVE PATIENTS IN A REAL-WORLD COHORT OF PORTUGAL

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Background: The patent expiration of the original etanercept in Europe has facilitated the development of biosimilar products. Non-significant differences in efficacy and safety were noted in clinical trials which are not expected to influence clinical performance. Nonetheless, daily practice data should be gathered to support the claim for biosimilarity.

Objectives: To compare the effectiveness and safety of original and biosimilar etanercept, in biological-Disease Modifying Antirheumatic Drug (bDMARD)-naïve patients.

Methods: A retrospective multicenter non-interventional study, using data collected prospectively from Reuma.pt (The Rheumatic Diseases Portuguese Register) was done, including patients with: age ≥ 18 years old; diagnosis of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Spondyloarthritis (SpA) (axial or peripheral); active disease who initiated treatment with etanercept as first line of biological treatment after 2010. Kaplan-Meier was used to calculate the persistence rate in treatment. Disease activity at baseline and follow-up data at 6, 12, 18 and 24 months of treatment was compared using the chi-square for categorical variables and t-student or Mann-Whitney tests for continuous variables. Reasons for discontinuing therapy were summarized using descriptive statistics. Statistical significance was assumed for 2-sided p-values >0.05 .

Results: We included 1694 patients (413 on biosimilar and 1280 on original etanercept) 864 with RA, 335 with PsA and 494 with SpA. The population's baseline characteristics were not significantly different among both groups, except concomitant treatment in RA (higher use of conventional DMARDs in biosimilar group and higher use of NSAIDs in original group) and in SpA patients (higher use of corticosteroids in original group).

At baseline, a higher joint count was found in patients treated with original etanercept with a statistical difference for swollen ($p=0.03$) and tender ($p=0.01$) joints count (SJC and TJC, respectively) in RA and in TJC in SpA patients ($p=0.02$). In RA patients, CDAI and SDAI were higher in patients who started original ($p=0.03$; $p=0.04$, respectively). Pain measured by visual analogic scale was higher in SpA patients treated with biosimilar ($p=0.03$).

The 3-year PR was not significantly different between both treatment groups in RA, PsA and SpA (Figure1). In RA, PR in biosimilar was 72.6%, with a median time-on-drug (TOD) of 28.3 months; for original etanercept PR was 63.6%, with a median TOD of 27.4 months ($p=0.566$). In PsA patients, the PR for biosimilar was 70.6%, with a median TOD of 27.6 months, and in original drug 67.0%, with a median TOD of 28.1 months ($p=0.743$). In SpA patients, the PR were 78.4% for biosimilar (median TOD of 27.4 months) and 71.5% for original treatment (median TOD of 28.0 months ($p=0.816$)).

Figure 1. Drug survival in biosimilar and original etanercept in Rheumatoid Arthritis, Psoriatic Arthritis and Spondyloarthritis

In RA patients, we did not find differences between the two treatment groups for the proportion of patients in remission or low disease activity by CDAI ≤ 10 , SDAI ≤ 11 or DAS28 < 3.2 at 6, 12, 18 and 24 months of treatment. For PsA, no differences were found in the same timelines for DAPSA ≤ 14 , DAS28 < 3.2 , BASDAI < 4 , ASDAS < 2.1 or PsARC response. Also, in SpA patients, no differences were found in BASDAI < 4 , BASFI < 4 , ASDAS < 2.1 , ASDAS response and BASDAI response in all the timelines with the exception of BASDAI response at 18 months, which was achieved in fewer patients in biosimilar therapy ($p=0.02$). Overall, 535 (31.6%) patients stopped etanercept (428 patients on original and 107 patients on biosimilar). Discontinuations due to inefficacy were the most frequent, but there were no significant differences between both groups as for adverse events. Discontinuations due to "other reasons" were higher for the original group, both in RA ($p=0.01$) and in SpA ($p=0.04$).

Conclusion: Biosimilar and original used as first-line biological treatment showed similar effectiveness and safety in our long-term cohort of patients with RA, PsA, and SpA

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