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Treatment Discontinuation in Patients With Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease

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IMPORTANCE Therapeutic deescalation strategies are increasingly considered in demyelinating diseases to mitigate the risks associated with prolonged immunosuppression. The impact of treatment discontinuation in myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) is not established.

OBJECTIVE To assess the relapse risk following treatment discontinuation in adult patients with MOGAD and to evaluate factors associated with disease reactivation.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study including 41 centers was conducted using the French NOMADMUS database. Adult patients with MOGAD diagnosed between January 2013 and April 2024 were included. Data were extracted on July 1, 2024. A total of 1047 patients with MOGAD were screened, and 705 patients fulfilled the inclusion criteria. Among them, 319 (45.2%) received at least 1 maintenance therapy.

EXPOSURE All instances of treatment discontinuation were collected and categorized according to their underlying reasons. Only discontinuations that were scheduled or related to adverse events were analyzed.

MAIN OUTCOMES AND MEASURES Time to first relapse was estimated using Kaplan-Meier survival curves, and differences between groups were assessed using the log-rank test.

RESULTS A total of 83 patients (median [IQR] age, 42.7 [28.9-53.3] years; 52 [63.7%] female) discontinued either oral immunosuppressants (azathioprine or mycophenolate mofetil) or rituximab in 60 (72.1%) and 23 (27.7%) individuals, respectively. Discontinuations were scheduled (n = 54 [65.1%]) or related to adverse events (n = 29 [34.9%]). After discontinuation, 7 patients relapsed, with a median (IQR) time to relapse of 0.5 (0.1-1.4) years. The Kaplan-Meier estimated cumulative incidence of relapse at 1 year after discontinuation was 8.7% (95% CI, 1.0-15.9). Severity of relapses was mild, with a median (IQR) change in the Expanded Disability Status Scale score of 0 (0-1) points. Factors associated with an increased relapse risk were a treatment duration of less than 1 year (7 relapses [19.4%] vs 0 relapses; log-rank $P = .002$) and a time since last relapse of less than 2 years (7 relapses [15.9%] vs 0 relapses; log-rank $P = .01$).

CONCLUSIONS AND RELEVANCE The low risk of disease reactivation found in this study suggests that discontinuing treatment may be considered in selected adult patients with MOGAD. Future clinical trials are necessary to confirm these results and establish guidelines in this situation.

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Supplemental content

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Group Information: The members of the NOMADMUS group appear in Supplement 2.

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Myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) is a recently characterized inflammatory demyelinating disorder of the central nervous system.[1] Unlike multiple sclerosis and neuromyelitis optica spectrum disorder, which carry a high relapse risk,[2,3] MOGAD may exhibit monophasic or relapsing patterns.[4] In relapsing cases, evidence supports a nonlinear disease course with a higher relapse risk during the first 2 years after onset, followed by a marked decline over time.[5,6] Early relapses within the first year also increase long-term relapse risk in adults.[7]

Currently, prolonged oral steroids, conventional immunosuppression such as azathioprine, mycophenolate mofetil, rituximab, and tocilizumab are commonly prescribed off label in adult patients with MOGAD to prevent further relapses.[8-12] While these treatments are generally well tolerated, long-term use raises concerns regarding infectious complications and malignancies. Intravenous immunoglobulins (IVIG) have also been shown to be effective with a favorable safety profile, but their use may be limited by cost or availability.[13]

To balance disease control with the risks of prolonged treatment, deescalation strategies represent a current challenge in chronic diseases.[14] In neuromyelitis optica spectrum disorder, discontinuing maintenance therapy is discouraged.[15] Given the natural history of MOGAD, treatment discontinuation may often be considered after several years of evolution. A cohort study[16] reported comparable relapse rates in patients who discontinued or maintained immunosuppressive treatment; however, without accounting for follow-up duration and therefore not reflecting a similar relapse risk over time. Here we investigated the outcomes after discontinuing maintenance therapy in a large national multicentric adult cohort of patients with MOGAD.

Key Points

Question What is the impact of maintenance therapy discontinuation on relapse risk in patients with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD)?

Findings In this cohort study of 705 adult patients with MOGAD, 83 discontinuations were analyzed, with a1-year relapse risk of 8.7%. Relapse risk was significantly decreased in patients with a prior treatment duration greater than 1 year and a time since last relapse greater than 2 years.

Meaning The findings suggest that treatment discontinuation may be considered in selected adult patients with MOGAD.

Methods

Ethics

All patients enrolled in The French Cohort and Biobank of Devic's Neuromyelitis Optica and Related Neurological Disorders (NOMADMUS) gave written informed consent to be included in the Observatoire Français de la Sclérose en Plaques (OFSEP) registry. In accordance with the French legislation, OFSEP was approved by both the French data protection agency (Commission Nationale de l' Informatique et des Libertés [CNIL]) and a French ethical committee (Comité de Protection des Personnes [CPP]). This study was declared compliant to the MR-004 of the CNIL by the institutional board of Hospices Civils de Lyon. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Data Source

This retrospective multicenter cohort study was conducted using the French NOMADMUS database (ClinicalTrials.gov Identifier: NCT02850705), a nested cohort of the French Multiple Sclerosis Database (Observatoire Français de la Sclérose En Plaques [OFSEP][17]). This database covers all major neuroimmunology units in France and MOGAD management is coordinated through the NOMADMUS expert group and multiple sclerosis referral centers. Data are collected retrospectively by clinicians at first visit then prospectively by clinicians and clinical research assistants during follow-up using EDMUS software.[18]

Patients

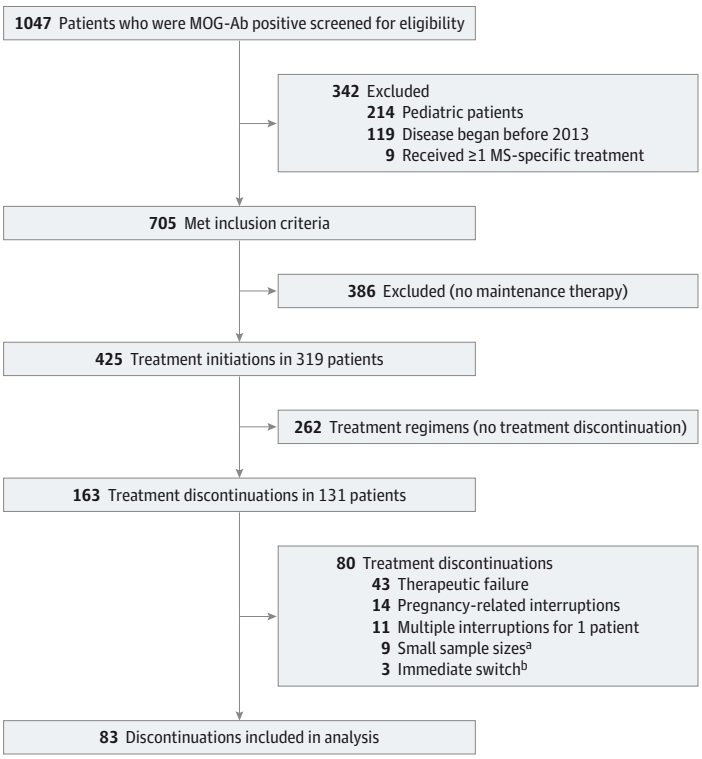
Patients included in the study fulfilled the following criteria: adult patients, diagnosis of MOGAD according to acknowledged criteria[1] defined by at least 1 acute central nervous system demyelinating event and clear positivity of myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) and a date of disease onset between January 1, 2013, and April 30, 2024. This time frame corresponds to the availability of MOG-Ab testing in France, to include only incident cases. MOG-Ab testing had been centralized using an in-house flow cytometry live cell-based assay with high titers (1:640 or greater) at the Lyon reference center and samples were mainly tested during attacks.[19] Patients who had received at least 1 multiple sclerosis-specific treatment during follow-up were excluded as this could indicate a false-positive MOG-Ab result.

Data Collection

Data were extracted on July 1, 2024, and collected until patients' last available follow-up. For each patient, we collected demographic and clinical data including age at onset, sex, date of disease onset, initial phenotype, and baseline Expanded Disability Status Scale (EDSS) score. Relapses were reported by the treating neurologist. EDSS were performed by certified neurologists (neurostatus.net).

Data on acute phase treatment and maintenance therapy were extracted, including initiation and discontinuation dates and reason for discontinuation. Among maintenance therapies, azathioprine, mycophenolate mofetil, and methotrexate were grouped under oral immunosuppressants. Patients enrolled in clinical trials or receiving less common treatments, such as mitoxantrone, were categorized under other. Given the evolution of clinical practices over time and the heterogeneous use of oral corticosteroids as maintenance therapy, this treatment was not considered such in the present study.

Figure 1. Study Flow Diagram



MOG-Ab indicates myelin oligodendrocyte glycoprotein antibody; MS, multiple sclerosis.

[a]Intravenous immunoglobulin, n = 3; tocilizumab, n = 1; and other treatments, n = 5.

[b]Initiation of a new treatment on the same day as the previous treatment discontinuation.

Assessment of Treatment Discontinuation

Treatment discontinuation was defined as an interruption beyond a predefined duration: for oral immunosuppressants, a cessation of at least 1 month; for interval-based therapies, a cessation of at least 1 year for rituximab, 2 months for tocilizumab, and 3 months for IVIG, to account for the possibility of extended dosing intervals.

All instances of treatment discontinuation were recorded, reviewed retrospectively by 2 expert neurologists, and categorized into 4 distinct groups: scheduled, adverse events or intolerance, pregnancy related, or therapeutic failure. Scheduled discontinuation could be initiated by the physician or the patient and included a predefined end of treatment, discontinuation due to the patient's age or the need to treat another condition, or the patient's personal convenience. There were no standardized regimens for interval-based therapies and treatment intervals could therefore be adjusted at the discretion of the treating neurologist. Therapeutic failure was defined as the occurrence of a relapse under maintenance therapy.

To assess the outcomes of treatment discontinuation in a context most representative of a deescalation strategy, only scheduled discontinuations and discontinuations related to adverse events were included in the main analysis. Pregnancy-related discontinuations were studied separately due to specific confounding factors and discontinuations related to therapeutic failure were not analyzed. Due to small sample sizes, discontinuations of IVIG and tocilizumab were not included in the main analysis but studied separately in a descriptive manner. To investigate the applicability of our results, the characteristics of patients who discontinued maintenance therapy were compared with those who continued treatment.

Evaluation of Relapse Risk Following Discontinuation

Due to the retrospective study design and the possibility of treatment resumption following any discontinuation, the permanence of treatment discontinuation could not be determined in advance. Thus, to evaluate the relapse risk only in the absence of subsequent treatment, we retained only the last treatment discontinuation in cases where a patient experienced several, and patients were censored from the analysis upon initiation of a new maintenance therapy.

Statistical Analysis

Continuous variables were summarized using medians with IQRs, and categorical variables were presented as counts and proportions. Factors associated with time to discontinuation among patients who initiated maintenance therapy were evaluated using a log-rank test.

Time to first relapse following maintenance therapy discontinuation was estimated using Kaplan-Meier survival curves, with censoring at the initiation of a new maintenance therapy or the end of patient follow-up. Associations between binary variables and time to first relapse were assessed using a log-rank test.

Continuous variables were dichotomized at their rounded median value. Statistical significance was defined as a P value <.05. All analyses were conducted using R

Table 1. Characteristics of the 83 Discontinuations Analyzed

Characteristic	Rituximab (n = 23)	Oral immunosuppressants (n = 60)	Total (N = 83)
Age at onset, median (IQR), y	36.6 (28-50.7)	37.9 (25.7-48.7)	37.6 (26.8-49.7)
Sex, No. (%)			
Female	17 (73.9)	35 (58.3)	52 (62.7)
Male	6 (26.1)	25 (41.7)	31 (37.3)
Phenotype at onset, No. (%)			
Myelitis	10 (43.5)	16 (26.7)	26 (31.3)
Optic neuritis	6 (26.1)	38 (63.3)	44 (53.0)
Optic neuritis + myelitis	5 (21.7)	4 (6.7)	9 (10.8)
Other[a]	2 (8.7)	2 (3.3)	4 (4.8)
EDSS score at onset, median (IQR)	3 (1.3-5)	2 (1-3)	2 (1-4)
No. of relapses, median (IQR)	1 (1-2)	1(1-2)	1 (1-2)
No. of treatments, median (IQR)	1 (1-1.5)	1 (1-2)	1 (1-2)
Prolonged use of oral corticosteroids during disease course, No. (%)			
No	21 (91.3)	53 (88.3)	74 (89.2)
Yes	2 (8.7)	7 (11.7)	9 (10.8)
Time between last administration of oral corticosteroids and discontinuation, median (IQR), y	0.9 (0.8-1)	2.1 (0.6-4)	1.1 (0.8-3.1)
Reason for discontinuation, No. (%)			
Adverse event	2 (8.7)	27 (45.0)	29 (34.9)
Scheduled	21 (91.3)	33 (55.0)	54 (65.1)
Age at discontinuation, median (IQR), y	43.6 (31.9-54)	41.9 (28.6-51.9)	42.6 (28.9-53.3)
Disease duration, median (IQR), y	3.8 (1.7-5.5)	2.1 (0.9-4.6)	2.3 (1.1-4.7)
Treatment duration, median (IQR), y	2.2 (1.3-4)	0.7 (0.2-1.8)	1.3 (0.4-3.5)
Last EDSS score before discontinuation, median (IQR)	2 (1-2.9)	1 (0-2)	1.5 (0-2.3)
Missing data	9	23	32
Time between EDSS score and discontinuation, median (IQR), y	0.2 (0-0.5)	0.2 (0-0.4)	0.2 (0-0.5)
Disease course at discontinuation, No. (%)			
Monophasic	15 (65.2)	37 (61.7)	52 (62.6)
Relapsing	8 (34.8)	23 (38.3)	31 (27.3)
Follow up duration, median (IQR), y	2.2 (1.7-3)	1.7 (0.4-3.3)	1.9 (0.7-3.2)
Oral corticosteroids at discontinuation, No. (%)			
No	23 (100)	58 (96.7)	81 (97.6)
Yes	0	2 (3.3)	2 (2.4)

Abbreviation: EDSS, Expanded Disability Status Scale.

[a] Other included brainstem, optic neuritis + brainstem, and brain involvement + other/unknown.

software version 4.4.2 (R Core Team), a language and environment for statistical computing developed by the R Foundation for Statistical Computing. As this was an exploratory study, no adjustment for multiple comparisons was made.

Results

Description of the Whole Cohort

Overall, 1047 patients with positivity of MOG-Ab were screened and 705 fulfilled inclusion criteria (**Figure 1**). Among them, 378 (53.6%) were female, with a median (IQR) age at disease onset of 37.4 (28.9-51.7) years. The median (IQR) follow-up duration was 2.1 (0.4-4.7) years. The most frequent initial clinical presentation was optic neuritis in 413 patients (58.6%), myelitis in 190 patients (27%) and the association of optic neuritis and myelitis in 47 patients (6.7%); the remaining presentations were brainstem syndrome in 16 (2.3%), other associations in 33 (4.7%), or unknown in 6 patients (0.9%). The median (IQR) baseline EDSS score at nadir was 1 (0-2) (eTable 1 in Supplement 1).

Among 319 patients (45.2%), 425 maintenance therapy initiations were observed after a median (IQR; range) of 1 (1-2; 1-8) relapse. Oral immunosuppressants (n = 222 [52.2%]) and rituximab (n = 149 [35.1%]) were the most frequently initiated therapies. Median time from disease onset to initiation was 0.5 (0.2-1.5) years for oral immunosuppressants and 0.6 (0.2-1.4) years for rituximab (eTable 2 in Supplement 1). IVIG and tocilizumab were initiated in 24 (5.6%) and 16 (3.7%) individuals, respectively. Oral corticosteroids were prescribed in 91 patients (12.9%), including 61 as monotherapy, with a median

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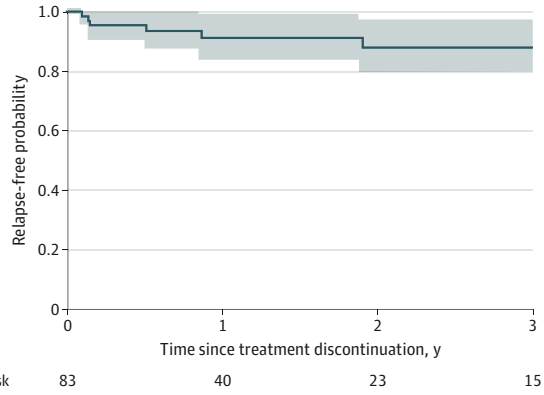
Figure 2. Kaplan-Meier Estimation of the Cumulative Incidence of Relapse Following Treatment Discontinuation



The cumulative incidence of relapse at 1 year was 8.7% (95% CI, 1.0-15.9) following treatment discontinuation.

(IQR) time to initiation of 25.6 (11-110) days, and a median (IQR) duration of 0.3 (0.2-0.5) years.

Treatment Discontinuation

A total of 163 treatment discontinuations were recorded in 131 patients, primarily following the use of oral immunosuppressants (n = 102 [62.6%]) and rituximab (n = 50 [30.7%]). Fewer discontinuations were observed following IVIG (n = 3 [1.8%]), tocilizumab (n = 2 [1.2%]), and other treatments (n = 6 [3.7%]). Treatment was stopped for therapeutic failure in 43 individuals (26.4%), while 14 pregnancy-related discontinuations (8.6%) were observed (eTable 2 in Supplement 1).

Main Analysis

Population Studied

Eventually, 83 discontinuations (50.9%) were analyzed as part of a deescalating strategy (median [IQR] age, 42.7 [28.9-53.3] years; 52 [62.7%] female and 31 [37.3%] male) (**Table 1**). Among them, 60 patients (72.3%) discontinued oral immunosuppressants (azathioprine: n = 34, mycophenolate mofetil: n = 26) and 23 patients (27.7%) discontinued rituximab. Discontinuation was scheduled in 54 patients (65%) and related to adverse events in 29 patients (35%). Rituximab was maintained for a longer duration before discontinuation, with a median (IQR) of 2.2 (1.3-4.0) years, compared to a median (IQR) of 0.7 (0.2-1.7) years for oral immunosuppressants (Table 1). After treatment discontinuation, the median (IQR) follow-up duration without new maintenance therapy initiation was 0.8 (0.2-2.3) years and 1.7 (1.1-2.7) years following rituximab.

Compared with patients who continued maintenance therapy, those who discontinued were more likely to have received oral immunosuppressants as a first treatment (59 patients [40%] vs rituximab in 28 [23.1%]; log-rank $P = .03$), to have a monophasic course at discontinuation (54 [32.9%] vs relapsing in 39 [25.1%]; log-rank $P = .03$) or to have experienced fewer relapses (1 relapse in 54 individuals [32.9%], 2 relapses in 24 [34.3%], ≥3 in 15 [17.6%]; log-rank $P = .008$). However, this difference was primarily driven by patients with 3 or more relapses, who were less represented in the discontinuation group (16.1%) compared with the continuation group (31%). The proportion of patients with 2 relapses, by contrast, was similar between groups (24 [25.8%] vs 46 [20.3%]). Neither initial phenotype nor initial disease severity was associated with discontinuation. Age and residual disability (last available EDSS score) were not associated with discontinuation either (eTable 3 in Supplement 1).

Relapse Risk Following Treatment Discontinuation

A relapse was observed in 7 of the 83 analyzed patients after treatment discontinuation, with a median (IQR; range) time to relapse of 0.5 (0.1-1.4; 0.1-4.0) years. Most relapses (n = 5, [1.4%]) occurred during the first year following treatment withdrawal (eFigure 1 in Supplement 1). The Kaplan-Meier estimated cumulative incidence of relapse at 1 year was 8.7% (95% CI, 1.0-15.9) (**Figure 2**). Relapses were observed following oral immunosuppressants discontinuation in 5 patients (cumulative incidence at 1 year: 10.2%; 95% CI, 0.0-19.3; azathioprine: n = 2, mycophenolate mofetil: n = 3) and following rituximab discontinuation in 2 patients (cumulative incidence at 1 year: 5.6%; 95% CI, 0.0-15.6), with no significant difference in relapse risk between the 2 treatments (log-rank $P = .68$). Similarly, relapse risk did not significantly differ between scheduled or adverse effect-related discontinuation (4 [7.4%] vs 3 [10.4%]; log-rank $P = .34$) (eFigure 2 in Supplement 1). Factors significantly associated with an increased relapse risk were a treatment duration of less than 1 year (7 relapses [19.4%] vs 0; log-rank $P = .002$) and a time since last relapse of less than 2 years (7 relapses [15.9%] vs 0; log-rank $P = .01$), with no relapses observed beyond those thresholds. No significant associations were found with age, sex, disease phenotype at onset, baseline EDSS score at nadir, monophasic or relapsing course, total number of relapses, disease duration, total number of maintenance therapies, prior use of prolonged oral corticosteroids, and last available EDSS score before discontinuation (**Table 2**).

In the subgroup of discontinuation due to adverse events alone, we observed consistent results regarding time since last relapse and treatment duration although statistical significance was lost due to reduced power. Relapse risk was not associated with the disease course or with the total number of previous relapses in this subgroup either (eTable 4 in Supplement 1).

Severity of Relapses Following Treatment Discontinuation

Among the 7 recorded relapses, there were 2 myelitis (28.6%), 2 brainstem syndromes (28.6%), 1 optic neuritis (14.2%) and 2 other phenotypes (28.6%). An EDSS measurement was available at least 1 month after the relapse in 4 patients and was either unchanged (n = 3) or improved (n = 1). In the remaining 3 patients, the last available EDSS score was the one recorded during the relapse and was either improved (n = 1), unchanged (n = 1) or had increased by 1 point (n = 1) compared to the previous assessment. Overall, the median (IQR) change in the EDSS was 0 (0-1) points and the last available EDSS score ranged from 0 to 2.5 (eTable 5 in Supplement 1).

Table 2. Factors Associated With Relapse After Maintenance Therapy Discontinuation

Variable	No. (%)		Log-rank *P* value
	No relapse	Relapse	
Treatment			
Rituximab	21 (91.3)	2 (8.7)	.68
Oral immunosuppressants	55 (91.7)	5 (8.3)	
Oral immunosuppressants			
Azathioprine	32 (94.1)	2 (5.9)	.39
Mycophenolate mofetil	23 (88.5)	3 (11.5)	
Reason for discontinuation			
Adverse event	26 (89.7)	3 (10.3)	.34
Scheduled	50 (92.6)	4 (7.4)	
Sex			
Female	48 (92.3)	4 (7.7)	.53
Male	28 (90.3)	3 (9.7)	
Baseline EDSS score at nadir			
≥1	59 (89.4)	7 (10.6)	.22
0	17 (100)	0	
Baseline EDSS score at nadir			
<4	54 (90)	6 (10)	.22
≥4	22 (95.7)	1 (4.3)	
No. of relapses			
<3	65 (91.5)	6 (8.5)	.46
≥3	11 (91.7)	1 (8.3)	
No. of treatments			
<2	52 (89.7)	6 (10.3)	.81
≥2	24 (96)	1 (4)	
Prolonged use of oral corticosteroids between onset and discontinuation			
No	67 (90.5)	7 (9.5)	.47
Yes	9 (100)	0	
Age at discontinuation, y			
≤40	41 (89.1)	5 (10.9)	.56
>40	35 (94.6)	2 (5.4)	
Age at discontinuation, y			
≤55	61 (89.7)	7 (10.3)	.26
>55	15 (100.0)	0	
Disease duration, y			
<2	31 (86.1)	5 (13.9)	.19
≥2	45 (95.7)	2 (4.3)	
Treatment duration, y			
≥1	47 (100.0)	0	.002
<1	29 (80.6)	7 (19.4)	
Phenotype			
Isolated optic neuritis	42 (95.5)	2 (4.5)	.28
Other phenotypes	34 (87.2)	5 (12.8)	
Disease course			
Monophasic	48 (92.3)	4 (7.7)	.46
Relapsing	28 (90.3)	3 (9.7)	
Time since last relapse, y			
≥2	39 (100.0)	0	.01
<2	37 (84.1)	7 (15.9)	
Last EDSS score before discontinuation			
≥1	33 (94.3)	2 (5.7)	.41
0	16 (100.0)	0	
Last EDSS score before discontinuation			
<4	42 (95.5)	2 (4.5)	.47
≥4	7 (100.0)	0	

Abbreviation: EDSS, Expanded Disability Status Scale.

Discontinuation of Other Maintenance Therapies

Scheduled discontinuations occurred in 3 of 24 patients (12.5%) receiving IVIG and in 1 of 16 patients (6.3%) receiving tocilizumab, respectively. No discontinuations related to adverse events were observed (eTable 2 in Supplement 1). No relapses were recorded following discontinuation of those treatments, with follow-up durations of between 0.8 and 1.8 years after IVIG and 2.4 years after tocilizumab.

Pregnancy-Related Discontinuations

Treatment was discontinued due to pregnancy planning in 14 cases: oral immunosuppressants (n = 6), rituximab (n = 7), and tocilizumab (n = 1). Among these patients, 4 were switched to azathioprine within the first year. One patient experienced a relapse with an interval of 0.85 years after rituximab discontinuation without any switch. Two years after discontinuation, 7 patients of 12 achieving follow-up (58.3%) remained treatment free.

Discussion

In this cohort study of adults with MOGAD, we analyzed the outcomes following maintenance therapy discontinuation. Among the 163 recorded treatment withdrawals, we analyzed the 83 discontinuations that were part of a deescalating strategy, highlighting the frequent use of this practice in clinical settings. We observed a low relapse risk, with an estimated cumulative incidence of 8.7% at 1 year after scheduled or adverse effect-related discontinuation of oral immunosuppressants or rituximab. Relapse risk was significantly decreased in patients with a prior treatment duration of greater 1 year and a time since last relapse of greater than 2 years.

A key finding is the absence of a rebound phenomenon following treatment discontinuation, either in relapse frequency or severity. This contrasts with previous observations of patients with neuromyelitis optica spectrum disorder[15,20] and on patients with multiple sclerosis after the withdrawal of anti-trafficking therapies.[21,22] Data on disease reactivation following treatment withdrawal in patients with MOGAD remain scarce. A study in Korea[16] evaluating treatment discontinuation outcomes in 41 patients found a higher

relapse risk of 24.4% after a median (IQR) interval of 8.2 (6.3-11.5) months. This difference may be partly explained by the heterogeneity of the study population, which included pediatric-onset cases, various treatment regimens, and discontinuation scenarios such as unplanned missed infusion intervals and pregnancy-related interruptions. In addition, the proportion of previously relapsing patients among those who discontinued treatment was higher than in our cohort. In that study, relapsing course was associated with increased relapse risk, a finding not confirmed in our analysis. However, they similarly observed that a treatment duration exceeding 1 year was associated with a reduced relapse risk after discontinuation. This consistency reinforces the validity of this protective effect, which is also consistent with studies[6,23] showing that early and sustained treatment was significantly associated with a reduction in risk of subsequent attacks. We also found that the relapse risk following treatment discontinuation was lower in patients with an interval of more than 2 years since their last attack. This finding aligns with the concept of attack clustering depicted in a substantial number of patients with MOGAD, especially in the first 3 years from disease onset.[5]

In real-world clinical practice, treatment strategies for MOGAD remain heterogeneous. A survey of MOGAD experts revealed that one-fourth of specialists would not consider stopping treatment, while among those open to discontinuation, nearly half would recommend waiting at least 5 years without relapse.[24] Based on our findings, we suggest that treatment discontinuation could be considered with a minimal risk of disease reactivation after at least 2 relapse-free years, aligning with proposed pediatric recommendations.[25] To mitigate the potential impact of relapse, patients should be made aware of the urgency of starting high-dose corticosteroids, considering the effect of treatment delay on recovery.[26]

Limitations

Our study has several limitations. First, its retrospective design may limit the applicability of our results. Patients with a monophasic course were more likely to discontinue treatment, but this difference was mainly driven by the lower rates of discontinuation in patients with 3 or more relapses; some of these patients still discontinued therapy. Moreover, relapse risk after discontinuation was similar between monophasic and relapsing patients, consistent with previous findings that disease course can evolve years after onset. Patients who discontinued treatment were otherwise comparable to those who continued regarding age, initial phenotype, and residual disability. Because baseline MOG-Ab titers were not routinely available to clinicians, we did not analyze this parameter, as it was unlikely to have influenced discontinuation decisions. Given the specific characteristics of pediatric patients in terms of phenotype, relapse risk, and treatment, they were not included in the study, limiting the generalizability of our results to this population.

Our cohort included a high proportion of patients treated with oral immunosuppressants or rituximab. In particular, other treatments, such as tocilizumab or IVIG, were underrepresented, although they are increasingly prescribed in patients with MOGAD with suggested efficacy. However, our findings remain relevant given the worldwide use of oral immunosuppressants. We did not evaluate the discontinuation of oral corticosteroids, which are typically prescribed immediately after the initial attack for a short, predefined period of 4 to 6 months, so that their discontinuation is not an issue in the same way as for other immunosuppressive treatments.

Another limitation concerns follow-up. Median disease duration and follow-up were both relatively short. We voluntarily excluded patients with a first attack prior to 2013 and those treated with multiple sclerosis–specific therapies to ensure a more homogeneous cohort of patients correctly diagnosed with and treated for MOGAD. However, this may have led to the exclusion of some patients with MOGAD whose long-term follow-up would have been informative.

Conclusion

Overall, our findings emphasize that maintenance therapy discontinuation is a frequent and possible strategy in select patients with MOGAD. The low relapse rate and the absence of severe early relapse highlight the potential for sustained remission in selected patients with at least 2 relapse-free years and at least 1 year of treatment exposure. Further prospective studies with longer follow-up and dedicated clinical trials are needed to refine discontinuation strategies and identify factors influencing disease reactivation.

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