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ARTICLE

Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder

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Abstract

Objective

Myelin oligodendrocyte glycoprotein–immunoglobulin G (MOG-IgG) associated disorder (MOGAD) often manifests with recurrent CNS demyelinating attacks. The optimal treatment for reducing relapses is unknown. To help determine the efficacy of long-term immunotherapy in preventing relapse in patients with MOGAD, we conducted a multicenter retrospective study to determine the rate of relapses on various treatments.

Methods

We determined the frequency of relapses in patients receiving various forms of long-term immunotherapy for MOGAD. Inclusion criteria were history of ≥1 CNS demyelinating attacks, MOG-IgG seropositivity, and immunotherapy for ≥6 months. Patients were reviewed for CNS demyelinating attacks before and during long-term immunotherapy.

Results

Seventy patients were included. The median age at initial CNS demyelinating attack was 29 years (range 3–61 years; 33% <18 years), and 59% were female. The median annualized relapse rate (ARR) before treatment was 1.6. On maintenance immunotherapy, the proportion of patients with relapse was as follows: mycophenolate mofetil 74% (14 of 19; ARR 0.67), rituximab 61% (22 of 36; ARR 0.59), azathioprine 59% (13 of 22; ARR 0.2), and IV immunoglobulin (IVIG) 20% (2 of 10; ARR 0). The overall median ARR on these 4 treatments was 0.3. All 9 patients treated with multiple sclerosis (MS) disease-modifying agents had a breakthrough relapse on treatment (ARR 1.5).

Conclusion

This large retrospective multicenter study of patients with MOGAD suggests that maintenance immunotherapy reduces recurrent CNS demyelinating attacks, with the lowest ARR being associated with maintenance IVIG therapy. Traditional MS disease-modifying agents appear to be ineffective. Prospective randomized controlled studies are required to validate these conclusions.

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Glossary

ADEM = acute disseminating encephalomyelitis; **AQP4** = aquaporin-4; **ARR** = annualized relapse rate; **IgG** = immunoglobulin G; **IVIG** = IV immunoglobulin; **MOG** = myelin oligodendrocyte glycoprotein; **MOGAD** = MOG-IgG associated disorder; **MS** = multiple sclerosis; **NMOSD** = neuromyelitis optica spectrum disorder.

Myelin oligodendrocyte glycoprotein (MOG) immunoglobulin G (IgG) associated disorder (MOGAD) is a recently described CNS demyelinating disease that often relapses and has the potential to cause severe morbidity.[1–3] The clinical phenotype can include optic neuritis, transverse myelitis, acute disseminating encephalomyelitis (ADEM), brainstem encephalitis, or combinations thereof.[1,4–8] MOG-IgG typically is not found in serum of patients with classic multiple sclerosis (MS) or aquaporin-4 (AQP4) IgG-positive neuromyelitis optica spectrum disorder (NMOSD).[9,10] Approximately 50% of patients with MOGAD will experience a recurrent demyelinating attack, most commonly optic neuritis.[1,4,8] Prior retrospective studies suggest that long-term immunosuppressant therapy may reduce the frequency of recurrent attacks, while most disease-modifying agents used to treat MS are likely ineffective.[2,11–14] Because there are few large studies on MOGAD long-term therapy, an optimal treatment strategy has not yet been determined. To better define the efficacy of maintenance immunotherapy in preventing recurrent attacks, we evaluated the relapse rates in a large multicenter cohort of patients with relapsing MOGAD who received different treatment modalities.

Methods

This was a multicenter observational retrospective case series of patients with MOGAD who received long-term immunotherapy. Included patients were seen at the Mayo Clinic between January 2001 and April 2019 or elsewhere between 2016 and 2019 with the following criteria: (1) clinically documented history of CNS inflammatory demyelinating disease, (2) seropositive for MOG-IgG1 by transfected cell-binding assay, and (3) received immunotherapy for ≥6 months with follow-up information available to review. Patients were stratified as pediatric (<18 years old) or adult (≥18 years old).

Forty-eight of the 70 study patients were included in earlier reports of autoimmune MOG-IgG optic neuritis, ADEM, and transverse myelitis, in which the primary goal was to describe clinical phenotypes rather than treatment response.[8,15,16]

Standard protocol approvals, registrations, and patient consents

The Mayo Clinic Institutional Review Board approved this retrospective study. For cases contributed by neuro-ophthalmologists from other medical centers, the pertinent institutional review boards approved the study with a waiver of informed consent due to the retrospective nature of the study. Data were shared in a deidentified manner with the lead site.

MOG-IgG assay

All MOG-IgG testing was performed by the Mayo Clinic Neuroimmunology Laboratory (technicians masked to diagnosis) using a flow cytometric cell based assay based on a technique that was previously described.[17] The MOG protein antigen was expressed on the surface of live human HEK293 cells by transient transfection with a recombinant expression vector that coexpressed an independent fluorescent marker protein, AcGFP, via an internal ribosomal entry site, pIRES2. Bound IgG was detected with Alexa Fluor 647–conjugated IgG specific for human IgG1-Fc region. An IgG binding index value ≥2.5 (ratio of median Alexa Fluor 647 fluorescence of green fluorescent protein–positive cells to that of green fluorescent protein–negative cells) was considered positive.[8] Seropositivity was considered persistent when value was ≥2.5 both in the initial sample and after 6 months or, if no sample was available at onset, the positive sample was obtained >1 year after disease onset. AQP4-IgG was tested by previously described live cell–based assay.[18]

Relapse rate and therapeutic efficacy

All patients' medical records were reviewed for number, dates, and types of CNS demyelinating events. A relapse was defined as any new CNS sign/symptom lasting at least 24 hours and supported by clinical examination or radiologic findings.[19] Immunotherapy modality and duration and number of relapses off and on treatment were recorded. Annualized relapse rate (ARR) was calculated as the ratio of the number of demyelinating attacks over years. The index event was excluded in calculations of pretreatment ARR, and patients required observation for at least 3 months before treatment for inclusion in the calculation to avoid an artificially high pretreatment ARR. Attacks were not counted as a relapse on treatment if they occurred within 3 months of starting azathioprine or mycophenolate mofetil or within 1 month of starting rituximab or MS disease-modifying agent due to the therapeutic time lag until peak immunosuppression. Prednisone at a dose of >10 mg daily for >6 months was defined as an adjunct therapy.

Data availability

Anonymized data not published within this article are available from the corresponding author on reasonable request from any qualified investigator.

Results

Seventy patients (59% female) with MOGAD received long-term immunotherapy and met the criteria for inclusion (49

seen at Mayo Clinic; 21 seen by neuro-ophthalmologists elsewhere). Fifty-four (77%) were white; the median age at neurologic symptom onset was 29 years (range 3–61 years; table 1); and 33% were <18 years of age. In 50 of 51 patients (98%) with serial samples or whose initial sample was obtained >1 year after the first demyelinating attack, MOG-IgG was persistently positive. No patient was seropositive for AQP4-IgG.

Fifty-four patients (77%) had at least 1 relapse before initiation of long-term immunotherapy; 47 (67%) had at least 1 relapse on treatment; and 66 (94%) had at least 1 relapse during the total period of observation (i.e., before and after initiation of therapy). The presenting demyelinating attack was isolated optic neuritis in 33 patients (47%), transverse myelitis in 8 (11%), AQP4-IgG–seronegative NMOSD (optic neuritis and transverse myelitis) in 7 (10%), and ADEM with or without optic neuritis/transverse myelitis in 22 patients (31%). Relapses in the follow-up period included optic neuritis in 67 (96%), transverse myelitis in 34 (49%), and ADEM in 28 (40%); 26 patients (37%) were assigned the diagnosis of AQP4-IgG–seronegative NMOSD. The median number of demyelinating attacks was 5 (range 1–11) in a median follow-up period of 4.5 years (range 1–19 years).

The pretreatment ARR was 1.6 attacks per year. Treatment efficacy was evaluated for azathioprine, mycophenolate mofetil, rituximab, maintenance IV immunoglobulin (IVIG), and MS disease-modifying agents (figures 1 and 2 and table 2). The overall posttreatment ARR in patients receiving long-term immunotherapy (excluding MS disease-modifying agents) was 0.3 attacks per year.

Azathioprine

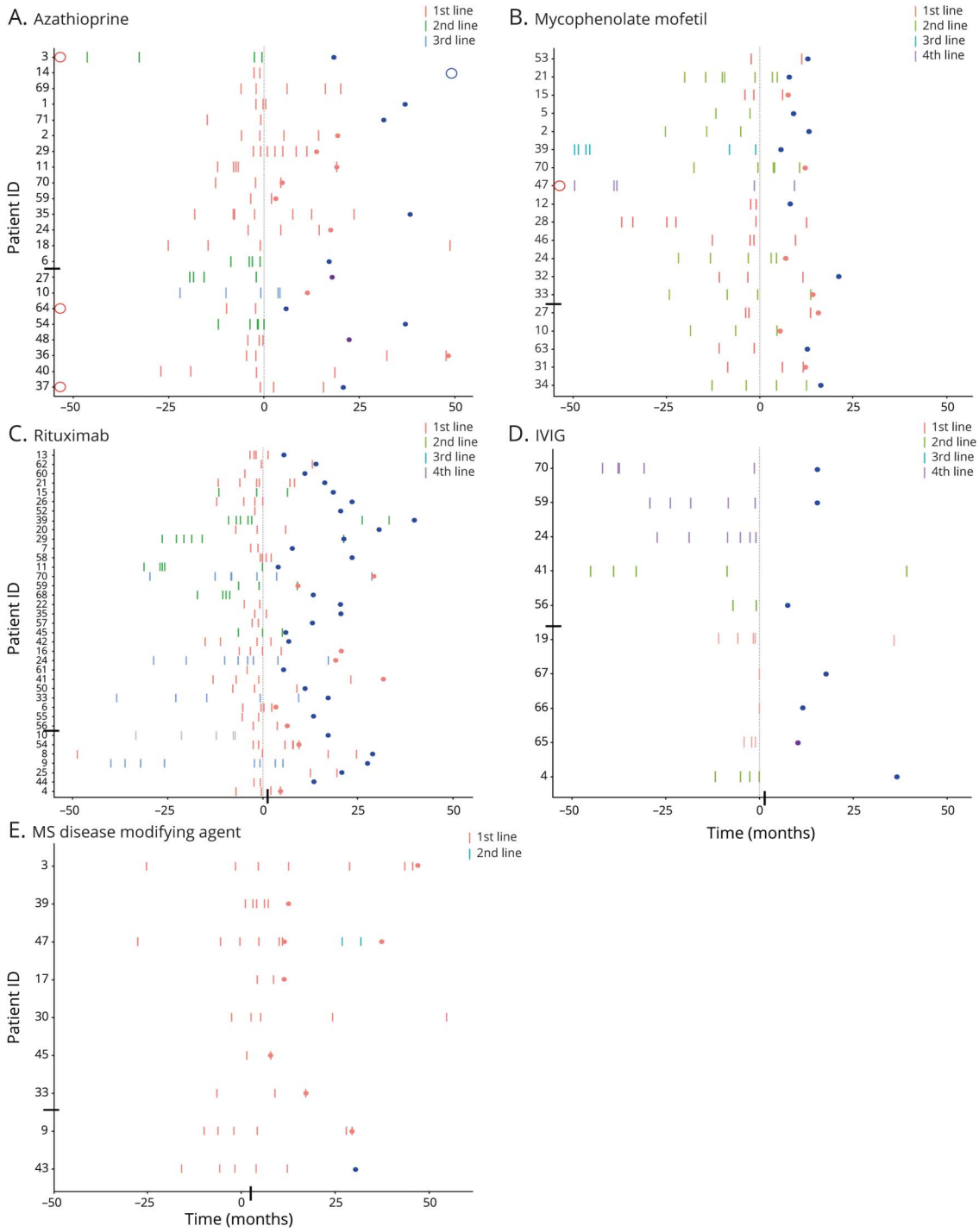
Twenty-two patients (36% pediatric) received azathioprine, 77% as first-line maintenance therapy (figures 1 and 2). Among those receiving azathioprine as their first maintenance

Table 1 Clinical characteristics of the MOGAD cohort

Clinical characteristics	Total cohort (n = 70)	Pediatric cohort (n = 23)	Adult cohort (n = 47)	*p* Value
Age at onset, median (range), y	29 (3–61)	13 (3–17)	40 (19–61)	NA
Female, %	58	61	57	0.79
Ethnicity, %				
White	77	74	79	0.23
Black	4	0	4	
Asian	4	13	0	
Hispanic	6	4	6	
Other/unknown	9	9	11	
Presenting demyelinating attack, n (%)				
ON	33 (47)	11 (48)	22 (47)	0.24
TM	8 (11)	1 (4)	7 (15)	
ON and TM	7 (10)	1 (4)	6 (13)	
ADEM	22 (31)	10 (43)	12 (26)	
Demyelinating attacks (ever), n (%)				
ON	67 (96)	21 (91)	46 (98)	0.10
TM	34 (49)	8 (35)	25 (53)	
ADEM	26 (37)	13 (57)	13 (28)	
Demyelinating attacks, median (range), n	5 (1–11)	5 (1–11)	5 (1–9)	0.34
Follow-up period, median (range), y	4.5 (1–19)	6.3 (1–19)	3.2 (1–18)	0.03
Pretreatment ARR (range)	1.6 (0–9.7)	1.3 (0–9.7)	2.2 (0.1–9.0)	0.84
ARR on treatment (range)	0.32 (0–1.9)	0.2 (0–1.7)	0.35 (0–1.9)	0.58

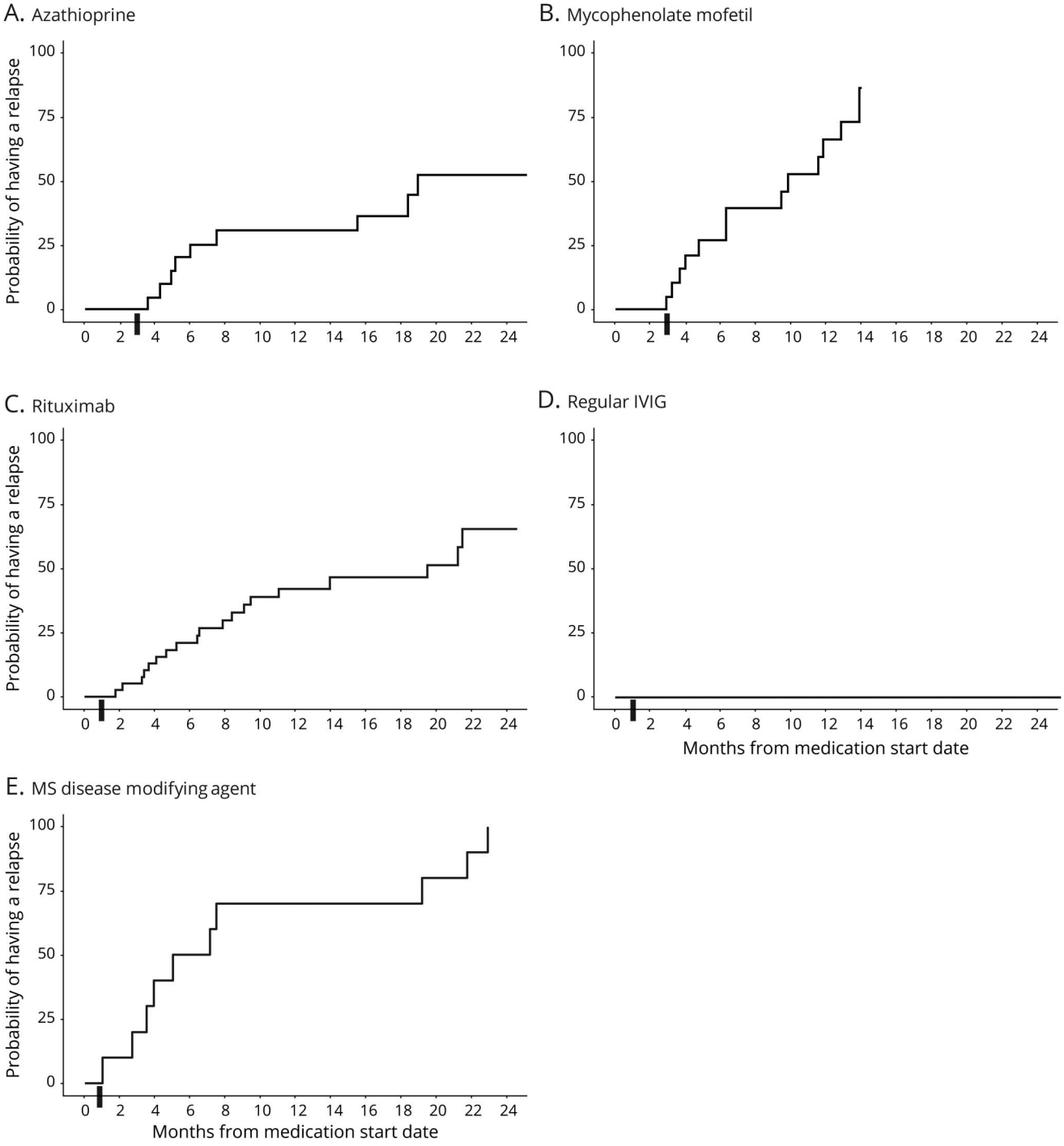
Abbreviations: ADEM = acute disseminating encephalomyelitis; ARR = annualized relapse rate; MOGAD = myelin oligodendrocyte glycoprotein–immunoglobulin G associated disorder; NA = not available; ON = optic neuritis; TM = transverse myelitis.
The *p* value is for the comparison between the pediatric and adult cohorts.

Figure 1 Disease activity of patients with MOG-IgG associated disorder on maintenance immunotherapy



Depictions of attacks before and after maintenance immunotherapy was started (time 0) for patients treated with (A) azathioprine, (B) mycophenolate mofetil, (C) rituximab, (D) maintenance IV immunoglobulin (IVIG), and (E) multiple sclerosis (MS) disease-modifying agents. Each dash represents a demyelinating attack (red indicates first-line therapy; green, second-line therapy; blue, third-line therapy; purple, fourth-line therapy). Red circle indicates immunotherapy switch, and purple indicates cessation of treatment. Blue circle indicates the last follow-up evaluation. The y-axis has the patient identifiers (IDs) arranged from old to young with a line demarking the split between adult and pediatric patients. Red open circle adjacent to the y-axis indicates relapses that occurred >50 months before the immunotherapy was started. Blue open circle at the right of the plot indicates a relapse >50 months after the immunotherapy was started. Dash along the x-axis demarks when the maintenance immunotherapy becomes fully active and a relapse is considered a failure of therapy. As an example, the top line (patient 3) in panel A shows an individual who was treated with azathioprine as a second-line therapy. Within the 50 months before starting azathioprine, the patient had 4 attacks (green hashmarks) while on a MS disease-modifying agent (E), and the red circle adjacent to the y-axis indicates there were relapses >50 months before azathioprine was initiated. At time point 0, the patient was changed to azathioprine and did not have any relapses over the 2 years of follow-up (blue circle).

Figure 2 Kaplan–Meier estimates of time to relapse on different maintenance therapies



Kaplan Meier curves showing time to relapse for patients treated with (A) azathioprine, (B) mycophenolate mofetil, (C) rituximab, (D) maintenance IV immunoglobulin (IVIG), and (E) multiple sclerosis (MS) disease-modifying agents. dash Along the x-axis demarks when the maintenance immunotherapy becomes fully active and a relapse is considered a failure of therapy.

therapy, 11 of 17 (64.7%) relapsed. Among the 5 patients receiving azathioprine as a second or later maintenance therapy, 2 patients relapsed. Overall, 13 of 22 (59%) had a relapse (median 1 attack [range 0–3], median follow-up period 1.7 years). Overall median ARR was 0.2 (range 0–3.2); median ARR was 0 (range 0–2.2) for pediatric patients and 0.43 (range 0–3.4) for adult patients (table 2). Ten of 20 (50%) received adjunct prednisone therapy for >6 months.

Mycophenolate mofetil

Nineteen patients (21% pediatric) received mycophenolate mofetil, 47% as first-line maintenance therapy (figures 1 and 2).

Table 2 Summary of maintenance immunotherapy modalities used for the MOGAD cohort

Medication	Patients, n (%)	Median age, y	Used as first-line therapy, n (%)	Pretreatment median ARR	Patients who relapsed, n (%)	Posttreatment median ARR	Median relapses, n	Time on medication, y
Mycophenolate mofetil	19	33.5 (13–58)	9 (47)	1.9 (0–9.7)	14 (74)	0.67 (0–5.2)	1 (0–2)	1.1
Pediatrics	4 (21)	14.6 (13–17.1)	3 (75)	2.1 (0–9.7)	3 (75)	1.5 (0–3.4)	1 (0–3)	1.1
Adults	15 (79)	44.1 (22–58)	6 (40)	1.9 (0–9.0)	11 (73)	0.4 (0–5.2)	1 (0–3)	1.1
Azathioprine	22	26.7 (4–58)	17 (77)	1.2 (0–9.7)	13 (59)	0.2 (0–3.2)	1 (0–3)	1.7
Pediatrics	8 (36)	15.5 (4–17.1)	5 (63)	0.9 (0–9.7)	4 (50)	0 (0–2.2)	0 (0–3)	1.7
Adults	14 (64)	45.5 (21–58)	12 (86)	1.4 (0–6.9)	9 (64)	0.43 (0–3.4)	1.5 (0–3)	1.8
Rituximab	37	33 (6–61)	25 (69)	1.8 (0–9.0)	22 (61)	0.59 (0–6.8)	1 (0–3)	1.2
Pediatrics	7 (19)	13.1 (3.1–16.1)	5 (71)	0.8 (0.1–3.4)	4 (57)	0.86 (0–5.1)	2 (0–2)	1.2
Adults	30 (81)	40 (19–61)	20 (67)	2.4 (0–9.0)	18 (62)	0.59 (0–6.8)	1 (0–3)	1.2
IVIG	10	18.2 (3–43)	4 (40)	2.8 (0–7.2)	2 (20)	0 (0–0.2)	0 (0–1)	1.2
Pediatrics	5 (50)	8.1 (3.1–17.4)	4 (80)	4.4 (0–7.2)	1 (20)	0 (0–0.2)	0 (0–1)	1.5
Adults	5 (50)	26.4 (19–43)	0 (0)	1.0 (0–2.8)	1 (20)	0.1 (0–0.2)	0 (0–1)	1.2
MS disease-modifying agents	9	32.3 (5–57.5)	9 (100)	1.8 (0–3.3)	9 (100)	1.5 (0.2–4.5)	2 (1–5)	1.5
Pediatrics	2 (22)	9.2 (5–13.1)	2 (100)	2.8 (2.3–3.2)	2 (100)	0.61 (0.2–1.0)	1.5 (1–2)	3.2
Adults	7 (78)	38.1 (22–57.5)	7 (100)	1.2 (0–3.3)	7 (100)	1.97 (0.3–4.5)	2 (1–5)	0.9

Abbreviations: ARR = annualized relapse rate; IVIG = IV immunoglobulin; MOGAD = myelin oligodendrocyte glycoprotein–immunoglobulin G associated disorder; MS = multiple sclerosis.

Among those receiving mycophenolate mofetil as their first maintenance therapy, 7 of 9 (77.8%) relapsed. Among the 10 patients receiving mycophenolate as a second or later maintenance therapy, 7 patients relapsed. Overall, 14 of 19 (74%) had a relapse (median 1 attack [range 0–2], median follow-up period 1.1 years). Overall median ARR was 0.67 (range 0–3.4); median ARR was 1.5 (range 0–3.4) for pediatric patients and 0.4 (range 0–5.2) for adult patients (table 2). Two of 19 (11%) received adjunct prednisone therapy for >6 months. The single patient with transient MOG-IgG positivity received mycophenolate mofetil and did not relapse.

Rituximab

Thirty-seven patients (19% pediatric) received rituximab, 68% as first-line maintenance therapy (figures 1 and 2). Among those receiving rituximab as their first maintenance therapy, 14 of 25 (56%) relapsed. Among the 12 patients receiving rituximab as a second or later maintenance therapy, 9 patients relapsed. Overall, 23 or 37 (62%) had a relapse (median 1 attack [range 0–3], median follow-up period 1.2 years). Overall median ARR was 0.59 (range 0–6.8); median ARR was 0.9 (range 0–5.1) for pediatric patients and 0.59 (range 0–6.8) for adult patients (table 2). Five of 36 (14%) received adjunct prednisone therapy for >6 months.

Maintenance IVIG

Ten patients (50% pediatric) received IVIG maintenance therapy (3 at interval of 3 weeks and 7 monthly), 40% as first-line maintenance therapy (figures 1 and 2). Among those receiving IVIG as their first maintenance therapy, 0 of 4 (0%) relapsed. Among the 6 patients receiving IVIG as a second or later maintenance therapy, 2 patients relapsed. Overall, 2 of 10 patients (20%) relapsed with a median follow-up period of 1.2 years. Overall median ARR was 0 (range 0–0.2); median ARR

was 0 (range 0–0.2) for pediatric and 0.1 (range 0–0.2) for adult patients (table 2). Two patients (20%) received adjunct prednisone therapy for >6 months.

Cyclophosphamide

Three patients (100% pediatric) received IV cyclophosphamide, 2 (67%) as first-line maintenance therapy. Among the 2 receiving cyclophosphamide as a first maintenance therapy, 1 of 2 (50%) relapsed. Overall, 2 patients (67%) relapsed while receiving cyclophosphamide, and both were later controlled by rituximab therapy.

MS disease-modifying agents

Nine patients (22% pediatric) received MS disease-modifying agents as first-line maintenance therapy: interferon beta-1a (n = 5) and glatiramer acetate (n = 4) (figures 1 and 2). All 9 patients relapsed while being treated with these agents; median ARR was 1.5 (range 0.2–4.5). One patient received fingolimod (n = 1) as a second-line agent after relapsing on interferon beta-1a and also relapsed while on fingolimod. One patient met 2017 McDonald criteria for MS diagnosis.

Discussion

This large multicenter cohort of MOG-IgG–positive patients demonstrates that maintenance immunotherapy was associated with a reduction in recurrent demyelinating attacks in both pediatric and adult patients, in contrast to those who received traditional MS disease-modifying agents (which appeared to be ineffective). Consistent with published reports, ADEM was more common in children with MOGAD than in adults.[1,13] Although pediatric MOGAD is often monophasic,[20] our pediatric cohort of patients had as high a pretreatment ARR as the adult cohort because the inclusion criteria of the study (requiring at least 6 months of maintenance immunotherapy) enriched for relapsing disease in both the pediatric and adult cohorts.

Maintenance IVIG (at 3- or 4-week intervals) was associated with the greatest reduction in relapse rate; only 20% of patients had a relapse (albeit only 10 patients were treated with IVIG in this study). In contrast, >50% of patients receiving other medications had relapses. Patients receiving maintenance IVIG had a pretreatment ARR similar to that in other treatment groups, suggesting that IVIG was more effective in suppressing attacks rather than there being a bias toward using IVIG in patients with more benign disease. In comparison, Ramanathan et al.[13] reported, from a review of the efficacy of immunotherapy for MOGAD in an Australian cohort, that the relapse rate was higher (3 of 7 patients) in patients receiving long-term IVIG therapy. However the median ARR for their cohort was 0, and the highest relapse rate in patients treated with IVIG was the lowest among the treatments evaluated (range 0–0.75). In addition, the relapse rate observed for their IVIG recipient group was lower than the relapse rate in the other immunotherapy modalities evaluated in our study. Other reports support the use of IVIG as maintenance therapy for MOGAD. Tsantes et al.[21] reported a patient with severe relapsing MOGAD who was unresponsive to all medications except IVIG at intervals of 3 weeks, similar to our observation in some of our patients. Hacohen et al.[11] retrospectively evaluated a cohort of pediatric patients with MOGAD and also found that maintenance IVIG was the most efficacious therapy for preventing relapse. Five of the 10 patients in our IVIG cohort were pediatric, which is further confirmation of the efficacy of this maintenance treatment modality at least for children. In sum, all of these studies support our findings that long-term IVIG is an effective maintenance immunotherapy for patients with MOGAD. They also make IVIG a strong candidate for study in a randomized controlled clinical trial. The recently reported efficacy of efgartigimod, a synthetic IgG1 Fc analog, as a substitute for IVIG in treating the IgG-mediated neuromuscular disorder myasthenia gravis[22] justifies consideration of its use in such a trial.

We found that azathioprine had the second lowest posttreatment ARR. However, the slightly lower pretreatment ARR for recipients of azathioprine compared to patients receiving the other therapies suggests that patients treated with azathioprine may have had more benign disease. In addition, a higher percentage of patients treated with azathioprine were receiving maintenance prednisone, which may have contributed to the apparently greater efficacy of azathioprine.

A recent multicenter study reported that rituximab reduces the relapse rate for MOGAD, but the benefit did not appear to be as great as for AQP4-IgG–positive NMOSD.[23] That observation concurs with our clinical experience, namely that maintenance therapy with rituximab is associated with a reduction in recurrent disease but that relapses can still occur.

Consistent with the reported Australian cohort,[13] mycophenolate mofetil conferred a more modest reduction in MOGAD relapses than the other agents that we compared for maintenance immunotherapy efficacy. However, the smaller numbers of patients in whom mycophenolate was used as first-line maintenance therapy compared to azathioprine and rituximab may have introduced bias toward patients with more severely relapsing disease, despite the groups having similar pretreatment ARRs. Cobo-Calvo et al.[14] recently reported a significant reduction in relapses in patients treated with mycophenolate mofetil in a cohort of Spanish and French adult patients with relapsing MOGAD. The fact that relapses occurred with almost all immunotherapy modalities emphasizes the need for randomized trials to determine the best treatment.

The overall higher relapse rate for all patients in the group receiving traditional MS disease-modifying agents is consistent with lower efficacy than for other immunotherapies, as has been reported by several groups.[2,11,12,14] This observation further supports that MOGAD is a different disease entity

from MS. However, our limited dataset did not reveal an increased relapse rate in patients with MOGAD who received MS disease-modifying agents. In contrast, there have been multiple reports that AQP4-IgG–positive NMOSD is worsened when treated with MS disease-modifying agents.[24]

Cyclophosphamide is one of the most potent immunosuppressive agents commonly used for managing immune-mediated CNS processes such as CNS vasculitis.[25] However, 2 of 3 patients had relapses during treatment with cyclophosphamide in our cohort. Similarly, 1 of 2 patients failed cyclophosphamide in the Australian cohort.[13] While the overall number of patients treated with IV cyclophosphamide is low, this lack of apparent efficacy may suggest that cytotoxic CD8 T cells are not key effectors of MOGAD pathogenesis. Alternatively, cyclophosphamide is often reserved for the most severe cases; therefore, its apparent failure may represent a bias toward its use in more refractory disease. However, the observation that 2 patients who experienced early relapses while receiving cyclophosphamide stabilized without further relapse when switched to rituximab suggests that cyclophosphamide may not be effective for MOGAD.

Limitations of this study include its retrospective nature, the variable periods of follow-up, and the selection of therapy by treating physician (potentially biasing assignment of therapy by personal practice experience or patient or disease characteristics, including cost and convenience of therapy). For example, maintenance IVIG was used as a first-line therapy in 40% of patients, while azathioprine was used as first-line treatment in 77%. In addition, the number of patients treated with IVIG was lower than that of the other treatments, and half of the patients treated with maintenance IVIG were pediatric, which could have biased apparent efficacy. However, the pretreatment ARR for the pediatric IVIG cohort was one of the highest among all groups. Being drawn mostly from tertiary care centers, the cohort was likely biased to more severe and recurrent disease by referral. This was reflected in the high percentage of patients with persistent MOG-IgG positivity, which has been associated with higher relapse risk.[1,15,26,27] Therefore, conclusions drawn from this study about the efficacy of immunotherapy apply best to MOG-IgG–positive patients with recurrent disease. Lastly, while qualitative comparisons between ARR can be made, statistical comparison is curtailed by the nonrandomized assignment of patients to treatment groups and the overlap between treatment groups (i.e., a single patient receiving multiple therapies would be counted in multiple groups).

In conclusion, long-term immunotherapy was associated with a reduction in relapse rate in this population of patients with MOGAD with relapsing disease. Traditional disease-modifying agents used for MS did not prevent or increase the relapse rate. Maintenance IVIG could be considered a promising candidate therapy for preventing relapse. Future prospective randomized controlled trials of relapse prevention medications are warranted for MOGAD.

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Disclosure

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Jiraporn Jitprapaikulsan, MD	Mayo Clinic, Rochester, MN	Acquisition of data; interpreted the data; revised the manuscript for intellectual content
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James P. Fryer, MS	Mayo Clinic, Rochester, MN	Interpreted the data; revised the manuscript for intellectual content
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Vanda A. Lennon, MD, PhD	Mayo Clinic, Rochester, MN	Interpreted the data; revised the manuscript for intellectual content
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Continued

Appendix *(continued)*

Name	Location	Contribution
Byron L. Lam, MD	Bascom Palmer Eye Institute, University of Miami, FL	Acquisition of data; interpreted the data; revised the manuscript for intellectual content
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Sean J. Pittock, MD	Mayo Clinic, Rochester, MN	Acquisition of data; interpreted the data; revised the manuscript for intellectual content

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