












OPEN ACCESS

Original research

Apheresis therapies in MOGAD: a retrospective study of 117 therapeutic interventions in 571 attacks

Carolyn Schwake ¹, Theodoros Ladopoulos,¹ Vivien Häußler ², Ingo Kleiter,³ Marius Ringelstein ^{4,5}, Orhan Aktas,⁴ Tania Kümpfel ⁶, Daniel Engels ⁶, Joachim Havla ⁶, Martin W Hümmert ⁷, Julian Reza Kretschmer,⁷ Daria Tkachenko,⁷ Corinna Trebst,⁷ Ana Beatriz Ayroza Galvão Ribeiro Gomes,⁸ Anne-Katrin Pröbstel,⁸ Mirjam Korporal-Kuhnke,⁹ Brigitte Wildemann,⁹ Sven Jarius,⁹ Refik Pul,¹⁰ Mosche Pomsch,¹¹ Markus Krämer,¹¹ Florian Then Bergh,¹² Clemens Gödel,¹² Patricia Schwarz,¹³ Markus C Kowarik,¹³ Paulus Stefan Rommer ¹⁴, Ioannis Vardakas,¹⁵ Makbule Senel ¹⁵, Alexander Winkelmann,¹⁶ Nele Retzlaff,¹⁶ Martin S Weber,^{17,18,19} Leila Hussein,¹⁸ Annette Walter,²⁰ Patrick Schindler,^{21,22,23} Judith Bellmann-Strobl,^{21,22} Friedemann Paul,^{21,22,23} Ralf Gold,¹ Ilya Aizenberg,¹ Neuromyelitis Optica Study Group (NEMOS)²⁴

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/jnnp-2024-334863>).

For numbered affiliations see end of article.

Correspondence to
Dr Ilya Aizenberg; ilya.aizenberg@rub.de

Received 19 August 2024
Accepted 14 October 2024

ABSTRACT

Background Incomplete attack remission is the main cause of disability in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). Apheresis therapies such as plasma exchange and immunoadsorption are widely used in neuroimmunology. Data on apheresis outcomes in MOGAD attacks remain limited.

Methods We retrospectively evaluated all apheresis treated attacks occurring in patients with MOGAD between 2008 and 2023 at 18 Neuromyelitis Optica Study Group centres. Treatment response was categorised as complete, partial or no remission. Preattack and follow-up Expanded Disability Status Scale (EDSS) and visual Functional System Scores (FSS) were used to calculate absolute outcomes (Δ EDSS/ Δ visual FSS). Predictors of complete remission were analysed using a generalised linear mixed model.

Results Apheresis was used for 117/571 (20.5%) attacks in 85/209 (40.7%) patients. Attacks with simultaneous optic neuritis and myelitis were treated more often with apheresis (42.4%, n=14) than isolated myelitis (25.2%, n=35), cerebral manifestation (21.0%, n=17) or isolated optic neuritis (17.6%, n=51). Apheresis was initiated as first-line therapy in 12% (4.5 (IQR 0–11) days after attack onset), second-line therapy in 62% (15 (IQR 6.75–31) days) and third-line therapy in 26% (30 (IQR 19–42) days). Complete remission was achieved in 21%, partial remission in 70% and no remission in 9% of patients. First-line apheresis (OR 2.5, p=0.040) and concomitant disease-modifying therapy (OR 1.5, p=0.011) were associated with complete remission. Both parameters were also associated with a favourable Δ EDSS. No differences in outcomes were observed between the apheresis types.

Conclusion Apheresis is frequently used in MOGAD attacks. An early start as first-line therapy and concomitant disease-modifying therapy predict full attack recovery.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Apheresis therapies are effective for treating disease attacks in multiple sclerosis and neuromyelitis optica spectrum disorder, with early intervention being crucial for better outcomes; however, data in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are limited.

WHAT THIS STUDY ADDS

⇒ This multicentre study demonstrates that apheresis therapies are commonly used in MOGAD attacks and identified early first-line apheresis therapy and prior disease-modifying treatment as two significant predictors of full attack recovery.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the importance of early initiation of apheresis therapy and the use of disease-modifying treatments in patients with MOGAD with recurrent disease attacks.

INTRODUCTION

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare autoimmune-inflammatory disease of the central nervous system (CNS). Despite a partial overlap in its clinical presentation with multiple sclerosis (MS) and aquaporin-4-IgG positive (AQP4-IgG⁺) neuromyelitis optica spectrum disorder (NMOSD), there are significant pathophysiological and clinical differences between these entities.¹

In contrast to MS, the accrual of disability in MOGAD is predominantly linked to disease attacks.² Although patients recover significantly



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Schwake C, Ladopoulos T, Häußler V, et al. *J Neurol Neurosurg Psychiatry* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jnnp-2024-334863

better from attacks than patients with AQP4-IgG⁺ NMOSD, relevant residual deficits are still common.³ Persistent visual impairment after optic neuritis (ON) has been reported in 7–24%,^{4–6} impaired ambulation in 14–25%^{6–7} and bladder dysfunction due to myelitis (MY) in 20–59% of patients with MOGAD.^{4–5} Cerebral manifestations are also possible and may result in long-term cognitive impairment, especially in patients with acute disseminated encephalomyelitis.^{8–9} Thus, prevention and optimal treatment of MOGAD attacks are crucial for preventing disability. While intravenous methylprednisolone (IVMP) is generally effective, some attacks remain corticosteroid refractory and require apheresis.¹⁰

Apheresis procedures such as plasma exchange (PLEX) and immunoadsorption (IA) have been reported to be highly effective in NMOSD^{11–12} and MS.¹³ In NMOSD, the very early use of apheresis (immediately after the onset of the attack) is considered even more critical, as previous studies have shown that early intervention significantly influences the clinical outcome.^{11–14} Thus, the American Society for Apheresis strongly recommends PLEX (grade 1B) and IA (grade 1C) for the treatment of NMOSD

attacks.¹⁵ Moreover, both treatment methods are included in the treatment guidelines of the Neuromyelitis Optica Study Group (NEMOS) and Guidelines of the German Neurological Society.¹⁶

Despite several studies on apheresis in MS and NMOSD,^{11–17–20} data on clinical outcomes after apheresis in acute MOGAD attacks remain lacking. Therefore, this study aimed (a) to describe clinical characteristics of attacks treated with apheresis in a large multicentre MOGAD cohort and (b) to identify variables predicting favourable post-apheresis outcomes.

MATERIALS AND METHODS

Patients with MOGAD were identified through the NEMOS registry (209 patients with 571 attacks) and all 85 patients who underwent PLEX and/or IA between January 2008 and December 2023 at 18 specialised centres in Germany, Switzerland and Austria were included in this retrospective, multicentre, cross-sectional study (figure 1). MOGAD was diagnosed at the respective centres with MOG-IgG testing by cell-based assays (CBA) at the discretion of each centre using the laboratory’s

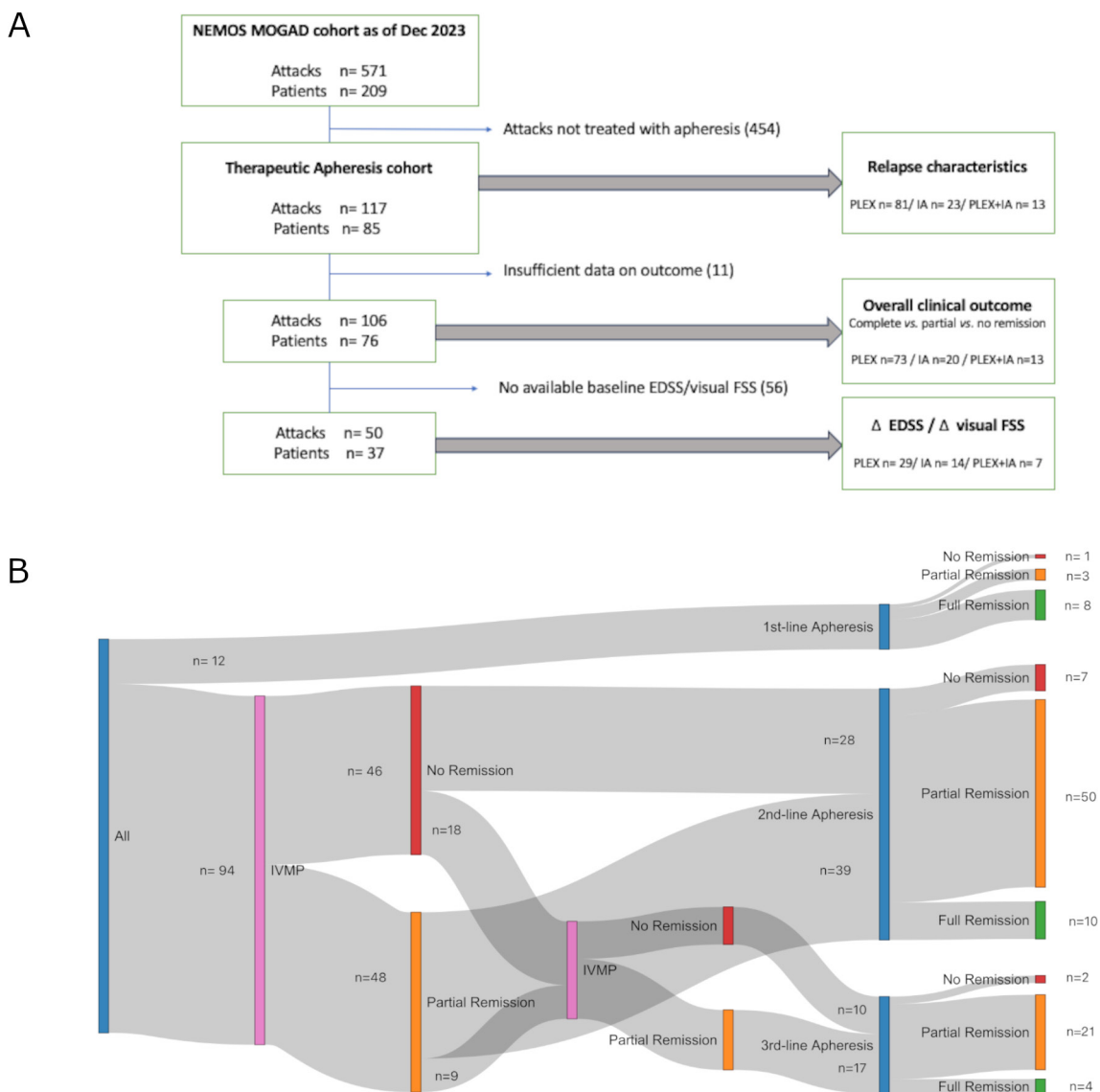


Figure 1 Study flow chart (A). Patient trajectories across attack treatments (n=106) (B). EDSS, Expanded Disability Status Scale; FSS, Functional System Score; IA, immunoadsorption; IVMP, intravenous methylprednisolone; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; NEMOS, Neuromyelitis Optica Study Group; PLEX, plasma exchange.

cut-offs (EUROIMMUN, Lübeck, Germany, fixed CBA, $\geq 1:10$; Medical University of Innsbruck, Innsbruck, Austria, live CBA, $\geq 1:160$; Labor Krone, Bad Salzflun, Germany, live CBA, $\geq 1:160$; Research Center for Neuroimmunology and Neuroscience, University of Basel, Basel, Switzerland, live CBA, flow cytometry, mean fluorescence intensity ≥ 3.0).

Demographic, clinical and apheresis-related data were retrieved from the NEMOS registry and supplemented through an experienced physician at the according site via review of medical records between March and October 2023.

This study followed the reporting guideline ‘Strengthening the Reporting of Observational Studies in Epidemiology’.

Main outcome and measures

Characteristics of all patients with MOGAD treated with PLEX and/or IA were analysed. Where available, clinical outcomes were further investigated to identify factors associated with a favourable post-apheresis result.

The clinical outcome was categorised into three groups¹²: (1) complete remission (disappearance of attack symptoms compared with baseline), (2) partial remission (gain in function without reaching the baseline) or (3) no remission (no neurological recovery).

If detailed clinical data on functional scores from the last study visit preceding and the first follow-up (FU) visit after the attack were accessible, we calculated the absolute clinical outcome using the following equation: $\Delta\text{visual FSS or } \Delta\text{EDSS} = \text{Follow-up score} - \text{baseline score}$. As the overall Expanded Disability Status Scale (EDSS) might not sufficiently represent visual impairments, we specifically assessed $\Delta\text{visual Functional System Score (FSS)}$ in the ON subgroup.

Statistical testing

Statistical analyses were performed using SPSS V.29.0 (IBM) and R (V.4.4.0) with a significance threshold set at $p < 0.05$. Continuous variables were compared using non-parametric statistical tests (Mann-Whitney U test for two groups, Kruskal-Wallis test for more than two groups). Correlation analysis was conducted using Spearman correlation. The χ^2 test was used to assess the association between two categorical variables.

Predictors of a favourable clinical outcome were identified through multivariate analysis using a generalised linear mixed model (GLMM). This model was employed to accommodate patients who underwent multiple apheresis therapies during their lifetime. Age, gender, line of therapy, type of apheresis, disease duration, disease-modifying therapy (DMT; yes/no), attack phenotype (ON/MY) and dosage of previous IVMP were defined as independent variables. Out of 106 attacks with known outcomes, 100 had complete data for all variables in the GLMM. A complete case analysis was implemented for the GLMM to ensure the robustness of our findings while minimising potential biases.

RESULTS

Cohort characteristics

209 patients of the whole NEMOS MOGAD cohort (female:male=130:79, median age at disease onset 33.5 (IQR 23.0–46.0) years) experienced 571 attacks (ON: n=289, MY: n=139, cerebral manifestation: n=81, simultaneous ON+MY: n=33, other: n=29) during a median disease duration of 5.8 years (IQR 3.2–11.1). Among these, 117 (20.5%) attacks in 85 (40.7%) patients were treated with apheresis (table 1). 80 of 85 patients

Table 1 Patient characteristics (n=209)

	Apheresis (n=85)	Non-apheresis (n=124)	P value
Female sex, n (%)	51/85 (60.0)	79/124 (63.7)	0.587*
Autoimmune comorbidities	12/72 (17.0%)	14/119 (11.3%)	0.378*
Ethnicity	n=80	n=110	0.846*
White	74/80 (93.0%)	104/110 (94.5%)	
Asian	1/80 (1.0%)	2/110 (1.8%)	
Arabic	4/80 (5.0%)	3/110 (2.4%)	
Hispanic (America)	1/80 (1.0%)	1/110 (0.8%)	
Clinical characteristics			
Age at disease onset, year, median (IQR)	34 (22.0–49.0) (n=83)	33 (23.0–43.0) (n=118)	0.254†
Apheresis at first attack, n (%)	50/85 (58.8)	–	
Age at apheresis, year, median (IQR)	38 (26.3–50.0) (n=80)	–	
Disease duration, year, median (IQR)	6.0 (3.7–9.9) (n=84)	5.5 (2.9–12.7) (n=118)	0.747†
Overall number of attacks	297 (n=85)	274 (n=118)	
Number of attacks treated with apheresis	117 (n=85)	–	
ARR until last FU, median (IQR)	0.4 (0.2–0.9) (n=84)	0.3 (0.2–0.6) (n=118)	0.109†
EDSS at last FU	2 (1.4–4.0) (n=82)	1.5 (1.0–2.5) (n=113)	<0.001†
* χ^2 test.			
†Mann-Whitney U test.			
ARR, annual relapse rate; EDSS, Expanded Disability Status Scale; FU, follow-up.			

(94%) fulfilled the recently proposed international MOGAD diagnostic criteria (supplemental table 1).²¹

Patient gender, ethnicity, occurrence of autoimmune comorbidities, age at disease onset, disease duration and annual relapse rate (ARR) at last FU did not differ between the non-apheresis and the apheresis cohort. However, the median EDSS at the last FU visit was significantly lower in the non-apheresis than in the apheresis group (1.5 vs 2.0, $p < 0.001$) (table 1).

Apheresis was initiated most frequently in multifocal attacks with simultaneous ON+MY (14/33, 42.4%), followed by MY (35/139, 25.2%), cerebral manifestation (17/81, 21.0%) and ON (51/289, 17.6%). 69 patients were treated with apheresis therapy once and further 16 patients for multiple (median 2.5 (IQR 2.0–5.0)) attacks.

81 attacks (69%) were treated with PLEX (median 5.0 (IQR 5.0–7.0) sessions), 23 (20%) with IA (median 6.0 (IQR 5.0–7.0) sessions) and 13 (11%) with a combination of PLEX and IA (median 2.0 (IQR 1.5–5.0) PLEX sessions; median 3.0 (2.5–4.5) IA sessions). Apheresis was administered as first-line therapy in 14 (12%), second-line therapy in 73 (62%) and third-line therapy in 30 (26%) attacks.

Among the 14 attacks receiving apheresis as first-line therapy, only two occurred at disease onset. All other first-line treated attacks occurred in patients already diagnosed with MOGAD; four of whom had a history of apheresis treatment.

The remaining 103 out of 117 attacks were initially treated with IVMP (cumulative median corticosteroid dose 5000 (IQR 5000–10 000) mg). The majority received one IVMP pulse (71% second-line apheresis, median corticosteroid dose 5000 (IQR 5000–5000) mg), while the rest received two IVMP pulses (29%

third-line apheresis, median corticosteroid dose 13 000 (IQR 9000–15 000)mg).

Only two attacks were treated with a combination of IVMP and intravenous immunoglobulins (125 and 145 g) before undergoing apheresis. 77/117 (65.8%) attacks occurred without concomitant DMT use and of these 50 (64.9%) at disease onset. Among patients with DMT use, B-cell depletion therapy was present in 17/117 attacks (14.5%), anti-interleukin-6 receptor therapy in 2 attacks (1.7%), azathioprine in 8 attacks (6.8%), mycophenolate mofetil in 4 attacks (3.4%) and a total of 9 attacks (7.7%) occurred during therapy with other MS-typical DMTs.

Clinical outcomes following apheresis therapy

The overall clinical outcome was available in 106/117 attacks (47 ON, 32 MY, 13 ON+MY, 14 cerebral manifestation) of 76 patients (female:male=45:31, median age at apheresis 38.0 (IQR 27.0–50.0) years) which were treated with 73 PLEX, 20 IA and 13 combined PLEX/IA procedures. Complete remission was achieved in 22 patients (21%), most patients improved partially (70%, n=74) and almost one in 10 patients did not improve at all (9%, n=10).

We could not identify any difference in remission status among the three types of apheresis (p=0.161, n=106), nor when comparing PLEX versus IA separately (p=0.315, n=93). There was no difference in remission status according to attack phenotypes (p=0.360) or focal/multifocal symptom manifestations (p=0.693). However, complete remission occurred significantly more often in patients with concomitant use of DMT

(p=0.003) as well as after first-line apheresis (n=8/12, 67%, p=0.001) compared with second-line (n=10/67, 15%) or third-line (n=4/27, 15%) apheresis (figure 2). The delay to apheresis was significantly shorter in first-line (4.5 (IQR 0–11)days) than in second-line (15 (IQR 7–31)days, p<0.001) or third-line (30 (IQR 19–42)days, p<0.001) therapy. Apheresis was revealed to be most effective if started within 2 days of attack onset, with complete remission rates dropping radically afterwards (figure 3).

A multivariate GLMM analysis confirmed an association between the use of apheresis as first-line therapy and prophylactic DMT with a good response to apheresis therapy defined as complete remission (table 2).

Additional detailed responses could be calculated in 47% of attacks (50/106). We found no difference in the ΔEDSS between PLEX and IA+PLEX (n=29 vs 21; Δ2 (IQR 0.5–4.0) vs Δ1.5 (IQR 0–2.3), p=0.243) or focal and multifocal attacks (n=43 vs 7; Δ1.5 (IQR 0–3.5) vs Δ1.5 (0.5–5.0), p=0.989). The difference between relapse phenotypes was not significant (n=18 ON Δ0.75 (IQR 0–2) vs n=7 ON/MY Δ1.5 (0.5–3.5) vs n=17 MY Δ2.5 (1.5–4.25) vs n=8 cerebral manifestations Δ0.75 (–0.375 to 4.25), p=0.059).

However, patients with concomitant DMT had a significant lower ΔEDSS than those without DMT (n=20 vs 30, Δ0 (IQR 0–0.9) vs Δ2.5 (IQR 1.5–4.0), p<0.001). It was also significantly lower in first-line treated patients than in the rest of the cohort (n=7 vs 43, Δ0 (IQR 1–1.5) vs Δ2 (IQR 0–4.0), p=0.023). Neither patient age (p=0.719) nor apheresis delay correlated with the ΔEDSS (p=0.542).

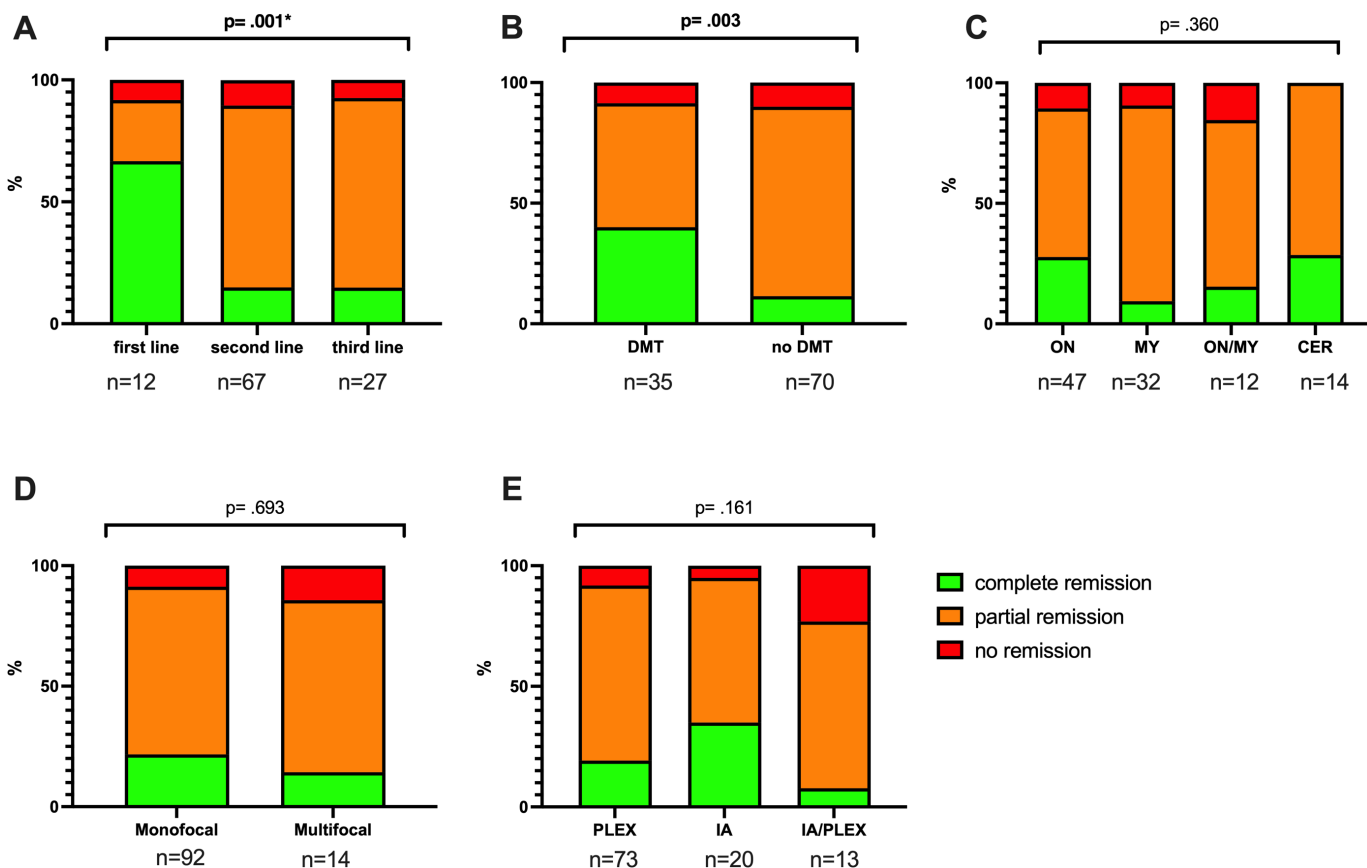


Figure 2 Overall clinical outcome in n=106 myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) attacks according to therapy line (A), DMT use (B), different attack phenotypes (C), the distribution of symptoms (D) and type of apheresis (E). X² test. Significant values (p<0.05) are shown in bold. CER, cerebral manifestation; DMT, disease-modifying therapy; IA, immunoadsorption; MY, myelitis; ON, optic neuritis; PLEX, plasma exchange.

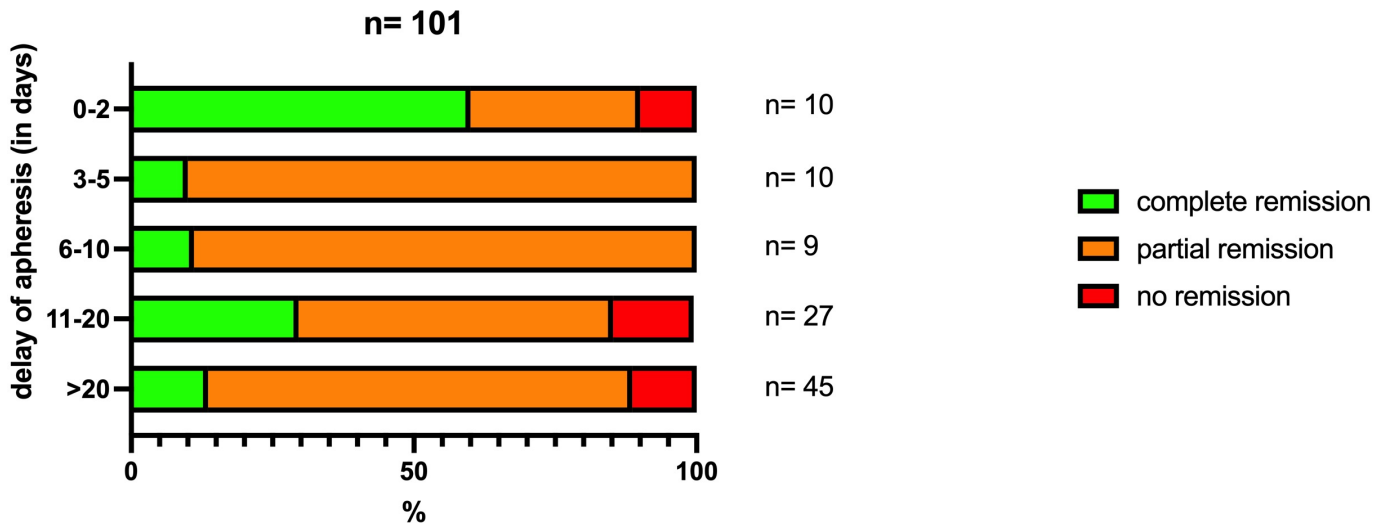


Figure 3 Bar chart showing the percentage of remission status based on apheresis delay (in days).

Considering the possible underestimation of visual deficits in the EDSS score, we additionally evaluated the Δ visual FSS, available in 22/50 (44%) of ON attacks. We likewise found no difference in the Δ visual FSS when comparing PLEX and IA+PLEX (n=13 vs 9, Δ 1 (IQR 0–3.5) vs Δ 0 (IQR 0–2.0), $p=0.430$). The Δ visual FSS did not differ in patients with and without DMT (n=11 vs 11, Δ 0 (IQR 0–1.0) vs Δ 2 (IQR 0–4.0), $p=0.105$) or first-line treated patients and the rest of the cohort (5 vs 17, Δ 0 (IQR 0–2.0) vs Δ 1 (IQR 0–2.0), $p=0.528$). However, the Δ visual FSS correlated with the patient's age at apheresis ($p=0.042$, $r=0.437$), indicating that younger patients benefited more.

Complications

Apheresis-related complications occurred in 8/117 treated attacks (7%), 5 during PLEX, 3 during combined PLEX/IA and none during IA. Four patients developed procedure-related systemic infections (2 PLEX, 2 PLEX/IA), one patient had heparin-induced thrombocytopenia, another patient had thrombocytopenia of unknown cause and one patient experienced transient cardiac arrhythmia (all PLEX). In one case, apheresis had to be stopped due to thrombosis of the internal jugular vein (PLEX/IA).

Table 2 Generalised mixed model analysis: factors associated with complete remission

	P value	OR	95% CI
Female (vs male)	0.217	1.006	–0.601 to 2.612
Age at attack (per year)	0.425	0.02	–0.029 to 0.069
Disease duration (per year)	0.208	–0.100	–0.258 to 0.057
ON (vs non-ON)	0.752	0.267	–1.406 to 1.941
MY (vs non-MY)	0.138	–1.519	–3.535 to 0.497
First line (vs second/third line)	0.032	2.579	0.225 to 4.933
DMT use (vs absence)	0.017	1.477	0.274 to 2.679
PLEX (vs IA+PLEX)	0.230	0.811	–0.521 to 2.144
IVMP dose (g)	0.627	0.042	–0.130 to 0.215

Generalised mixed model analyses with remission status of attacks (complete remission vs partial remission and no remission) as the dependent variable, n=100 attacks, $p=0.040$.

Significant values ($p<0.05$) are shown in bold.

DMT, disease-modifying therapy; IA, immunoadsorption; IVMP, intravenous methylprednisolone; MY, myelitis; ON, optic neuritis; PLEX, plasma exchange.

DISCUSSION

In this study, we systematically investigated the frequency and effectiveness of apheresis therapy in a large multicentre MOGAD cohort. Early start of apheresis, as first-line therapy, and concomitant use of DMT were associated with favourable clinical outcomes. Notably, the type of apheresis had no impact on the remission status.

Although MOGAD attacks are generally considered steroid sensitive,^{1,22} the prevalence of steroid refractory relapses remains unknown. Data regarding the effectiveness of apheresis therapy in MOGAD attacks are also limited. Most previous studies on therapeutic apheresis in autoimmune CNS conditions lack adequate representation of patients with MOGAD, likely due to its rarity and only recent recognition as a distinct disease entity. We demonstrate that the use of apheresis in MOGAD is not uncommon in German-speaking countries, with every fifth MOGAD attack being treated with apheresis. Similarly, a study on treatment regimens by the French NOMADMUS study group observed that 28% of the included 67 MOGAD attacks underwent PLEX.²² Moreover, every fourth patient in a large international study examining PLEX outcomes in ON (n=395) tested positive for MOG-IgG.²³

In contrast, a prospective single-centre study in China evaluating the efficacy of PLEX in a heterogeneous cohort of patients with ON included only a minority of MOGAD-ON (6/124, 4.8%).¹⁰ It is unclear whether this is due to different genetic backgrounds or different therapeutic approaches.

We suppose that steroid refractory relapses are not uncommon in MOGAD, with 20% of attacks and 41% of patients in our cohort being treated at least once with apheresis. The majority of patients (88%) received apheresis treatment as a second-line (after a median of 5000 mg IVMP) or third-line treatment (after a median of 13000 mg IVMP). Moreover, the disability level at the last FU was significantly higher in the apheresis group compared with the non-apheresis group, despite similar disease duration and ARR.

Analysing factors associated with a favourable post-apheresis outcome, we identified that early use of apheresis as first-line therapy is beneficial for achieving complete remission from MOGAD attacks. Our observation is in line with multiple previous studies on other demyelinating CNS disorders including MS and NMOSD.^{11 12 14 17 24 25} A meta-analysis also confirmed that the timepoint of PLEX initiation significantly influenced the

outcome, as indicated by EDSS reduction.²⁶ Moreover, in our study, complete remission was most frequently achieved in a very early apheresis initiation, specifically within the first 2 days after attack onset. This finding is also consistent with the results of two previous studies in AQP4-IgG⁺ NMOSD, which identified a comparable optimal apheresis period of 0–2 days.^{11,14}

Early elimination of disease-mediating antibodies can result in rapid clinical improvement. Despite demonstrating less robust complement activation compared with AQP4-IgG due to its bivalent binding pattern,²⁷ MOG-IgG can nonetheless activate the complement system. Interestingly, neuropathological findings in MOGAD are similar to MS pattern II lesions,²⁸ which are known to be particularly responsive to apheresis therapy.¹³ Early removal of the autoantibodies and probably further inflammation-promoting factors could prevent further damage at the cellular level, similar to the reversible dysfunction as demonstrated in AQP4-IgG⁺ NMOSD.¹⁷

Because of a possible monophasic disease course, the use of long-term immunotherapy in MOGAD remains a matter of debate. However, our results indicate that the presence of DMT in patients with severe relapses has a significant impact on post-apheresis clinical outcomes, especially in MY and cerebral manifestations. This finding was not significant in ON attacks, probably due to the smaller size of the ON subgroup. Data from other previous studies are controversial. Abboud *et al* reported comparable effects in NMOSD: preventive DMT resulted in a higher likelihood of reaching baseline EDSS after the attack.²⁹ Interestingly, their cohort consisted of mostly non-ON (69% MY, brain and brainstem) cases as well. In contrast, two other studies demonstrated no effect of concomitant DMT use on NMOSD attack recovery.^{11,30} However, one of these studies investigated patients with ON attacks only.³⁰ It seems to be plausible that DMT prevents relapses and can reduce severity and neuroaxonal damage in those relapses that occur. Reduced relapse severity under DMT has been demonstrated in previous studies in NMOSD and MS.^{31,32} Nevertheless, it remains unclear whether this effect differs between ON and non-ON attacks.

Depending on the relapse phenotype, there seem to be other factors relevant to the attack recovery. In ON attacks, the severity of vision loss at attack nadir and higher age at the attack were two additional risk factors for worse outcomes, as shown by Chen *et al*.²³ Interestingly, in a previous study comparing adult and paediatric patients with MOGAD, a younger age at ON onset demonstrated an even stronger association with visual outcomes compared with the grade of subsequent retinal atrophy involvement. This likely indicates a significant role of age-dependent cortical neuroplasticity in the visual cortex.³³ The patient's age might be a positive influencing factor in MOGAD-ON independent of an attack therapy.

In contrast to PLEX, which removes the entire blood plasma, IA selectively filters antibodies from the patient's blood. IA was shown to be effective in MS³⁴ and NMOSD.^{35–37} Some studies even propose a better long-term outcome after attack treatment with IA in MS,¹⁸ others found no differences between PLEX and IA in MS and NMOSD.^{11,38} In line with these findings, clinical outcomes in our MOGAD cohort did not differ among different types of apheresis (PLEX, IA, PLEX/IA).

Apheresis was generally well tolerated, similar to findings from previous studies.^{18,39} However, apheresis-related complications occurred in 7% of attacks, and in one case, apheresis had to be stopped due to thrombosis of the internal jugular vein.

Despite several strengths, including the large number of included attacks in this rare disease and the multicentre study design, our study has several limitations. The retrospective

nature of the study and the inclusion of patients from university hospitals only could result in a selection bias, potentially skewing the data towards more severe cases. Baseline and FU EDSS data were not available for all patients. We cannot exclude prolonged effects of high-dose corticosteroids in patients receiving second-line and third-line apheresis therapies that might have influenced clinical outcomes. Additionally, we were unable to analyse other clinical and paraclinical findings, such as the grade of retinal atrophy and exact visual acuity in ON, or levels of neurofilament light chain and glial fibrillar acidic protein, due to a lack of biosamples. Although highly suggestive of MOGAD based on (para)clinical characteristics, 5/85 patients (6%) did not fully meet the proposed diagnostic criteria. Further, ideally prospective comparative studies are needed to confirm our findings.

Our study revealed that severe relapses requiring apheresis therapy are not rare, affecting approximately every fifth MOGAD attack in our cohort. All types of apheresis seem to be equally effective for the treatment of attacks in MOGAD. An early, first-line apheresis improved the outcome substantially. DMT was another relevant factor associated with a favourable outcome. This evidence is supporting the recommendation for long-term immunotherapy in patients with MOGAD with severe relapses.

Author affiliations

- ¹Department of Neurology, St Josef Hospital, Ruhr University Bochum, Bochum, Germany
- ²Neurology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
- ³Behandlungszentrum Kempfenhausen für Multiple Sklerose Kranke gemeinnützige, Berg, Germany
- ⁴Department of Neurology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany
- ⁵LVR-Klinikum Düsseldorf, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany
- ⁶Institute of Clinical Neuroimmunology, LMU University Hospital, LMU Munich, Munich, Germany
- ⁷Department of Neurology, Hannover Medical School, Hannover, Germany
- ⁸Departments of Neurology, Biomedicine and Clinical Research and Research Center for Neuroimmunology and Neuroscience, University of Basel, Basel, Switzerland
- ⁹Molecular Neuroimmunology Group, Department of Neurology, Heidelberg University, Heidelberg, Germany
- ¹⁰Department of Neurology, University of Duisburg-Essen, Duisburg, Germany
- ¹¹Department of Neurology, Alfred Krupp Hospital Rüttenscheid, Essen, Germany
- ¹²Department of Neurology, Leipzig University, Leipzig, Germany
- ¹³Department of Neurology, University of Tübingen, Tübingen, Germany
- ¹⁴Department of Neurology, Medical University of Vienna, Vienna, Austria
- ¹⁵Department of Neurology, Ulm University, Ulm, Germany
- ¹⁶Department of Neurology, University of Rostock, Rostock, Germany
- ¹⁷Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Göttingen, Germany
- ¹⁸Department of Neurology, University Medical Center Göttingen, Göttingen, Germany
- ¹⁹Institute of Neuropathology, University Medical Center, Göttingen, Germany
- ²⁰Department of Neurology, Herford Hospital, Herford, Germany
- ²¹Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine, Berlin, Germany
- ²²Neuroscience Clinical Research Center, Charité Universitätsmedizin Berlin, a corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany
- ²³Department of Neurology and Experimental and Clinical Research Center, a cooperation between the Max Delbrück Center for Molecular Medicine in the Helmholtz Association and Charité-Universitätsmedizin Berlin, Charité-Universitätsmedizin Berlin, Berlin, Germany
- ²⁴c/o Department of Neurology, University Hospital Düsseldorf, Düsseldorf, Germany

X Joachim Havla @NeuroVisionLab

Acknowledgements The authors thank all patients for participating in the study and all contributors of the Neuromyelitis Optica Study Group (NEMOS) for their support.

Collaborators Coinvestigators within the Neuromyelitis Optica Study Group (NEMOS): Philipp Albrecht, MD, Klemens Angstwurm, MD, Susanna Asseyer, MD,

Antonios Bayas, MD, Stefanie Behnke, MD, Achim Berthele, MD, Felix Bischof, MD, Stefan Bittner, MD, Tobias Böttcher, MD, Franziska Buetow, Mathias Buttmann, MD, Eva Dawin, Ankelen Duchow, MD, Thorleif Etgen, MD, Barbara Ettrich, MD, Juergen H Faiss, Katinka Fischer, MD, Martina Flaskamp, Benedikt Frank, MD, Tim Friede, Achim Gass, MD, Christian Geis, MD, Katrin Giglhuber, MD, Stefan Gingele, MD, Jonas Graf, Matthias Grothe, MD, Sergiu Groppa, MD, Julia Gutbrod, MD, Kerstin Guthke, MD, Axel Haarmann, MD, Eva Marie Habedank, MD, Hans-Peter Hartung, MD, Maria Hastermann, Kerstin Hellwig, Bernhard Hemmer, MD, Marielle Herfurth, Marina Herwerth, Frank Hoffmann, MD, Olaf Hoffmann, MD, Ulrich Hofstadt-van Oy, MD, Jutta Junghans, MD, Matthias Kaste, MD, Barbara Kaulen, MD, Peter Kern, MD, Karsten Kern, Pawel Kermer, MD, Christoph Kleinschnitz, MD, Luisa Klotz, MD, Wolfgang Köhler, MD, Kimberly Körbel, MD, Melanie Korsen, MD, Markus Kowarik, MD, Markus Krumbholz, MD, Natalia Kurka, MD, Ann-Sophie Lauenstein, MD, Stefan Langel, MD, Sarah Laurent, MD, De-Hyung Lee, MD, Dominik Lehnrieder, MD, Frank Leyboldt, MD, Martin Liebetrau, MD, Ralf Linker, MD, Gero Lindenblatt, MD, Lisa Lohmann, MD, Felix Luessi, MD, Peter Luedemann, Michelle Maiworm, Martin Marziniak, MD, Christoph Mayer, MD, Stefanie Meister, MD, Arthur Melms, MD, Matthias Mering, MD, Imke Metz, MD, Sven Meuth, MD, Jasmin Naumann, MD, Oliver Neuhaus, MD, Tradite Neziraj, MD, Moritz Niederschweiberer, MD, Sabine Niehaus, MD, Carolin Otto, MD, Florence Pache, MD, Thivya Pakeerathan, MD, Sarah Passoko, MD, Mark Pawlitzki, MD, Hannah Pelkofer, MD, Hans-Ulrich Puhlmann, MD, Sebastian Rauer, MD, Arne Riedlinger, MD, Veith Rothhammer, MD, Kevin Rostásy, MD, Lioba Rückriem, MD, Klemens Ruprecht, MD, Rebekka Rust, MD, Christoph Ruschil, MD, Sven Schippling, MD, Olivia Schreiber-Katz, Charlotte Schubert, Matthias Schwab, MD, Maria Seipelt, MD, Jörn Peter Sieb, MD, Nadja Siebert, Claudia Sommer, MD, Annette Spreer, MD, Till Sprenger, MD, Alexander Stefanou, MD, Andreas Steinbrecher, MD, Jan-Patrick Stellmann, MD, Heike Stephanik, MD, Muriel Stoppe, MD, Klarissa Stürmer, MD, Marie Süße, MD, Björn Tackenberg, MD, Athanasios Tarampanis, MD, Simone Tauber, MD, Johannes Tünnerhoff, MD, Hayrretin Tumani, MD, Anna Walz, MD, Klaus-Peter Wandering, MD, Clemens Warnke, MD, Jens Weise, MD, Robert Weissert, MD, Klaus-Dieter Wernecke, PhD, Jonathan Wickel, MD, Heinz Wiendl, MD, Christian Wilke, MD, Yavor Yalachkov, MD, Lena Zeltner, MD, Uwe K Zettl, MD, Ulf Ziemann, MD, Frauke Zipp, MD.

Contributors CS was responsible for drafting and revising the manuscript, including medical writing for content, played a major role in data acquisition, contributed to the study concept/design and was involved in data analysis or interpretation. TL was responsible for drafting and revising the manuscript, including medical writing for content, and contributed to the study concept/design. VH, IK, MR, OA, TK, DE, JH, MWH, JRK, DT, CT, MK-K, BW, SJ, ABAGRG, A-KP, PSR, RP, MP, MK, FTB, CG, PSchw, MCK, IV, MS, AW, NR, MSW, LH, AWA, PSchi, FP, JB-S and RG were responsible for drafting and revising the manuscript, including medical writing for content. IA (guarantor) was responsible for drafting and revising the manuscript, including medical writing for content, contributed to the study concept/design and was involved in data analysis or interpretation.

Funding The NEMOS registry is partially supported by Horizon Therapeutics/Amgen, Alexion/AstraZeneca Rare Disease and Roche.

Competing interests CS has received speaker honoraria from Alexion and travel support from Novartis and UCB, all not related to the content of this manuscript, as well as research support from FORUM (clinician scientist position), medical faculty Ruhr-Universität Bochum. TL has received travel support from UCB. VH has received research support from NEMOS independent of this project. IK has received personal compensation for consulting, serving on a scientific advisory board, speaking or other activities with Alexion, Almirall, Bayer, Biogen, GlaxoSmithKline, Hexal, Horizon, Merck, Neuraxpharm, Roche/Chugai and Sanofi, none related to this study. MR received speaker honoraria from Novartis, Bayer Vital, Roche, Alexion, Horizon and Ipsen and travel reimbursement from Bayer Schering, Biogen Idec, Merz, Genzyme, Teva, Roche, Alexion, Horizon and Merck, none related to this study. OA has received personal fees from Alexion, Bayer HealthCare, Biogen, Celgene, Merck Serono, MedImmune, Novartis, Roche, Teva and Zambon, outside the submitted work. TK has received speaker honoraria and/or personal fees for advisory boards from Novartis Pharma, Roche Pharma, Alexion/AstraZeneca, Horizon Therapeutics/Amgen, Merck, Chugai Pharma and Biogen. The institution she works for has received compensation for serving as a member of a steering committee from Roche. TK is a site principal investigator in several randomised clinical trials and her institution has received compensation for clinical trials from Novartis Pharma, Roche Pharma and Sanofi Genzyme; all outside the present work. DE received speaker honoraria and/or travel reimbursement from Alexion, Amgen/Horizon and Merck, all not related to the presented work. JH reports a grant for OCT research from the Friedrich-Baur-Stiftung, Horizon and Merck, personal fees and non-financial support from Alexion, Amgen, Bayer, Biogen, BMS, Merck, Novartis and Roche and non-financial support from the Sumaira Foundation and Guthy-Jackson Charitable Foundation, all outside the submitted work. MWH received institutional research support from Myelitis, German Federal Joint Committee/Innovation Fund and NEMOS, speaker honoraria from selpers og, Horizon and Alexion and travel grants and compensation for serving on an advisory board from Alexion. None of these interfered with the current manuscript. CT received honoraria for consultation and

expert testimony from Alexion Pharma Germany. None of these interfered with the current report. MK-K received speaker honoraria from BMS, Merck and Novartis. BW received research grants from Deutsche Forschungsgemeinschaft, German Ministry of Education and Research, Dietmar Hopp Foundation, Klaus Tschira Foundation, Novartis and Roche, and personal fees from Alexion, INSTAND, Novartis and Roche, all unrelated to this work. ABAGRG has received travel grants from Roche and Biogen, outside the submitted work. A-KP received speaker honoraria and research support from Biogen, none related to this study. RP received honoraria for lectures from Alexion, Bayer Healthcare, Biogen, Celgene, Horizon/Amgen, Novartis, Merck, Roche, Sanofi-Aventis and Teva. He received research grants from HERZ Burgdorf, Novartis and Merck. MK received honoraria from Roche Pharma and Chugai Pharma. FTB has received, over his academic career, research support and travel grants for attending scientific meetings, through his institution, from the German Science Fund (DFG), German Federal Ministry of Education and Science (BMBF), Bayer-Schering, Diamed, Fresenius, Merck, Novartis, Pfizer, Roche, Sanofi and Teva; speaker fees and compensation for advisory boards from Actelion, Alexion, Bayer, Biogen, CSL Behring, Fresenius, Horizon, Merck, Novartis, Roche, Sanofi-Genzyme, Takeda and Teva. None of these are related to this work. CG received honoraria from Merck. MCK has served on advisory boards and received speaker fees/travel grants from Merck, Sanofi-Genzyme, Novartis, Biogen, Janssen, Alexion, Celgene/Bristol-Myers Squibb and Roche. He has received research grants from Merck, Roche, Novartis, Sanofi-Genzyme, Janssen and Celgene/Bristol-Myers Squibb. PSR has received honoraria for lectures/consultancy from Alexion (AstraZeneca), Almirall, Amicus, Biogen, Genzyme, Horizon (Amgen), Merck, Novartis, Roche and Teva, served on advisory boards for Alexion (AstraZeneca), Amicus, Genzyme, Horizon (Amgen), Merck, Roche and Sandoz and received research grants from Amicus, Roche, Merck and the Austrian Science Fund (FWF). IV has received travel support from Alexion. MS has received consulting and/or speaker honoraria from Alexion, Bayer, Biogen, Bristol-Myers Squibb/Celgene, Merck, Horizon, Roche and Sanofi-Genzyme. AW received speaker honoraria, consultant fees and travel reimbursement from Alexion, Bayer, Biogen, GlaxoSmithKline, Hexal, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme and UCB, none related to this study. MSW Our research is supported by research grants (Startförderung) of the Universitätsmedizin Göttingen, the National Multiple Sclerosis Society (NMSS; PP 1660), Novartis, Teva, Biogen Idec, Roche, Merck, the ProFutura Programme of the Universitätsmedizin Göttingen and the Deutsche Forschungsgemeinschaft (WE 3547/4-1; WE 3547/5-1; WE3547/7-1; project A8, SFB TRR 274). LH has received research support and speaker honoraria from Novartis. She is supported by the Deutsche Forschungsgemeinschaft (DFG Clinician Scientist Kolleg 'Zelldynamik in Pathogenese und Therapie'). AWA received speaker honoraria and meeting expenses from Novartis, Bayer, Biogen, Sanofi-Genzyme, Teva, Roche and Merck. PSchi received travel reimbursement from UCB. FP has received research support, speaker honoraria and travel reimbursement from Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi-Genzyme, UCB and Teva; is supported by the German Research Council (DFG Exc 257) and the German Competence Network for Multiple Sclerosis; received travel reimbursement from the Guthy-Jackson Charitable Foundation; and serves on the steering committee of the OCTIMS study sponsored by Novartis. JB-S has received institutional research support from NEMOS, Alexion and Bayer, personal fees from Alexion, speaker honoraria and travel grants from Bayer Healthcare, Horizon/Amgen, Novartis and Sanofi-Aventis/Genzyme, as well as grants for participating in a scientific advisory board from Roche and Merck, all unrelated to the present work. RG has received speaker and board honoraria from Baxter, Bayer Schering, Biogen Idec, CLB Behring, Genzyme, Merck Serono, Novartis, Stendhal, Talecris and Teva. His department received grant support from Bayer Schering, Biogen Idec, Genzyme, Merck Serono, Novartis and Teva. All not related to the content of this manuscript. IA received personal fees from Roche, Alexion, Horizon, Sanofi-Aventis/Genzyme and Merck and received research support from Diamed, none related to this study.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and data were retrieved from the NEMOS registry. Written informed consent was obtained from all patients prior to inclusion. Following the lead vote from the Technical University of Munich (No 2016-424_3-5-SR and No 424/16 S), ethics boards of all participating NEMOS centres have approved the data collection in the NEMOS registry. The study was conducted according to the Declaration of Helsinki (1964) in its currently applicable version. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The anonymised data that support the findings of this study are available from the corresponding author upon reasonable request, provided there are no legal or data protection objections.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and

responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Carolin Schwake <http://orcid.org/0000-0003-3669-7244>

Vivien Häußler <http://orcid.org/0000-0002-7787-7391>

Marius Ringelstein <http://orcid.org/0000-0003-3618-8407>

Tania Kümpfel <http://orcid.org/0000-0001-7509-5268>

Daniel Engels <http://orcid.org/0000-0002-9877-6987>

Joachim Havla <http://orcid.org/0000-0002-4386-1340>

Martin W Hümmert <http://orcid.org/0000-0002-5928-2343>

Paulus Stefan Rommer <http://orcid.org/0000-0001-5209-6647>

Makbule Senel <http://orcid.org/0000-0002-2737-7495>

REFERENCES

- Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. *J Neuroinflammation* 2016;13:280.
- Marignier R, Hacohen Y, Cobo-Calvo A, et al. Myelin-oligodendrocyte glycoprotein antibody-associated disease. *Lancet Neurol* 2021;20:762–72.
- Duchow A, Bellmann-Strobl J, Friede T, et al. Time to disability milestones and annualized relapse rates in NMOSD and MOGAD. *Ann Neurol* 2024;95:720–32.
- Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain (Bacau)* 2017;140:3128–38.
- Lopez-Chiriboga AS, Sechi E, Buciu M, et al. Long-term Outcomes in Patients With Myelin Oligodendrocyte Glycoprotein Immunoglobulin G-Associated Disorder. *JAMA Neurol* 2020;77:1575–7.
- Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry* 2018;89:127–37.
- Dubey D, Pittock SJ, Krecke KN, et al. Clinical, Radiologic, and Prognostic Features of Myelitis Associated With Myelin Oligodendrocyte Glycoprotein Autoantibody. *JAMA Neurol* 2019;76:301–9.
- Ayzenberg I, Ladopoulos T, Schwake C, et al. Cognitive impairment in MOGAD is associated with ADEM-like episodes and deep grey matter atrophy (S40.006). *Neurology (E-Cronicon)* 2023;100.
- Passoke S, Stern C, Häußler V, et al. Cognition in patients with myelin oligodendrocyte glycoprotein antibody-associated disease: a prospective, longitudinal, multicentre study of 113 patients (CogniMOG-Study). *J Neurol Neurosurg Psychiatry* 2024.
- Fu J, Wang Y, Li H, et al. Efficacy of Plasma Exchange Treatment for Demyelinating Optic Neuritis Associated with Various Serum Antibodies: A Prospective Cohort Study. *Neurol Ther* 2022;11:797–813.
- Kleiter I, Gahlen A, Borisow N, et al. Apheresis therapies for NMOSD attacks: A retrospective study of 207 therapeutic interventions. *Neurol Neuroimmunol Neuroinflamm* 2018;5:e504.
- Kleiter I, Gahlen A, Borisow N, et al. Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses. *Ann Neurol* 2016;79:206–16.
- Stork L, Ellenberger D, Reißbarth T, et al. Differences in the Responses to Apheresis Therapy of Patients With 3 Histopathologically Classified Immunopathological Patterns of Multiple Sclerosis. *JAMA Neurol* 2018;75:428–35.
- Bonnan M, Valentino R, Debeugny S, et al. Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. *J Neurol Neurosurg Psychiatry* 2018;89:346–51.
- Connelly-Smith L, Alquist CR, Aquino NA, et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. *J Clin Apher* 2023;38:77–278.
- Kümpfel T, Gighlhuber K, Aktas O, et al. Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) - revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. *J Neurol* 2024;271:141–76.
- Bonnan M, Cabre P. Plasma exchange in severe attacks of neuromyelitis optica. *Mult Scler Int* 2012;2012:787630.
- Dorst J, Fangerau T, Taranu D, et al. Safety and efficacy of immunoadsorption versus plasma exchange in steroid-refractory relapse of multiple sclerosis and clinically isolated syndrome: A randomised, parallel-group, controlled trial. *E Clin Med* 2019;16:98–106.
- Lipphardt M, Wallbach M, Koziolok MJ. Plasma Exchange or Immunoadsorption in Demyelinating Diseases: A Meta-Analysis. *J Clin Med* 2020;9:1597.
- Weinshenker BG, O'Brien PC, Petterson TM, et al. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. *Ann Neurol* 1999;46:878–86.
- Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol* 2023;22:268–82.
- Demuth S, Guillaume M, Bourre B, et al. Treatment regimens for neuromyelitis optica spectrum disorder attacks: a retrospective cohort study. *J Neuroinflammation* 2022;19:62.
- Chen JJ, Flanagan EP, Pittock SJ, et al. Visual Outcomes Following Plasma Exchange for Optic Neuritis: An International Multicenter Retrospective Analysis of 395 Optic Neuritis Attacks. *Am J Ophthalmol* 2023;252:213–24.
- Keegan M, Pineda AA, McClelland RL, et al. Plasma exchange for severe attacks of CNS demyelination: predictors of response. *Neurology (E-Cronicon)* 2002;58:143–6.
- Llufriu S, Castillo J, Blanco Y, et al. Plasma exchange for acute attacks of CNS demyelination: Predictors of improvement at 6 months. *Neurology (E-Cronicon)* 2009;73:949–53.
- Huang X, Wu J, Xiao Y, et al. Timing of plasma exchange for neuromyelitis optica spectrum disorders: A meta-analysis. *Mult Scler Relat Disord* 2021;48:102709.
- Lerch M, Schanda K, Lafon E, et al. More Efficient Complement Activation by Anti-Aquaporin-4 Compared With Anti-Myelin Oligodendrocyte Glycoprotein Antibodies. *Neurol Neuroimmunol Neuroinflamm* 2023;10:e200059.
- Höftberger R, Guo Y, Flanagan EP, et al. The pathology of central nervous system inflammatory demyelinating disease accompanying myelin oligodendrocyte glycoprotein autoantibody. *Acta Neuropathol* 2020;139:875–92.
- Aboud H, Petrak A, Mealy M, et al. Treatment of acute relapses in neuromyelitis optica: Steroids alone versus steroids plus plasma exchange. *Mult Scler* 2016;22:185–92.
- Gonzalez C, Vargas D, Contreras K, et al. Therapeutic plasma exchange for optic neuritis attacks in patients with neuromyelitis optica spectrum disorders. *Ther Apher Dial* 2022;26:1274–80.
- Hosny HS, Shehata HS, Ahmed S, et al. Predictors of severity and outcome of multiple sclerosis relapses. *BMC Neurol* 2023;23:67.
- Kleiter I, Trabouisee A, Palace J, et al. Long-term Efficacy of Satralizumab in AQP4-IgG-Seropositive Neuromyelitis Optica Spectrum Disorder From SAKuraSky and SAKuraStar. *Neurol Neuroimmunol Neuroinflamm* 2023;10:e200071.
- Havla J, Pakeerathan T, Schwake C, et al. Age-dependent favorable visual recovery despite significant retinal atrophy in pediatric MOGAD: how much retina do you really need to see well? *J Neuroinflammation* 2021;18:121.
- Heigl F, Hettich R, Arendt R, et al. Immunoadsorption in steroid-refractory multiple sclerosis: Clinical experience in 60 patients. *Atheroscler Suppl* 2013;14:167–73.
- Yasuda T, Mikami T, Kawase Y. Efficacy of Tryptophan Immunoadsorption Plasmapheresis for Neuromyelitis Optica in Two Cases. *Ther Apher Dial* 2015;19:411–2.
- Faissner S, Nikolayczik J, Chan A, et al. Immunoadsorption in patients with neuromyelitis optica spectrum disorder. *Ther Adv Neurol Disord* 2016;9:281–6.
- Heigl F, Hettich R, Fassbender C, et al. Immunoadsorption as maintenance therapy for refractory neuromyelitis optica spectrum disorder. *Ther Adv Neurol Disord* 2023;16.
- Lipphardt M, Mühlhausen J, Kitz B, et al. Immunoadsorption or plasma exchange in steroid-refractory multiple sclerosis and neuromyelitis optica. *J Clin Apher* 2019;34:381–91.
- Basic-Jukic N, Kes P, Glavas-Boras S, et al. Complications of therapeutic plasma exchange: experience with 4857 treatments. *Ther Apher Dial* 2005;9:391–5.

Supplemental Table 1. Characteristics of MOG-IgG+ patients not meeting the 2023 MOGAD criteria

ID	Gender	Age at onset	MOG-titer	Relapses	Disease duration	OCB	Additional information/ Comment
1	m	34y	Positive w/o titer (fixed CBA)	Isolated ADEM	7y	NA	Episode of severe encephalopathic syndrome, monophasic course, no further attacks (without DMT), suggestive of MOG-IgG+ ADEM (initial MRI not available)
2	m	53y	Low positive 1:50 (fixed CBA)	Isolated Myelitis	8y	neg	Isolated Myelitis, monophasic course, OCB negative, suggestive of MOGAD
3	m	50y	Low positive 1:32 (fixed CBA)	3x ON unilateral	9y	NA	(Recurrent) isolated ON suggestive of MOGAD with early relapse after steroid tapering, no data on papilledema/OCT or MRI in the acute stage available
4	m	42y	Low positive 1:32 (fixed CBA)	6x ON unilateral	2y	neg	
5	f	30y	Low positive 1:32 (fixed CBA)	1x ON unilateral	7y	NA	

Abbr.: ADEM= acute disseminated encephalomyelitis, CBA= cell-based assay, DMT= disease modifying therapy, f= female, m= male, MRI= magnetic resonance imaging, MS= multiple sclerosis, MOGAD= myelin oligodendrocyte glycoprotein antibody-associated disease, NA= not available, OCB= oligoclonal bands, OCT= optical coherence tomography, ON= optic neuritis, w/o= without, y= years.

Supplemental Table 1. Characteristics of MOG-IgG+ patients not meeting the 2023 MOGAD criteria

ID	Gender	Age at onset	MOG-titer	Relapses	Disease duration	OCB	Additional information/ Comment
1	m	34y	Positive w/o titer (fixed CBA)	Isolated ADEM	7y	NA	Episode of severe encephalopathic syndrome, monophasic course, no further attacks (without DMT), suggestive of MOG-IgG+ ADEM (initial MRI not available)
2	m	53y	Low positive 1:50 (fixed CBA)	Isolated Myelitis	8y	neg	Isolated Myelitis, monophasic course, OCB negative, suggestive of MOGAD
3	m	50y	Low positive 1:32 (fixed CBA)	3x ON unilateral	9y	NA	(Recurrent) isolated ON suggestive of MOGAD with early relapse after steroid tapering, no data on papilledema/OCT or MRI in the acute stage available
4	m	42y	Low positive 1:32 (fixed CBA)	6x ON unilateral	2y	neg	
5	f	30y	Low positive 1:32 (fixed CBA)	1x ON unilateral	7y	NA	

Abbr.: ADEM= acute disseminated encephalomyelitis, CBA= cell-based assay, DMT= disease modifying therapy, f= female, m= male, MRI= magnetic resonance imaging, MS= multiple sclerosis, MOGAD= myelin oligodendrocyte glycoprotein antibody-associated disease, NA= not available, OCB= oligoclonal bands, OCT= optical coherence tomography, ON= optic neuritis, w/o= without, y= years.