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Full Length Article

Comparative efficacy of rituximab versus azathioprine in the treatment of MOG antibody-associated disease (MOGAD)

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ABSTRACT

Background: Azathioprine (AZA) and rituximab (RTX) are frequently used drugs in the treatment of Myelin Oligodendrocyte Glycoprotein Associated Disease (MOGAD).
Objectives: The aim of this study was to evaluate the efficacy and safety data of AZA and RTX treatments in MOGAD.
Methods: Patients diagnosed according to the 2023 MOGAD diagnostic criteria and receiving AZA or RTX treatment were included in the study.
Results: In 142 patients included in the study, the female/male value was 1.2. The rate of OCB positivity in MOGAD patients was 22.6 %. Patients on RTX had higher EDSS values than patients on AZA. However, the RTX group demonstrated a more pronounced improvement in disability, reflected by a greater negative trend in the ΔEDSS values. The attack-free rate was 78 % in the RTX group and 68 % in the AZA group during their treatment period. Both groups had no difference in the time of the first attack. The main factor affecting the time to first attack was having a higher EDSS at the time of treatment initiation. The survival analysis found that EDSS scores improved significantly in patients treated with RTX.
Conclusion: Although survival analyses for both treatments appear to be similar, using RTX provides better EDSS scores.

1. Introduction

Neuromyelitis optica spectrum disorders (NMOSD) refer to a group of conditions primarily affecting the optic nerve and spinal cord, characterized by the presence of aquaporin-4 antibodies (AQP4-IgG) in many patients (Wingerchuk et al., 2015). However, a subset of patients presenting with clinical features resembling NMOSD lack AQP4-IgG antibodies and have traditionally been categorized as seronegative NMOSD (Lopez-Chiriboga et al., 2018). The discovery of myelin oligodendrocyte glycoprotein antibodies has revealed that some of these seronegative cases actually represent a distinct disease entity, now recognized as Myelin Oligodendrocyte Glycoprotein Associated Disease (MOGAD) (Jarius et al., 2016; Jarius et al., 2018). Recently published guidelines have established diagnostic criteria for MOGAD, providing essential recommendations to distinguish it from NMOSD and ensure accurate diagnosis (Banwell et al., 2023).

Although the clinical, laboratory, and radiologic characteristics of MOGAD have been well defined in both children and adults, a standardized treatment algorithm has yet to be established. Medications such as azathioprine (AZA) and rituximab (RTX), commonly used in the management of AQP4-IgG-positive patients, are frequently employed in clinical practice for the treatment of MOGAD. However, clinical practice is primarily guided by limited observational and cross-sectional studies evaluating the efficacy and safety of these treatment options (Whittam et al., 2020; Barreras et al., 2022; Montcuquet et al., 2017; Ramanathan et al., 2018; Cobo-Calvo et al., 2019; Mao et al., 2019; Zhou et al., 2019; Chen et al., 2020; Albassam et al., 2020; Tzartos et al., 2020; Pedapati et al., 2020; Durozard et al., 2020). In this study, we not only present the clinical and demographic features of MOGAD but also share our efficacy and safety findings for treatments involving AZA and RTX.

2. Methods

2.1. Study design and data collection

Patients aged 18 years and older who met the 2023 diagnostic criteria for MOGAD and had received either AZA treatment for at least six months or at least two doses of RTX with a six-month interval were included in the study. Patients who were not sufficiently differentiated from other diseases when diagnosing MOGAD were not included in the study. Patients who had previously received a diagnosis other than MOGAD and therefore received any treatment other than RTX and AZA were not included in the study.

The research was designed as a multicenter, retrospective study. A standardized form was developed to collect data on MOGAD-specific clinical, laboratory, radiologic, and treatment-related characteristics. Data were extracted from medical records using structured forms that captured demographic information, comorbidities, disease onset features, diagnostic criteria, treatment initiation dates, dosages, infusion reactions, relapse characteristics, neurological examination findings, Expanded Disability Status Scale (EDSS) scores, and laboratory and radiological results.

The collected data included demographic features, age at disease onset, the most recent relapse prior to treatment, the total number of relapses, and all relapses occurring during treatment. Laboratory findings encompassed results for oligoclonal bands (OCB) and myelin oligodendrocyte glycoprotein antibodies. Radiologic evaluations recorded both the imaging characteristics at disease onset and the most recent findings prior to the initiation of AZA or RTX treatment. During the treatment period, radiologic features were categorized for both the brain and spinal cord (cervical and thoracic) as new T2 lesions, lesions with enhancement, or enlarging T2 lesions. Ethical approval for the study was granted by the Ondokuz Mayıs University Clinical Research Ethics Committee (2023/000342).

2.2. Data preparation

Missing data imputation was performed using the missRanger package (Mayer M, 2024. https://CRAN.R-project.org/package=missRanger), a random forest-based approach, which iteratively imputes missing values by predicting each variable based on others in the dataset. A model with 1000 trees and a fixed seed (seed = 3) was applied to ensure reproducibility. EDSS values were rounded to 0.0 or 0.5 increments to align with clinical standards, capturing consistent disability gradation.

2.3. ΔEDSS calculation and EDSS categorization

To assess disability progression, ΔEDSS scores were calculated at three time points: first year post-intervention - baseline, second year - first year, last recorded EDSS - baseline. These scores were derived to quantify EDSS progression or improvement, and further analyses assessed differences across treatment groups. A new categoric variable was generated to classify baseline EDSS into two categories for further analysis: scores between 0 and 2, and scores of 2 or higher.

2.4. Descriptive and comparative analysis

Summary statistics of demographic and clinical characteristics were stratified by treatment group. *P*-values were computed using chi-square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables.

2.5. Survival analysis

The time to the first relapse was analyzed using Kaplan-Meier survival analysis, stratified by treatment group. Time was calculated from treatment initiation to either first relapse or end of follow-up. The survival curves with 95 % confidence intervals, and survival distributions were compared using log-rank tests.

2.6. Propensity score matching

To adjust for baseline differences in disability, nearest neighbor matching on Mahalanobis distance was conducted between RTX and AZA groups using the MatchIt package (Ho et al., 2011). Baseline EDSS score was selected as the matching variable due to its clinical relevance, with replacement allowed to optimize match quality. The matched dataset was assessed to ensure comparability of baseline EDSS scores across groups, reducing confounding effects in subsequent analysis.

2.7. Cox proportional hazards regression models

To explore factors associated with relapse timing, univariate and multivariate Cox proportional hazards regression models were applied. Covariates included treatment group, baseline EDSS score, age, sex, initial attack symptoms, total attacks before treatment, and time from diagnosis to treatment. Each univariate model estimated the effect of a single variable on relapse risk, with hazard ratios (HRs) and *p*-values for each factor. A multivariate model was fitted to assess the independent effects of each covariate while adjusting for potential confounding.

Post-matching, a Cox proportional hazards model evaluated the treatment effect on time to first relapse. The outcome variable was the time from treatment initiation to the first relapse or end of follow-up, with treatment group as the primary predictor. Relapse events were coded as binary indicators. Hazard ratios from this model provided estimates of relapse risk between the treatment groups, adjusted for matching.

2.8. Inverse probability weighting

To further address confounding, inverse probability weighting (IPW) based on propensity scores was applied. Propensity scores were generated from a logistic regression model with treatment group as the outcome and predictors including total pre-treatment attacks and baseline EDSS. The IPW was calculated as:

$$IPW = T_i/p_i + (1 - T_i)/(1 - p_i)$$

where T_i is the treatment indicator and p_i the propensity score. This weighting balanced baseline characteristics between groups. The weighted Cox proportional hazards model estimated relapse risk, yielding adjusted hazard ratios and confidence intervals for the effect of RTX compared to AZA.

All statistical analyses, data imputation, and visualizations were conducted using the R statistical software (version 4.3.3; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Study population

The study included 142 patients with a definite diagnosis of MOGAD. Patients with low-titer positive anti-MOG antibody results obtained via fixed cell-based immunoassay or those not tested with live cell-based immunoassay were excluded in line with the updated MOGAD diagnostic criteria. Additionally, no patients with positive anti-AQP4 antibody results were included in the study. The cohort comprised 95 patients receiving RTX and 47 patients treated with AZA.

3.2. Demographic and clinical characteristics

Of the patients, 77 were female and 65 were male, with a female to male ratio of 1.2. The age range was 19.5–72.7 (IQR = 39) years. Disease duration was 0.8–33.6 (IQR = 4) years. Follow-up duration was 0.5–3.7 (IQR = 1) years in the RTX group and 0.2–4.9 (IQR = 1.9) years in the AZA group. The most common mode of disease onset was unilateral or bilateral optic neuritis (58 %). Bilateral optic neuritis was the initial symptom in only six patients. Myelitis was the second most common (% 28) initial symptom. Pyramidal signs, area postrema symptoms, brainstem involvement and other findings were also present, although to a lesser extent (%13). Among all patients, a total of 119 patients were evaluated for OCB. OCB type-1 (negative) was found in 93 of these patients, type-2 in 17, type-3 in 4 and type-4 in 6. The rate of OCB positivity in MOGAD patients was 22.6 %. The total number of attacks ranged from 1 to 22 (IQR = 2).

Before disease modifying therapy (DMT), most patients had only one attack and there was no difference in the number of relapses between the RTX and AZA groups ($p = 0.2$). The EDSS before treatment ranged between 0 and 8 (IQR = 2). In addition, in terms of the mean and median EDSS values before the start of DMT, patients receiving RTX (2.6 and 2) had higher values than those receiving AZA (1.4 and 1) and this was statistically significant ($p < 0.001$).

The first-year, second-year, and final EDSS scores, along with ΔEDSS, were analyzed for patients receiving DMT. The difference in EDSS scores between the groups was evident even before the initiation of DMT. However, the RTX group demonstrated a more pronounced improvement in disability, reflected by a greater negative trend in the ΔEDSS values. Additionally, the number of relapses during DMT was evaluated. In both groups, the majority of patients remained relapse-free, with 78 % in the RTX group and 68 % in the AZA group achieving this outcome (Table 1).

3.3. Relapses and disability

Survival analyses were performed for the patients until their first attack under DMT. There was no difference in time to first episode for patients on RTX and AZA. (Fig. 1a) Similarly, survival analyses were performed for clinical and demographic characteristics. No differences were found between the groups for gender, first attack type and last attack type before DMT. (Fig. 1b, c, d) When survival analysis was performed on the baseline EDSS values of the patients at the time of DMT initiation, it was found that patients with more disability had an earlier attack. (Fig. 1e).

Cox regression analysis was performed to evaluate clinical and demographic factors affecting the time to first attack. The multivariate analysis revealed that the baseline EDSS value prior to the initiation of DMT was the only significant factor influencing outcomes (Table 2).

For the survival analysis, propensity score matching based on EDSS was applied to enable a more efficient evaluation. There was no significant difference in the time to the first relapse between patients receiving RTX and AZA (log-rank test, $p = 0.9$) (Fig. 1f). Similar matching was conducted using the total number of relapses prior to DMT and baseline EDSS. The differences between the groups were not statistically significant.

The EDSS values of patients prior to initiating DMT were compared with their first-year, second-year, and final EDSS values under treatment. Baseline EDSS scores differed between groups, with the RTX group showing higher baseline disability (Fig. 2a-b). However, during the follow-up period, the ΔEDSS analysis revealed that patients receiving RTX consistently demonstrated lower levels of disability progression. This finding indicates that EDSS scores improved significantly in patients treated with RTX, suggesting that relapses in this group resulted in fewer long-term sequelae. (Fig. 2c-d).

Table 1
Demographic and clinical data.

	RTX (n = 95)	AZA (n = 47)	p-value
Sex, n (%)			0.2
Female	55 (58)	22 (47)	
Male	40 (42)	25 (53)	
Age, IQR (mean)	39 (27.5)	40 (32.5)	0.2
Disease duration, IQR (mean)	4 (2.8)	4 (2.8)	0.5
First attack symptom, n (%)			**0.024**
Myelitis	32 (34)	8 (17)	
Optic neuritis	48 (51)	35 (74)	
Others	15 (16)	4 (9)	
Oligoclonal bands, n (%)			**0.013**
Negative or unexamined	72 (76)	43 (91)	
Type 2 positive	16 (17)	1 (2)	
Type 3 positive	4 (4)	0 (0)	
Type 4 positive	3 (3)	3 (6)	
Total number of attacks before DMT, IQR (min-max)	2.00 (1.00–3.00)	2.00 (1.00–3.00)	0.2
1, n (%)	40 (42)	29 (62)	
2, n (%)	23 (24)	8 (17)	
3, n (%)	12 (13)	8 (17)	
4, n (%)	6 (6)	0 (0)	
5 and over, n (%)	14 (15)	2 (4)	
Last attack type before DMT, n (%)			0.076
Myelitis	4 (36)	12 (26)	
Optic neuritis	41 (43)	31 (66)	
Others	20 (21)	4 (8)	
Last EDSS before DMT, IQR (min-max)	2.00 (1.00–3.50)	1.00 (1.00–2.00)	**<0.001**
Last EDSS before DMT, n (%)			**<0.001**
0- <2	26 (27)	33 (70)	
2- <4	46 (48)	12 (26)	
≥4	23 (24)	2 (4.3)	
First year EDSS under DMT, IQR (min-max)	2.00 (1.00–3.00)	1.50 (1.00–2.50)	**0.018**
Second year EDSS under DMT, IQR (min-max)	2.00 (1.00–3.00)	1.50 (1.00–2.50)	0.089
Last EDSS under DMT, IQR (min-max)	2.00 (1.00–3.00)	1.00 (1.00–2.00)	**0.004**
ΔEDSS-1 (first year post intervention – baseline)	0.00 (−1.00–0.00)	0.00 (0.00–0.00)	**<0.001**
ΔEDSS-2 (second year - first year)	0.00 (0.00–0.00)	0.00 (0.00–0.50)	**0.012**
ΔEDSS-3 (last recorded EDSS - baseline)	0.00 (−1.00–0.00)	0.00 (0.00–0.50)	**0.015**
Total number of attacks under DMT, n (%)			0.3
0	74 (78)	32 (68)	
1	14 (15)	11 (23)	
2	7 (7.4)	3 (6.4)	
4	0 (0)	1 (2.1)	
Follow-up time, IQR (min-max)	1.00 (0.50–2.77)	1.99 (0.22–4.93)	0.2
ARR before DMT, IQR (min-max)	2.14 (0.82–5.14)	2.97 (0.75–5.15)	0.9
ARR after DMT, IQR (min-max)	0.00 (0.00–0.03)	0.00 (0.00–0.15)	0.5

RTX = Rituximab, AZA = Azathioprine, IQR = Median, DMT = Disease Modifying Therapy, EDSS = Expanded Disability Status Scale, ARR = Annual Relapse Rate.

3.4. Magnetic resonance imaging

Magnetic resonance imaging (MRI) was evaluated at the end of the first and second years to assess the presence of new or enlarging T2 lesions with contrast enhancement following treatment initiation. This analysis required the availability of brain, cervical, thoracic, or orbital MRI. MRI results were available for 57 patients in the first year and 32 patients in the second year. Among the 57 patients who underwent MRI in the first year, 19 (33.3 %) showed radiological activity, while 7 (21.9 %) exhibited radiological activity in the second year. All patients who experienced a clinical relapse during follow-up had corresponding MRI findings, whereas those without MRI findings exhibited a stable disease course. MRI characteristics were comparable between the AZA and RTX groups (Table 3).

3.5. Adverse events

The occurrence of side effects during the treatment period was also evaluated. Among patients receiving RTX, 9 (9.5 %) experienced adverse events, with 7 reporting mild infusion reactions or mild infections. Two patients developed serious adverse events, which necessitated the discontinuation of treatment. In the AZA group, side effects were observed in 8 patients (17 %), all of which were mild. No serious adverse events were reported in patients treated with AZA.

4. Discussion

Myelin oligodendrocyte glycoprotein-associated disease (MOGAD) may present as either a recurrent or a monophasic disorder. The clinical and demographic features of MOGAD vary significantly between pediatric and adult populations (Trewin et al., 2025). As well as defining the demographic characteristics of the disease, our study also provides information in terms of treatment response and clinical course. In our study, the proportion of female patients was found to be 54 %; consistent with those reported in the existing literature. In the literature, the reported female-to-male ratio has been observed to vary widely, with values ranging between 50 % and 80 %, reflecting a degree of variability across different studies (Whittam et al., 2020; Trewin et al., 2025; Contentti et al., 2023). This rate may be as high as 90 % in series with smaller patient cohorts (21). This may be due to geographical and ethnic differences. The age of disease onset for adults is generally found to be between 20 and 45 years. Our cohort exhibits result that align with these data (Whittam et al., 2020; Trewin et al., 2025; Rojas et al., 2023; Rempe et al., 2024).

In our study, optic neuritis was the most common initial symptom. Optic neuritis was present in 58 % of patients. Mostly unilateral onset of optic neuritis was found to be bilateral in only 6 patients (6/83). The onset of bilateral optic neuritis is a recognized clinical manifestation of MOGAD, occurring in 7 % of patients. Although there are studies in the literature showing the presence of bilateral optic neuritis up to 40 %, this rate was lower in our series (Contentti et al., 2023).

The diagnosis of MOGAD requires a comprehensive differential diagnosis, primarily to distinguish it from multiple sclerosis (MS). Therefore, the presence of intrathecal OCB, which are 90 % specific for MS (Arrambide et al., 2018), is frequently evaluated in MOGAD patients during the diagnostic process. In our study, this analysis was performed for the majority of patients, with OCB positivity detected in 27 individuals, corresponding to approximately 19 %. The literature on OCB positivity in MOGAD is limited, with previous studies reporting positivity rates of 10–15 %. A recent review published in January 2025, encompassing 4699 MOGAD patients, reported an OCB positivity rate of 12 % (Trewin et al., 2025). The rate observed in our study was slightly higher.

The treatment strategy for patients with MOGAD remains unclear, as no phase-3 studies have been completed, and no therapeutic agents have received official approval. Similar to other demyelinating diseases, acute attacks can be managed with treatments such as corticosteroids, plasmapheresis, or intravenous immunoglobulin (Schiro et al., 2024). For preventive therapy, treatment approaches in adult patients largely rely on prior experience with NMOSD patients. Preventive options include AZA, RTX, mycophenolate mofetil, IL-6 receptor antagonists, oral maintenance steroids, and booster intravenous immunoglobulin (Trewin et al., 2025; Schiro et al., 2024). Among these, AZA and RTX are the most commonly employed therapies.

Large-scale comparative studies evaluating the efficacy and safety of AZA and RTX in MOGAD patients are lacking, and data on disease activity outcomes with these therapies remain limited. However, in more than half of the patients studied, both treatments demonstrated efficacy in controlling disease activity and preventing relapses (Whittam et al.,

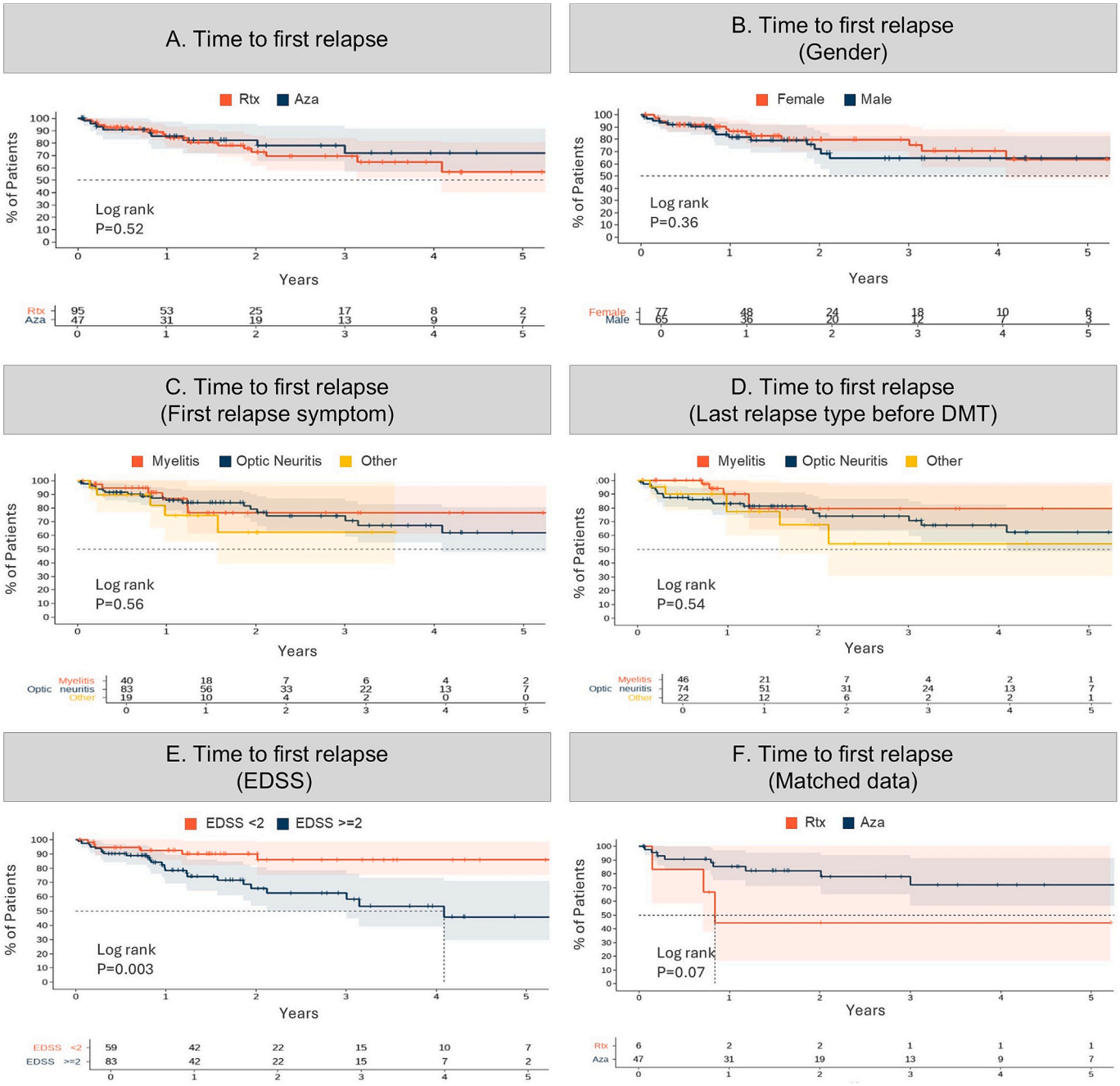

Fig. 1. Time to first relapse by treatment group and clinical subgroups. Kaplan-Meier survival analyses evaluating the time to first clinical relapse after treatment initiation, stratified by various patient characteristics. A: Rtx and Aza treatment groups, B: Sex-based differences, C and D: Relapse-free survival based on the first relapse symptom and the last relapse type before initiation of DMT, E: Survival differences between patients with baseline EDSS scores <2 versus those with scores ≥2, F: Relapse-free survival between treatment groups using data matched by Mahalanobis distance on baseline EDSS. Each panel displays survival curves with 95 % confidence intervals and includes p-values from log-rank tests.

2020; Barreras et al., 2022; Albassam et al., 2020; Durozard et al., 2020; Spagni et al., 2023; Nepal et al., 2022; Bai et al., 2021). Despite these findings, direct comparisons between the two therapies remain difficult due to the heterogeneity of MOGAD patients and the variability in age and comorbid conditions across study populations. Our study aimed to assess the efficacy and adverse effects of RTX and AZA. While patients treated with RTX and AZA experienced a comparable number of attacks, those receiving RTX had a higher prevalence of prior myelitis and greater baseline EDSS scores. These findings indicate that, in Türkiye, clinicians may preferentially prescribe RTX for MOGAD patients with a history of myelitis and more significant disability.

There was no significant difference between the two groups in the time to the next attack under treatment. Furthermore, factors such as gender, the type of the first attack, and the type of the last attack before treatment initiation did not influence this outcome. Regardless of the DMT used, patients with higher disability at treatment initiation experienced an earlier onset of the next attack, a finding confirmed by Cox regression analysis. In the multivariate analysis, baseline EDSS was identified as the only significant predictor for the time to the next attack.

When EDSS scores were matched to allow a direct comparison between the two therapies, no significant difference in attack rates was observed. Notably, the most striking result of our study was that the change in EDSS values over time was more favorable in patients treated with RTX. This finding suggests that RTX may offer superior benefits in

Table 2
Time until first attack.

	Univariate		Multivariate	
	HR (95 %CI)	p-value	HR (95 %CI)	p-value
DMT				
RTX	–	–	–	–
AZA	0.8 (0.4–1.7)	0.52	1.4 (0.6–3.7)	0.4
First attack type				
Myelitis	–	–	–	–
Optic neuritis	1.3 (0.5–3.2)	0.59	1.5 (0.6–4.0)	0.4
Others	1.9 (0.6–6.3)	0.29	2.9 (0.8–10.3)	0.10
Gender				
Female	–	–	–	–
Male	1.4 (0.7–2.8)	0.37	1.2 (0.6–2.6)	0.6
Age	1.0 (1.0–1.0)	0.82	1.0 (1.0–1.0)	0.8
Total attacks before DMT	1.1 (1.1–1.2)	**<0.001**	1.1 (1.0–1.2)	0.13
Disease duration	1.1 (0.9–1.4)	0.12	1.1 (1.0–1.3)	0.3
Basal EDSS before DMT	1.3 (1.0–1.5)	**0.016**	1.3 (1.0–1.7)	**0.022**

HR = Hazard Ratio, CI = Confidence Interval, RTX = Rituximab, AZA = Azathioprine, DMT = Disease Modifying Therapy.

reducing disability and may lead to relapses with fewer residual sequelae compared to AZA in MOGAD patients.

In our study, we also analyzed the radiological findings of the patients. MRI data were obtained for 57 patients in the first year and 32 patients in the second year. MRI activity was observed in 33 % of patients during the first year and 22 % during the second year. No significant differences were identified in MRI findings between the RTX and AZA groups. These results align with our other findings, which demonstrated comparable annual relapse rates and time to the first attack for both therapies. We also obtained side effect results for the use of RTX and AZA therapies in MOGAD. Except for a serious adverse event during infusion in only two patients using RTX, we did not obtain any treatment safety outcomes. These findings are consistent with the clinical observations and outcomes associated with AZA and RTX, which have been utilized for many years in the treatment of demyelinating diseases.

Our study has several limitations. One primary limitation is the variability in treatment protocols across the multicenter study design. While AZA dosing is standardized based on patient weight, RTX dosages may differ between centers, potentially influencing treatment outcomes. Another limitation is related to MRI findings. We lack standardized

Table 3
Magnetic resonance imaging results.

	MRI activity	RTX	AZA	Total
First year MRI progression, n (%)	Yes	15 (34.1 %)	4 (30.8 %)	19 (33.3 %)
	No	29 (65.9 %)	9 (69.2 %)	38 (66.7 %)
	Total	44 (100 %)	13 (100 %)	57 (100 %)
Second year MRI progression, n (%)	Yes	6 (25.0 %)	1 (12.5 %)	7 (21.9 %)
	No	18 (75.0 %)	7 (87.5 %)	25 (66.7 %)
	Total	24 (100 %)	8(100 %)	32 (100 %)

RTX = Rituximab, AZA = Azathioprine, MRI = Magnetic resonance imaging.

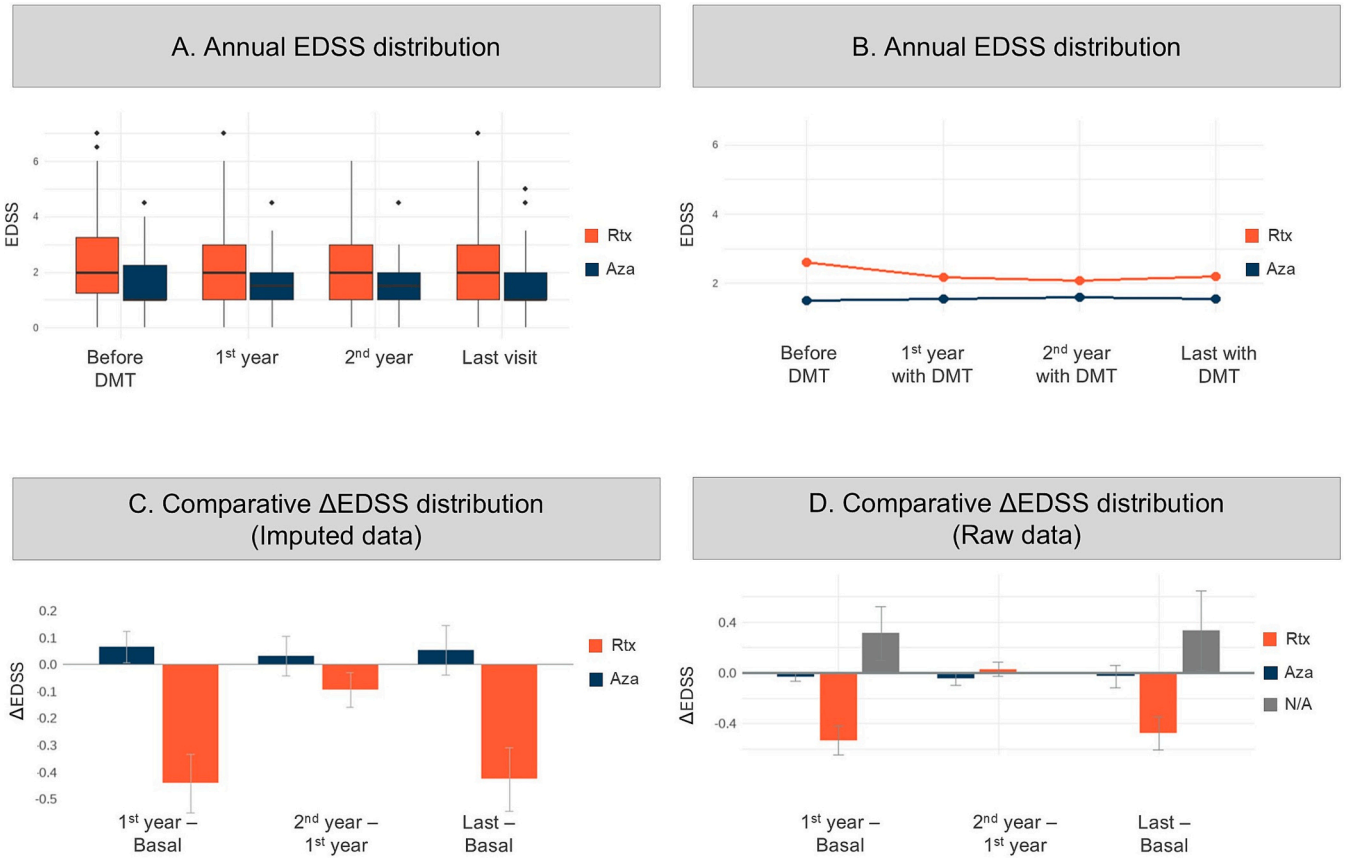

Fig. 2. Distribution and changes in EDSS scores across treatment groups. The progression of disability, across two treatment groups, at multiple time points. A: EDSS scores at four key time points; before disease-modifying therapy (DMT), and at the 1st year, 2nd year, and last clinical visit. B: Mean EDSS scores over the same time points. C: Change in EDSS (ΔEDSS) across three time intervals using imputed data. D: ΔEDSS comparisons based on raw (non-imputed) data, including a third category for patients with missing group data (gray bars).

brain and spinal cord MRI data for all patients, as these imaging studies were not standardized. This lack of standardized imaging complicates the comparison and interpretation of radiological outcomes.

5. Conclusion

RTX and AZA have been shown to be effective and reliable treatment options for patients with MOGAD. RTX was more commonly prescribed for patients with greater baseline disability. No significant difference was observed between the two treatments in terms of annual relapse rates or the time to relapse during treatment. However, RTX treatment appeared to contribute to greater improvement in EDSS, suggesting its potential to enhance outcomes for patients with MOGAD.

CRediT authorship contribution statement

Sedat Şen: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Murat Kürtüncü:** Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Serkan Demir:** Investigation, Data curation. **Tuncay Gündüz:** Investigation, Data curation. **Ezgi Demirel:** Investigation, Data curation. **Melih Tütüncü:** Investigation, Data curation. **Cihat Uzunköprü:** Investigation, Data curation. **Damla Cetinkaya Tezer:** Investigation. **Ferah Kızılay:** Investigation. **Belgin Petek Balcı:** Investigation. **Gökhan Arslan:** Methodology, Formal analysis, Data curation. **Caner Feyzi Demir:** Investigation. **Nazire Pınar Acar Özen:** Investigation. **Yeşim Beckmann:** Investigation. **İpek Güngör Doğan:** Investigation. **Uğur Uygunoğlu:** Investigation. **Serkan Özakbaş:** Investigation. **Mesrure Köseoğlu:** Investigation. **Haluk Gümüş:** Investigation. **Nuray Bilge:** Investigation. **Dürdane Bekar Aksoy:** Investigation. **Ahmet Kasım Kılıç:** Investigation. **Mehmet Fatih Yetkin:** Investigation. **Aylin Akçalı:** Investigation. **Sibel Canbaz Kabay:** Investigation. **Özlem Ethemoğlu:** Investigation. **Nermin Tepe:** Investigation. **Vedat Çilingir:** Investigation. **Sena Destan Bunul:** Investigation. **Dilcan Kotan:** Investigation. **Şeyda Figül Gökçe:** Investigation. **Nazlı Gamze Bülbül:** Investigation. **Fatma Akkoyun Arıkan:** Investigation. **Sabahattin Saip:** Investigation. **Murat Terzi:** Investigation. **Hüsnü Efendi:** Investigation. **Rana Karabudak:** Investigation. **Aksel Siva:** Supervision, Methodology, Investigation. **Aslı Tuncer:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization.

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Declaration of competing interest

None.

Data availability

The datasets generated and analyzed during this study contain patient-related data and are not publicly available due to privacy and ethical restrictions. However, the data may be available from the corresponding author upon reasonable request and with appropriate institutional and ethical approvals.

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