

Real-world outcomes after rituximab and abatacept initiation in rheumatoid arthritis: a retrospective single-centre cohort study

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Abstract

Background

To describe clinical outcomes, treatment exposure, follow-up, and available safety data among patients with rheumatoid arthritis (RA) who initiated rituximab (RTX) or abatacept (ABA) in routine care at a tertiary rheumatology centre.

Methods

This retrospective single-centre cohort included 86 patients treated with RTX between August 2007 and March 2013 and 27 treated with intravenous ABA between March 2011 and March 2013. Clinical and laboratory variables, joint counts, HAQ-DI, follow-up, treatment exposure, and adverse events were abstracted from clinical records. The primary within-cohort analysis evaluated change in four-variable DAS28-ESR from baseline to the first evaluable follow-up; three-variable DAS28-ESR was analysed as a supportive outcome because patient global assessment was incompletely recorded. Paired *t* tests and Wilcoxon signed-rank tests were used. No direct comparative or causal inference was intended.

Results

In the RTX cohort, paired four-variable DAS28-ESR data were available for 9/86 patients and decreased from 5.45 ± 1.04 to 3.55 ± 1.25 (mean change 1.91, 95% CI, 0.99–2.82; $P = .001$ by paired *t* test, $P = .008$ by Wilcoxon). Three-variable DAS28-ESR in 25 patients decreased from 4.85 ± 0.88 to 3.61 ± 1.10 (mean change 1.24, 95% CI, 0.79–1.70; $P < .001$ by both tests). Swollen and tender joint counts, ESR, and CRP also decreased in available paired samples. Safety follow-up was documented in 66/86 patients; 12/66 (18.2%) had a recorded adverse event, including one death following empyema after the first infusion and one possible hepatitis B event. In ABA, four-variable DAS28-ESR decreased from 5.22 ± 1.23 to 3.61 ± 1.49 in 6/27 patients (mean change 1.62, 95% CI, 0.34–2.89; $P = .023$ by paired *t* test, $P = .063$ by Wilcoxon), while three-variable DAS28-ESR decreased from 4.36 ± 1.09 to 3.07 ± 1.22 in 11 patients ($P = .002$ and $P = .005$, respectively). Two mild infusion reactions were recorded among 18 patients with available ABA safety follow-up.

Conclusions

Disease-activity measures decreased after RTX or ABA initiation among patients with evaluable paired data, but complete longitudinal outcome data were limited. Findings are descriptive and hypothesis-generating and should not be interpreted as evidence of comparative effectiveness, treatment persistence, or causality.

Background

Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disease characterised by persistent synovitis, progressive structural damage, disability, and systemic complications. Disease-modifying antirheumatic drugs (DMARDs) and treat-to-target strategies have substantially improved outcomes, although some patients have inadequate responses or intolerance to conventional synthetic DMARDs or biologic therapies.

Rituximab (RTX), a chimeric anti-CD20 monoclonal antibody, produces B-cell depletion, whereas abatacept (ABA), a CTLA-4-Ig fusion protein, modulates T-cell co-stimulation through the CD80/CD86–CD28 pathway. Both agents have demonstrated efficacy in RA populations with inadequate response to previous therapies, including patients with inadequate response to tumour necrosis factor inhibitors (TNFi).^{1–3}

The present cohort was assembled between 2007 and 2013, when the therapeutic landscape differed substantially from current practice. It therefore provides historical real-world evidence rather than a contemporary treatment-sequencing study. The 2025 EULAR update, published online in March 2026, includes RTX and ABA among available biologic DMARDs and recommends adjustment of therapy when treatment targets are not achieved, while emphasising individualised decisions based on efficacy, safety, comorbidities, risks, and patient preferences.⁴

The aim of this study was to describe outcomes after RTX or ABA initiation in routine care at a tertiary rheumatology centre, including patients with and without previous TNFi exposure. The study was descriptive and was not designed to establish superiority of one biologic over the other.

Methods

Study design and setting

This was a retrospective observational cohort study conducted at the Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Türkiye. Clinical records were reviewed for patients who initiated RTX between 27 August 2007 and 15 March 2013 or intravenous ABA between 16 March 2011 and 15 March 2013. Data were abstracted from the clinical records following ethics committee approval.

The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement,⁵ with additional reference to the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement given the use of routinely collected clinical records.⁶

Ethics

The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (approval no. GO 13/148 – 12; 27 March 2013). Given the retrospective design, the requirement for individual informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki.

Eligibility and treatment exposure

Eligible patients fulfilled the 1987 American Rheumatism Association/American College of Rheumatology classification criteria for RA ⁷ and received RTX or ABA during the specified periods. Patients who switched from RTX to ABA or vice versa during the observation period were excluded, according to the source thesis. No additional exclusions were documented. The final cohorts comprised 86 RTX-treated and 27 ABA-treated patients.

RTX was administered as two 1000-mg intravenous infusions separated by two weeks, with subsequent retreatment according to clinical judgement. The mean number of RTX courses was 2.8 ± 1.9 , mean cumulative dose 5593 ± 3860 mg, and mean observed exposure duration 17.2 ± 14.8 months. ABA was administered intravenously using weight-based dosing in routine practice; mean cumulative dose was 4076 ± 2558 mg and mean observed exposure duration was 7.2 ± 4.9 months.

Anti-TNF exposure groups

Within each treatment cohort, patients were classified descriptively as anti-TNF-experienced if they had received at least one prior TNFi and subsequently switched because of inadequate response or intolerance, and as anti-TNF-naïve if they had not previously received a TNFi and were treated after inadequate response to conventional synthetic DMARDs. RTX included 54/86 (62.8%) anti-TNF-experienced and 32/86 (37.2%) anti-TNF-naïve patients; ABA included 20/27 (74.1%) and 7/27 (25.9%), respectively. These groups reflect clinical treatment history and were not randomised.

Outcomes and statistical analysis

The primary outcome was within-patient change in four-variable DAS28-ESR from baseline to the first evaluable follow-up, using erythrocyte sedimentation rate (ESR), 28-joint tender and swollen joint counts, and patient global assessment. Because patient global assessment was incompletely recorded, a three-variable DAS28-ESR excluding patient global assessment was analysed separately as a supportive outcome. DAS28-CRP, joint counts, ESR, CRP, rheumatoid factor (RF), HAQ-DI, and EULAR response were also evaluated where paired data were available.

Baseline characteristics were summarised descriptively. Within-cohort paired comparisons used paired t tests and Wilcoxon signed-rank tests. Mean paired changes and 95% confidence intervals are reported where available. Subgroup comparisons by previous TNFi exposure were exploratory. No formal

between-treatment comparison was performed because treatment allocation was non-randomised, cohort sizes were unequal, follow-up timing differed, and no confounding-adjustment strategy had been prespecified.

Missing data were reported by outcome and analysis. Because reasons for missing follow-up measurements were not systematically documented, complete-case analyses may be subject to selection bias. Nominal p values were interpreted as exploratory rather than confirmatory because of the number of outcomes and the small paired samples.

The source thesis reported percentages of patients returning for successive follow-up visits. These figures are presented, when relevant, as follow-up visit continuation rather than drug retention, because discontinuation dates, censoring rules, and reasons for non-attendance were not systematically recorded. A Kaplan–Meier persistence analysis was therefore not possible.

Results

Study population and baseline characteristics

The dataset comprised 113 patients: 86 treated with RTX and 27 with ABA. Women accounted for 82.6% and 81.5% of the respective cohorts. Mean age was 52.7 ± 11.2 years in the RTX cohort and 45.0 ± 15.8 years in the ABA cohort. Mean disease duration was 152.3 ± 101.7 months ($n = 84$) and 123.8 ± 88.6 months, respectively. Prior TNFi exposure was present in 54/86 (62.8%) RTX-treated patients and 20/27 (74.1%) ABA-treated patients.

Baseline four-variable DAS28-ESR was 5.50 ± 0.85 ($n = 56$) in the RTX cohort and 5.22 ± 1.20 ($n = 13$) in the ABA cohort. Baseline three-variable DAS28-ESR was 5.07 ± 0.87 ($n = 55$) and 4.53 ± 1.09 ($n = 18$), respectively. At least one comorbidity was recorded in 55/86 (64.0%) RTX and 14/27 (51.9%) ABA patients. (Table 1).

Table 1
Baseline characteristics of the study cohorts.

Characteristic	RTX (n = 86)	ABA (n = 27)
Women, n (%)	71 (82.6)	22 (81.5)
Age, years, mean $\pm$ SD	52.7 $\pm$ 11.2	45.0 $\pm$ 15.8
Disease duration, months, mean $\pm$ SD	152.3 $\pm$ 101.7 (n = 84)	123.8 $\pm$ 88.6
Prior TNFi exposure, n (%)	54/86 (62.8)	20/27 (74.1)
RF positive, n (%)	59/77 (76.6)	11/22 (50.0)
Baseline DAS28-ESR, 4-variable	5.50 $\pm$ 0.85 (n = 56)	5.22 $\pm$ 1.20 (n = 13)
Baseline DAS28-ESR, 3-variable	5.07 $\pm$ 0.87 (n = 55)	4.53 $\pm$ 1.09 (n = 18)
Baseline DAS28-CRP, 4-variable	4.87 $\pm$ 0.85 (n = 47)	4.87 $\pm$ 1.10 (n = 10)
HAQ-DI, mean $\pm$ SD	1.16 $\pm$ 0.69 (n = 27)	1.01 $\pm$ 0.75 (n = 12)
≥ 1 comorbidity, n (%)	55 (64.0)	14 (51.9)
Malignancy before biologic, n (%)	3 (3.5)	2 (7.4)

Rituximab outcomes

Sixty-two of 86 patients (72%) had a recorded first follow-up visit, at a mean of 7.1 ± 1.9 months after initiation. Paired outcome data were available for smaller, outcome-specific subsets.

For the primary four-variable DAS28-ESR outcome, paired data were available for 9 patients. Mean DAS28-ESR decreased from 5.45 ± 1.04 to 3.55 ± 1.25 , corresponding to a mean paired change of 1.91 (95% CI, 0.99–2.82; $P = .001$ by paired t test; $P = .008$ by Wilcoxon signed-rank test).

The supportive three-variable DAS28-ESR analysis included 25 patients and showed a decrease from 4.85 ± 0.88 to 3.61 ± 1.10 (mean change 1.24, 95% CI, 0.79–1.70; $P < .001$ by both tests). DAS28-CRP also decreased in its available paired samples. Swollen and tender joint counts, ESR, and CRP decreased significantly in the available paired analyses. RF titre decreased as well, although this laboratory change was not interpreted as an independent clinical efficacy endpoint.

HAQ-DI could not be meaningfully analysed longitudinally because only one patient had paired values. Cross-sectional HAQ-DI values are therefore not interpreted as within-patient change.

Using four-variable DAS28-ESR, EULAR response was evaluable in 9 patients: 3 good, 4 moderate, and 2 with no response. Using the three-variable DAS28-ESR, 10/25 (40%) had a good response, 7/25 (28%) a moderate response, and 8/25 (32%) no response. [8] (Table 2).

Table 2

Changes in disease activity and selected clinical and laboratory measures after rituximab initiation.

Parameter	n	Baseline	First follow-up	Mean change (95% CI)	P (t test/Wilcoxon)
DAS28-ESR, 4-variable	9	5.45 ± 1.04	3.55 ± 1.25	1.91 (0.99–2.82)	.001 / .008
DAS28-ESR, 3-variable	25	4.85 ± 0.88	3.61 ± 1.10	1.24 (0.79–1.70)	< .001 / <.001
DAS28-CRP, 4-variable	6	5.04 ± 0.96	3.06 ± 1.08	1.99 (0.48–3.49)	.019 / .031
DAS28-CRP, 3-variable	23	4.39 ± 0.79	3.29 ± 0.93	1.10 (0.63–1.57)	< .001 / <.001
Swollen joint count	30	3.43 ± 2.39	1.37 ± 1.69	2.07 (1.05–3.08)	< .001 / <.001
Tender joint count	30	6.43 ± 3.50	3.33 ± 3.11	3.10 (1.73–4.47)	< .001 / <.001
ESR, mm/h	60	45.6 ± 25.8	26.9 ± 18.2	18.7 (13.5–24.0)	< .001 / <.001
CRP, mg/dL	54	3.44 ± 3.88	1.45 ± 1.80	1.99 (1.15–2.84)	< .001 / <.001
RF titre, IU/mL	39	200.5 ± 304.9	94.7 ± 234.1	105.8 (56–156)	< .001 / <.001

Mean time to first follow-up: 7.1 ± 1.9 months.

Rituximab follow-up and safety

The source thesis reported 92% attendance at approximately 6 months, 76% at approximately 12 months, and 11% at approximately 57 months. These figures represent attendance at successive follow-up visits rather than a censored estimate of treatment persistence. The records did not reliably distinguish treatment discontinuation from transfer of care, loss to follow-up, or missed visits.

Safety follow-up was documented in 66/86 patients (76.7%). Twelve of these 66 patients (18.2%) had a recorded adverse event. Four patients (6.1%) had allergic-type reactions; other recorded events included fever, headache, dyspnoea, palpitations, dry mouth, low back pain, one possible hepatitis B event, and one death. One patient died following empyema after the first RTX infusion. The temporal association is reported without assigning causality. No patient was documented to discontinue RTX because of an adverse event.

In the exploratory comparison by prior TNFi exposure, no statistically significant difference in magnitude of change was detected for measures with adequate subgroup data. Given the small subgroups and absence of a prespecified power calculation, these findings should be interpreted as failure to detect a difference rather than evidence of equivalence.

Abatacept outcomes

Eighteen of 27 patients (66.7%) had a recorded first follow-up visit, at a mean of 4.6 ± 1.4 months. Four-variable DAS28-ESR decreased from 5.22 ± 1.23 to 3.61 ± 1.49 in 6 patients (mean change 1.62, 95% CI, 0.34–2.89; $P = .023$ by paired t test; $P = .063$ by Wilcoxon). Three-variable DAS28-ESR decreased from 4.36 ± 1.09 to 3.07 ± 1.22 in 11 patients (mean change 1.29, 95% CI, 0.62–1.95; $P = .002$ and $P = .005$, respectively).

Swollen joint count, tender joint count, and CRP showed decreases in their available paired samples, whereas ESR did not show a consistent statistically significant change across the two tests. HAQ-DI had paired data in only two patients and was not analysed inferentially.

Four-variable DAS28-ESR EULAR response was evaluable in 6 patients: 1 good, 4 moderate, and 1 no response. Using the three-variable DAS28-ESR in 11 patients, 5 had a good response, 3 a moderate response, and 3 no response. [8] (Table 3).

Safety follow-up was documented for 18/27 patients (66.7%). Two patients (11.1%) had mild infusion reactions. No deaths or serious infections were recorded in the available follow-up; this should not be interpreted as proof of a favourable safety profile because one third of the cohort lacked documented safety follow-up.

Table 3
Changes in disease activity and selected clinical and laboratory measures after abatacept initiation.

Parameter	n	Baseline	First follow-up	Mean change (95% CI)	P (t test/Wilcoxon)
DAS28-ESR, 4-variable	6	5.22 ± 1.23	3.61 ± 1.49	1.62 (0.34–2.89)	.023 / .063
DAS28-ESR, 3-variable	11	4.36 ± 1.09	3.07 ± 1.22	1.29 (0.62–1.95)	.002 / .005
DAS28-CRP, 4-variable	6	4.76 ± 1.00	3.42 ± 1.13	1.34 (– 0.17–2.85)	.071 / .156
DAS28-CRP, 3-variable	11	4.08 ± 0.75	3.04 ± 0.81	1.04 (0.30–1.78)	.011 / .042
Swollen joint count	11	2.91 ± 1.51	0.55 ± 0.93	2.36 (1.15–3.58)	.002 / .004
Tender joint count	11	5.73 ± 4.22	2.27 ± 1.79	3.45 (0.43–6.48)	.029 / .051
ESR, mm/h	18	33.9 ± 18.2	29.1 ± 23.7	4.8 (– 2.2–11.9)	.165 / .050
CRP, mg/dL	17	2.64 ± 2.96	1.58 ± 1.89	1.06 (0.14–1.98)	.027 / .051

Mean time to first follow-up: 4.6 ± 1.4 months.

Discussion

The principal message of this historical cohort is not simply that disease-activity measures decreased after RTX or ABA initiation, but that the completeness of longitudinal outcome capture was limited. Once analysis was restricted to genuinely paired same-patient measurements, four-variable DAS28-ESR was available for only 9/86 RTX-treated and 6/27 ABA-treated patients. The larger three-variable analyses showed a consistent direction of improvement, but they remain complete-case analyses and therefore cannot be assumed to represent all treated patients.

The RTX findings are directionally compatible with randomised and registry evidence supporting the efficacy of RTX in active RA, including populations with inadequate response to methotrexate or TNFi.^{1,2,9} However, direct numerical comparison with those studies is inappropriate because the present cohort was retrospectively assembled, outcome capture was incomplete, follow-up timing was variable, and treatment practices have changed over time.

The ABA cohort was substantially smaller and had limited paired data. The observed decrease in disease-activity measures is compatible with the established efficacy of ABA in RA, including the ATTAIn trial in patients with inadequate response to TNFi, but the present data are too sparse to provide a reliable estimate of treatment effect.³

The analysis by previous TNFi exposure did not detect statistically significant differences in the magnitude of improvement between TNFi-experienced and TNFi-naïve RTX-treated patients. This result should not be interpreted as evidence that prior TNFi exposure has no influence on response. The analysis was exploratory, the subgroup sizes were modest, and the study had no power calculation for this question.

An important methodological caveat concerns the definition of the primary outcome. Because paired four-variable DAS28-ESR data were available for only 9/86 RTX-treated and 6/27 ABA-treated patients, this outcome lacked the precision to serve as a robust primary endpoint despite reaching nominal statistical significance in both cohorts. The three-variable DAS28-ESR, evaluable in larger subsets (25/86 and 11/27, respectively), is better regarded as the more informative descriptive outcome, and the four-variable analysis is best interpreted as a sensitivity analysis constrained by very small sample size rather than as the principal basis for inference.

The mechanism underlying missing follow-up data could not be established from the available records. Patients with and without evaluable paired outcomes were not systematically compared on baseline characteristics, so the possibility that missingness was related to disease severity, early treatment response, or early discontinuation (missing not at random) cannot be excluded. This constrains generalisation of the observed improvements to the full treated cohorts and should be borne in mind when interpreting the magnitude of change reported here.

The follow-up attendance figures deserve particular caution. The original thesis described these percentages as treatment retention, but the underlying data document attendance at successive visits rather than a time-to-discontinuation process. Without reliable discontinuation dates, censoring rules, and reasons for non-attendance, a Kaplan–Meier persistence estimate cannot be reconstructed. Reframing these values as follow-up continuation avoids attributing information to the dataset that it does not contain.

Safety findings also require a cautious interpretation. The available RTX records included one death following empyema after the first infusion and one possible hepatitis B event, while two mild infusion reactions were recorded in the ABA cohort. Because safety ascertainment was incomplete and adverse events were abstracted from routine records without consistent formal severity or causality grading, the study cannot establish comparative safety. If the original charts remain accessible, verification of the hepatitis B event and the empyema-related death—including baseline infection screening, prophylaxis, temporal sequence, and clinical outcome—would materially strengthen the report.

The different first-follow-up timing between RTX and ABA (approximately 7.1 versus 4.6 months) further limits any qualitative comparison. More importantly, the non-randomised treatment selection and unequal cohort sizes make confounding by indication likely. The study should therefore not be framed as a head-to-head comparison. Large registry analyses and randomised trials can provide comparative effectiveness evidence, but those approaches were not feasible in this historical dataset.^{9,10}

The contemporary relevance of this cohort is primarily historical and hypothesis-generating. The 2025 EULAR recommendations, published in 2026, retain RTX and ABA among available biologic DMARDs and recommend treatment adjustment when targets are not achieved, with selection informed by efficacy, safety, comorbidity, and risk considerations.⁴ The present data should not be used to infer current treatment sequencing; instead, they document real-world experience from an earlier therapeutic era.

Strengths and limitations

Strengths include the tertiary referral setting, inclusion of routine-care patients over a prolonged recruitment period, representation of both TNFi-experienced and TNFi-naïve patients, and transparent reporting of outcome-specific denominators. The reanalysis also distinguishes paired from cross-sectional data and avoids interpreting follow-up attendance as treatment persistence.

Limitations include retrospective design, confounding by indication, unequal cohort sizes, incomplete longitudinal capture of patient-reported and composite outcomes, small paired samples—particularly for the standard four-variable DAS28—uncertain reasons for missing follow-up, incomplete safety ascertainment, and absence of a contemporaneous comparator. No causal or direct comparative conclusion can be drawn.

Several additional limitations warrant emphasis. First, the primary four-variable DAS28-ESR analysis rested on very small paired samples (9 and 6 patients in the RTX and ABA cohorts, respectively), limiting

its precision as a primary endpoint; the larger three-variable analyses, although more informative, remain complete-case analyses. Second, because the mechanism underlying missing follow-up data could not be determined and baseline characteristics of patients with and without evaluable outcomes were not systematically compared, missing-not-at-random bias cannot be excluded. Third, as a tertiary referral centre, the cohort may over-represent patients with more severe or refractory disease, which may limit generalisability to broader RA populations treated in non-tertiary settings. Fourth, multiple outcomes and subgroup comparisons were evaluated without adjustment for multiplicity, so nominal P values should be interpreted with caution. Finally, adverse events were abstracted from routine clinical records without standardised causality or severity grading, which precludes any formal comparison of safety between the two treatments.

Conclusion

In this historical single-centre cohort, initiation of RTX or ABA was followed by decreases in disease-activity measures among patients with available paired data. The findings are most consistent for the larger three-variable DAS28 analyses, whereas the standard four-variable DAS28 analyses were limited by very small paired samples. Because of incomplete follow-up, non-randomised treatment selection, and the absence of a comparator, these results should be regarded as descriptive and hypothesis-generating rather than evidence of comparative effectiveness, treatment persistence, or causal efficacy.

ABA, abatacept; CRP, C-reactive protein; DAS28, Disease Activity Score in 28 joints; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; EULAR, European Alliance of Associations for Rheumatology; HAQ-DI, Health Assessment Questionnaire Disability Index; RA, rheumatoid arthritis; RECORD, REporting of studies Conducted using Observational Routinely-collected health Data; RTX, rituximab; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TNFi, tumour necrosis factor inhibitor.

Declarations

Ethics approval and consent to participate:

Approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (GO 13/148 – 12; 27 March 2013). Individual informed consent was waived because of the retrospective design.

Consent for publication:

Not applicable; no identifiable individual data or images are reported.

Competing interests:

The authors declare no competing interests.

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Author Contribution

ÖÖ contributed to data abstraction, statistical analysis, and manuscript drafting. SK contributed to study conception, clinical interpretation, and critical revision. Both authors approved the final manuscript.

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Availability of data and materials:

The underlying dataset is not publicly available because it contains potentially identifiable clinical information. De-identified data may be considered upon reasonable request, subject to institutional and ethics committee approval.

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