

eMethods

Details on the methodology of the study are reported below:

We retrospectively identified patients with MOGAD diagnosed according to the recently proposed diagnostic criteria in 24 different Italian centres between 01/2017 and 01/2025.

MOG-Abs testing was performed using live CBAs in 4 laboratories (Verona, Pavia, Florence, Bologna) and fixed CBAs in 5 local laboratories (Udine, Padova, Mestre, Siena).

Clinical and paraclinical data were obtained from referring physicians and included in a dedicated database. Patients with insufficient clinical/paraclinical data and with a follow-up of less than 1 year were excluded.

The parameters included in the MOG-AR Score (onset age ≥ 45 years, sex, attack phenotype, oral steroids use for at least 3 months, use of immunosuppressive treatment after the 1st event) were analysed to assess correlation with disease course. Patients were stratified in 4 groups based on the MOG-AR score (grade 1: 0-4, grade 2: 5-8, grade 3: 9-12, grade 4: 13-16).

Additionally, the following clinical (pediatric onset -i.e- <18 years old-, comorbidities, infectious or vaccinal triggers, EDSS, visual acuity), laboratory (serum and CSF MOG-Abs positivity, CSF oligoclonal bands), treatment (the use of acute treatment in addition to high-dose corticosteroids such as intravenous immunoglobulin or plasma exchange) and follow-up data (number of relapses, EDSS, and visual acuity at follow-up) were also collected and analyzed.

Relapse was defined as the occurrence of new or worsening neurological symptoms, lasting ≥ 24 hours, in the absence of fever or infection, and separated by at least 30 days from the onset of a preceding demyelinating event. Of note, decisions on treatment strategy were made independently by treating physicians.

For descriptive statistics, quantitative variables are expressed as median (interquartile ranges [IQR]) or mean (standard deviation [SD]), and categorical variables as percentages. Group comparisons were

assessed using nonparametric tests (χ^2 and Mann-Whitney tests). Receiving Operator Characteristic (ROC) curves were constructed to assess MOG-AR score performance.

Considering that a MOG-AR score of 9 or higher was considered predictive of MOGAD relapses¹¹, true positive cases were considered those relapsing and with a MOG-AR score ≥ 9 (TP), true negative cases were those monophasic and with a MOG-AR score < 9 (TN), false positive cases were defined as those monophasic and with a MOG-AR score ≥ 9 (FP), false negative patients as those relapsing and with a MOG-AR score < 9 (FN). Sensitivity (TP/TP+FN), Specificity (TN /FP+TN), positive predictive value (PPV= TP/TP+FP), negative predictive value (NPV= TN/TN+FN), accuracy (TP+TN/TP+TN+FP+FN) with 95% confidence interval (CI) were calculated accordingly.

Univariate binary logistic regression models were performed to assess the risk of relapsing disease according to age at onset (pediatric onset and age at onset ≥ 45), sex, clinical phenotype, presence of infectious/vaccine triggers, receiving an additional acute treatment (corticosteroids + plasma exchange and/or intravenous immunoglobulin), oral steroids use for at least 3 months, use of an immunosuppressive treatment after the 1st event. Variables resulting from the univariate analysis with a p -value ≤ 0.50 were included in a multivariate binary regression model. The results were expressed as odds ratio (OR) with 95% of CI. Kaplan–Meier survival curves were plotted to assess time to first relapse (for the relapsing patients) or time to last follow-up (for the monophasic course) according to MOG-AR score, as well as the same variables explored in the univariate logistic regression model. Differences between survival curves were compared using the log-rank test. Statistical analyses were performed using IBM SPSS 25.

The study was part of the research protocol approved by the Ethics Committees of the enrolling centers: BIOB-NEU-DNA-2014 and prog. 1052CESC Verona-Rovigo approved by the Ethics Committee of Verona University Hospital (Italy); protocol n. 16601_oss, approved by Area Vasta Centro—Regione Toscana (Florence, Italy); project code: 0020308/23 approved on April 14, 2023 by

the Institutional Review Board of the IRCCS Policlinico San Matteo, Pavia; Prot IRB (University of Udine): 209/2025