MOGAD:
Who, when and how to treat?

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Disclosures

In the last 3 years, E.S.

- Received speaker honoraria and/or support for attending scientific meetings from Alexion, Horizon, Roche and UCB.
- Served as editorial board member for BMC Neurology and Frontiers in Neurology.
- Served as medical advisory board member for the MOG project.

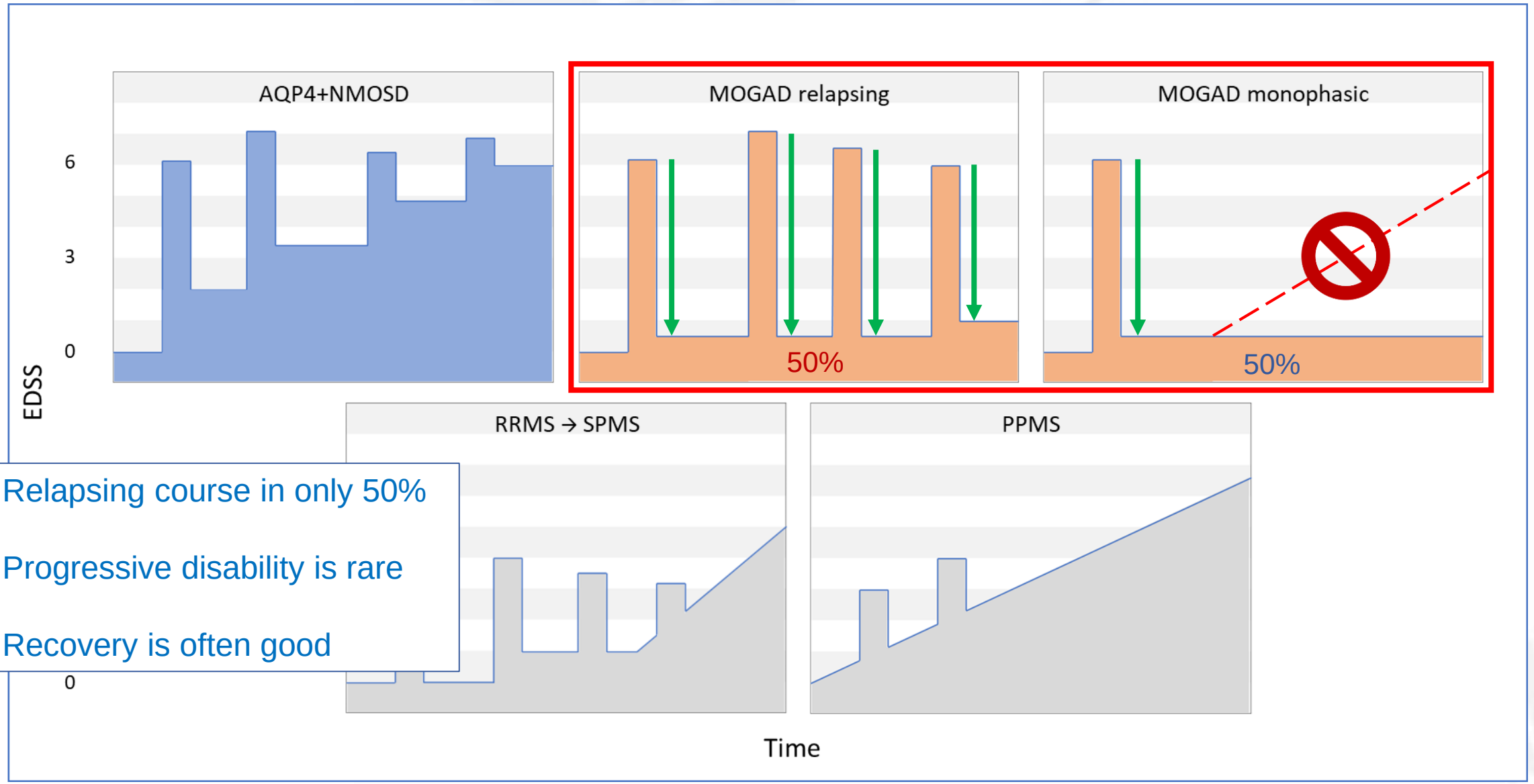
MOGAD treatment - Layout

1. General considerations

2. Treatment of disease attacks

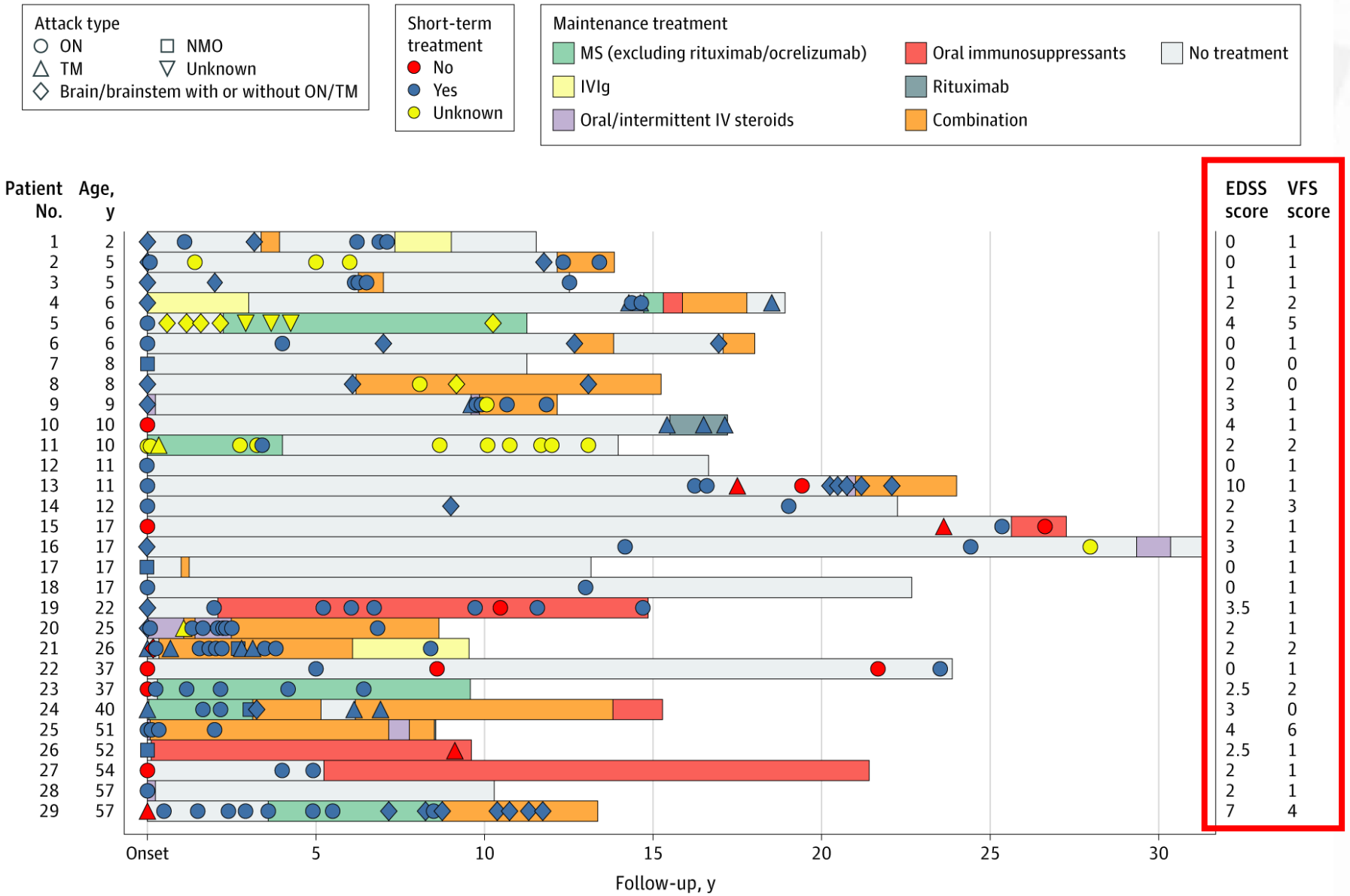
3. Maintenance treatment and disease monitoring

Disease course in MOGAD



- Relapsing course in only 50%
- Progressive disability is rare
- Recovery is often good

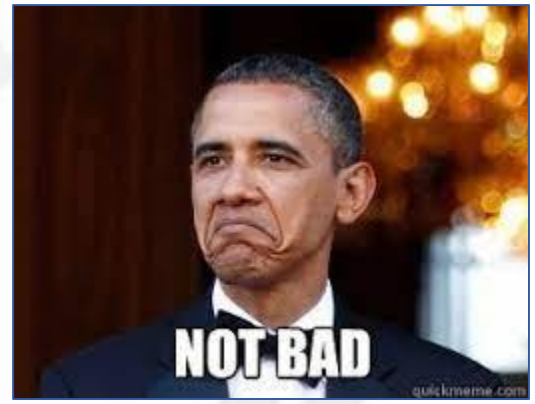
Disability accrual in MOGAD



- Median N. attacks/patient: 5 (range, 1-16)
- Median follow-up: 14 years (range, 9-31)
- Final EDSS >4: 2/29 (7%)
- Median VA: 20/20 (20/20 to count fingers)

Lopez-Chiriboga & Sechi et al. JAMA Neurol 2020

MOGAD treatment - Considerations



- Should we treat all patients long-term? NOT SURE

- Can we predict who is going to relapse? NO

- Can we predict who is going to have a poor outcome? NO

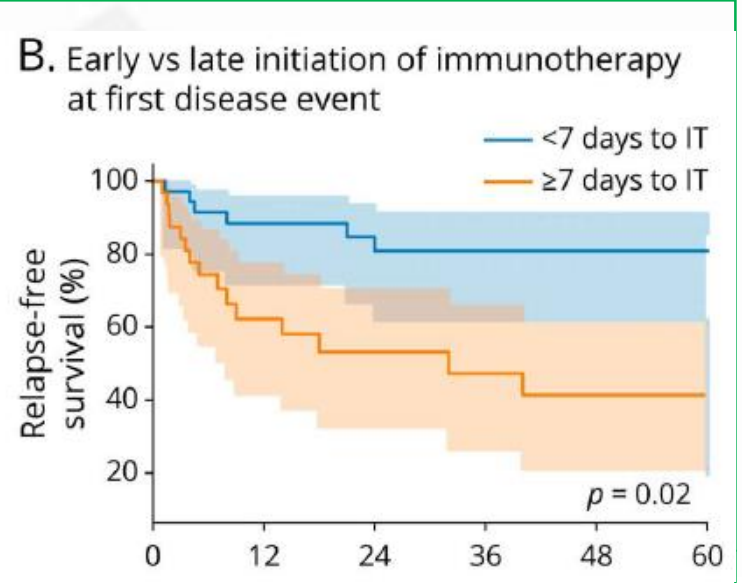
- Should we treat all disease attacks? YES

- Is our treatment strategy guided by solid evidences? NO

Treatment of MOGAD attacks

- Better outcome with early immunotherapy:
- IVMP (1 g/day for 5-7 days)

Steroids are often not sufficient!



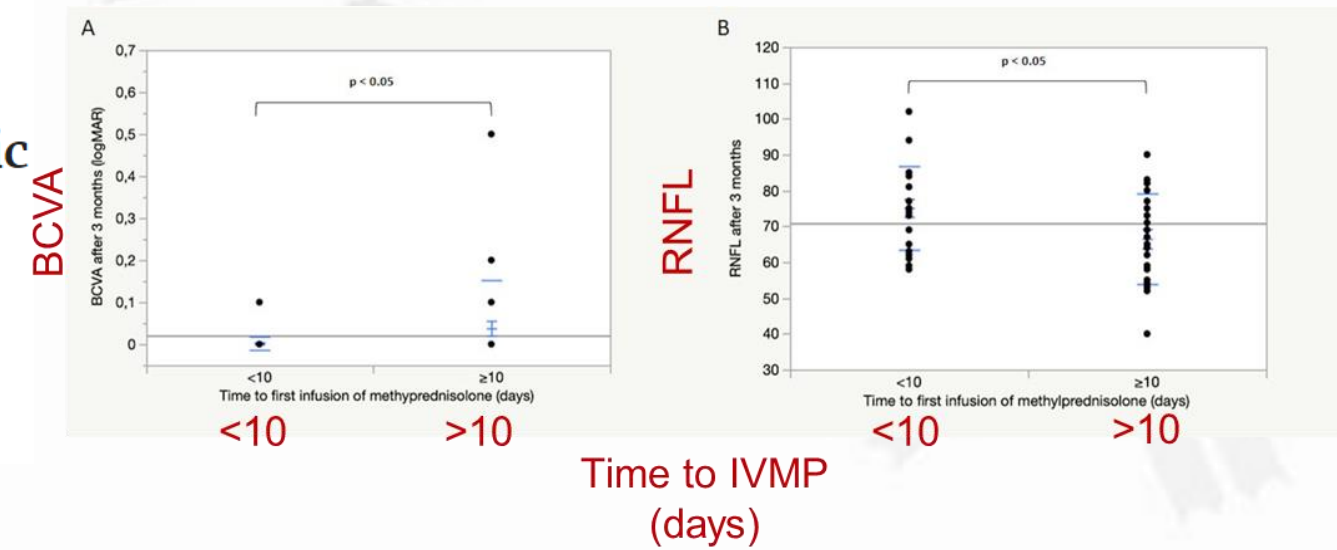
RESEARCH ARTICLE OPEN ACCESS

Early Immunotherapy and Longer Corticosteroid Treatment Are Associated With Lower Risk of Relapsing Disease Course in Pediatric MOGAD

J Neurol Neurosurg Psychiatry. 2023 Apr;94(4):309-313. doi: 10.1136/jnnp-2022-330360. Epub 2022 Dec 13.

Time to steroids impacts visual outcome of optic neuritis in MOGAD

Julie Rode [1], Julie Pique [2], Adil Maarouf [3 4], Xavier Ayrignac [5], Bertrand Bourre [6], Jonathan Ciron [7], Mikael Cohen [8], Nicolas Collongues [9], Romain Deschamps [10], Elisabeth Maillart [11], Alexis Montcuquet [12], Caroline Papeix [10], Aurelie Ruet [12], Sandrine Wiertlewski [13], Helene Zephir [14], Romain Marignier [2], Bertrand Audoin [3 4]



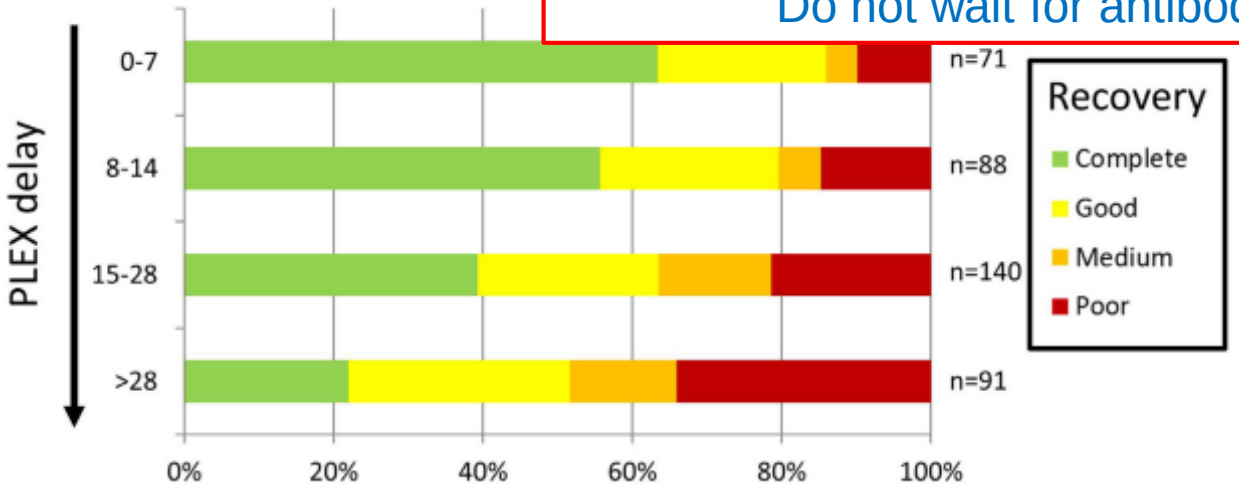
Treatment of MOGAD attacks

- Better outcome with early immunotherapy:

- IVMP (1 g/day for 5-7 days)
- PLEX (5-7 exchanges)

Start PLEX on day 4 of IVMP if no improvement!

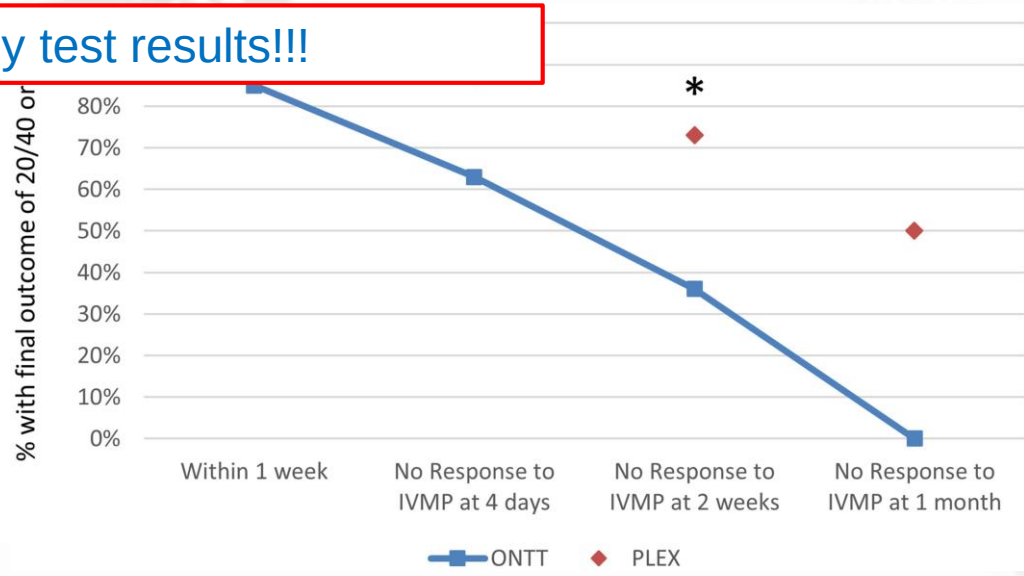
Do not wait for antibody test results!!!



AOS Thesis

Visual Outcomes Following Plasma Exchange for Optic Neuritis: An International Multicenter Retrospective Analysis of 395 Optic Neuritis Attacks

John J. Chen [1 2], Eoin P. Flanagan [2 3 4], Sean J. Pittock [2 3 4], Nicole Caroline Stern [1], Nanthaya Tisavipat [2], M. Tariq Bhatti [5], Kevin D. Chodnicki [1], Deena A. Tajfirouz [1 2], Sepideh Jamali [1], Amy Kunchok [2 4 6], Eric R. Eggenberger [7], Marie A. Di Nome [8 9], Elias S. Sotirchos [10], Eleni S. Vasileiou [10], Amanda D. Henderson [10 11], Anthony C. Arnold [12], Laura Bonelli [12], Heather E. Moss [13 14], Sylvia Elizabeth Villarreal Navarro [14], ... n Marignier [30]



Consider PLEX regardless of antibody serostatus

- Low risk compared to potential benefits
- Efficacy of PLEX demonstrated before AQP4-IgG discovery!

Annals of NEUROLOGY
An Official Journal of the American Neurological Association and the Child Neurology Society
ANA AMERICAN NEUROLOGICAL ASSOCIATION

Original Article

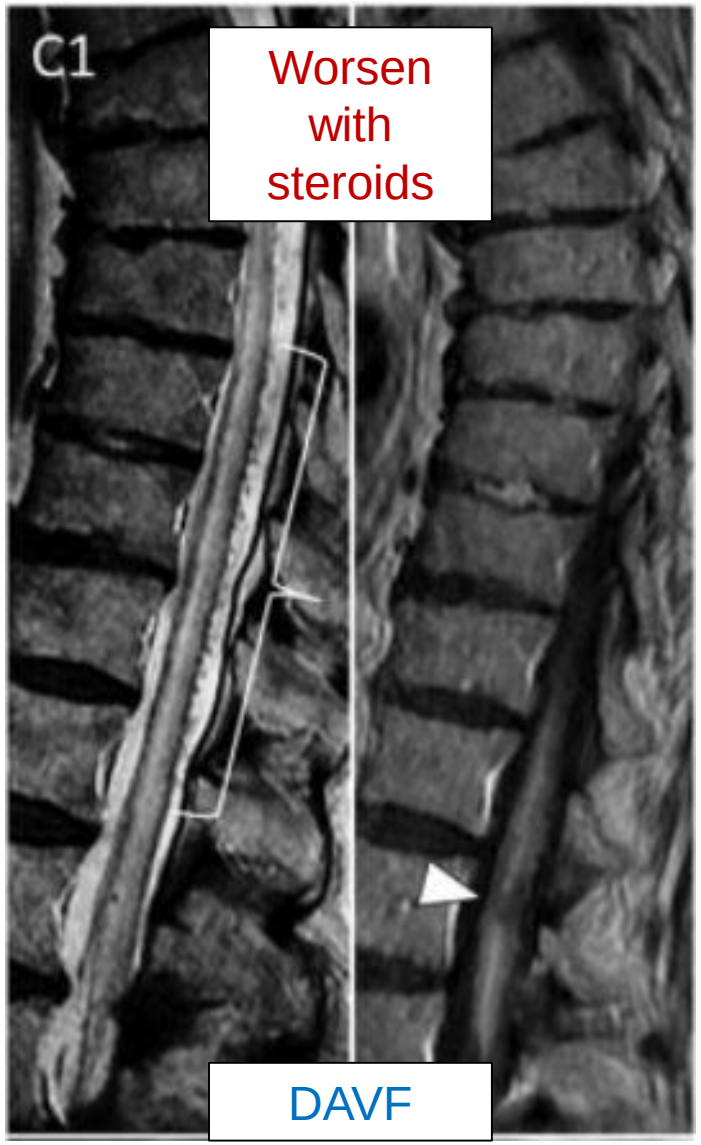
A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease

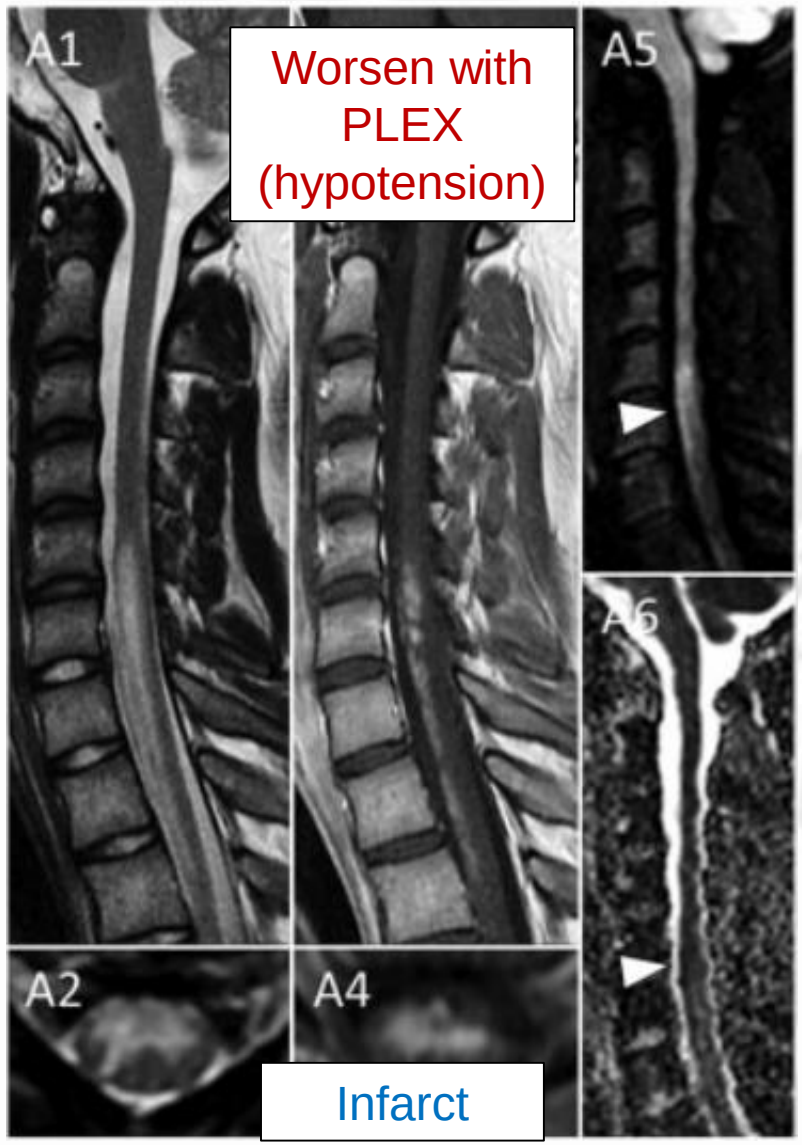
Brian G. Weinshenker MD, Peter C. O'Brien PhD, Tanya M. Petterson MSc, John H. Noseworthy MD, Claudia F. Lucchinetti MD, David W. Dodick MD, Alvaro A. Pineda MD ... See all authors

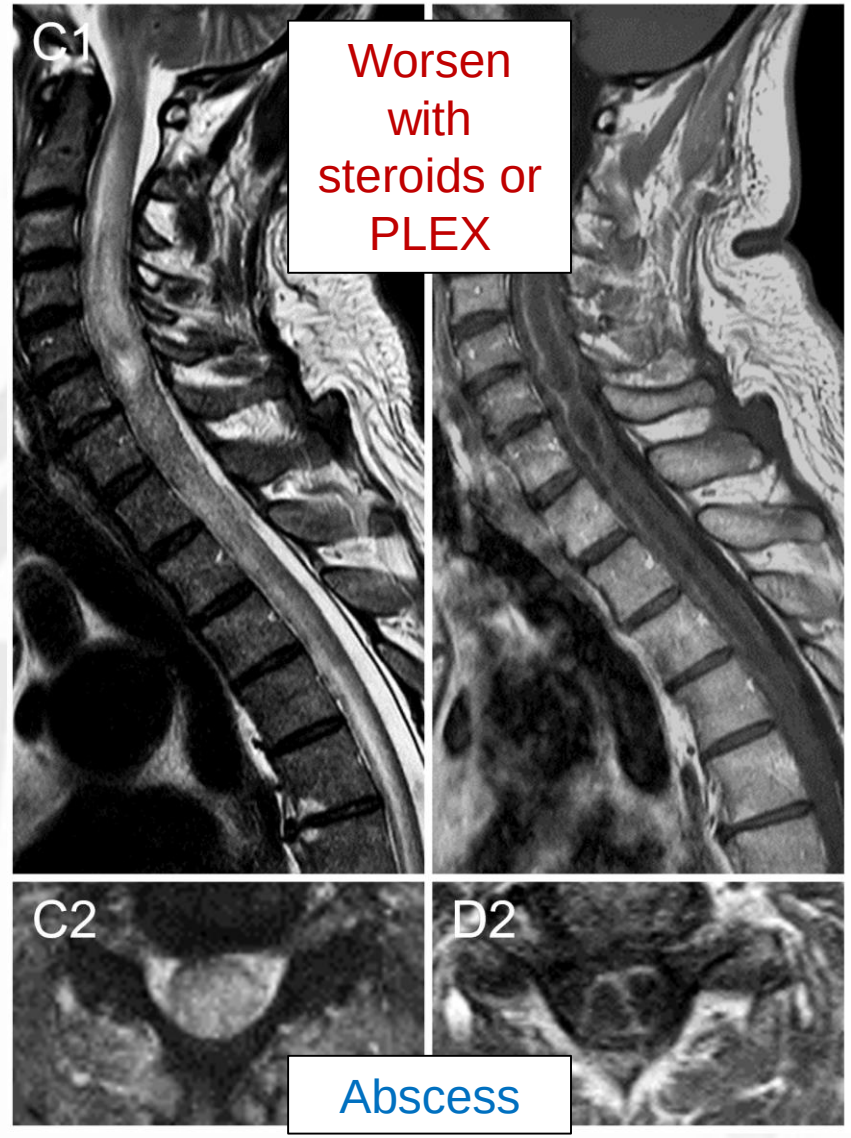
First published: 17 May 2001 |
https://doi.org/10.1002/1531-8249(199912)46:6<878::AID-ANA10>3.0.CO;2-Q | Citations: 608

- Randomized, sham-controlled, double masked, cross-over study
- 22 adult patients with severe attacks of CNS demyelination (10 MS, 12 other)
- Persistant deficit 14 days after corticosteroids onset
- Improvement in 8/19 (42%) vs 1/17 (6%); p=0.01

Early treatment - Caution if...







Sechi et al. Semin Neurol 2021; Zara et al Eur J Neurol 2023

Treatment of MOGAD attacks

- Better outcome with early immunotherapy:
- IVMP (1 g/day for 5-7 days)
- PLEX (5-7 exchanges)
- IVIg (various regimens)

IVIG treatment dose (protocol) (*N*, %)	
0.8 g/kg (0.4 g/kg × 2 days)	1 (2.6)
1 g/kg (1 g/kg × 1 day)	1 (2.6)
1.2 g/kg (0.4 g/kg × 3 days)	3 (7.7)
1.32 g/kg (0.66 g/kg × 2 days)	1 (2.6)
1.6 g/kg (0.4 g/kg × 4 days)	1 (2.6)
1.98 g/kg (0.66 g/kg × 3 days)	2 (5.2)
2 g/kg (0.4 g/kg × 5 days)	17 (43.6)
2 g/kg (1 g/kg × 2 days)	12 (30.8)
2.4 g/kg (0.4 g/kg × 6 days)	1 (2.6)
Additional treatments (*N*, %)	
IVMP	15 (38.5)
IVMP + oral CS	5 (12.8)
IVMP + TPE[a]	9 (23.1)
IVMP + oral CS + TPE[b]	5 (12.8)
None	5 (12.8)

In some patients first line treatments are not sufficient!

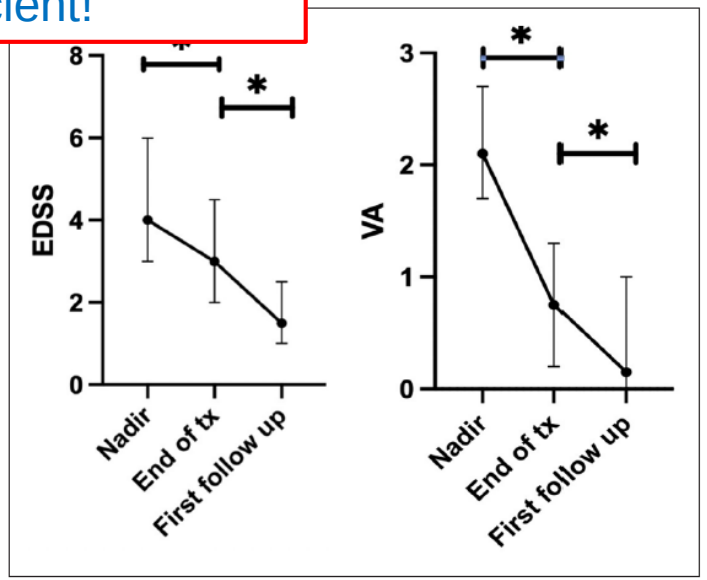
MULTIPLE SCLEROSIS JOURNAL | MSJ

39 pts (adults and children)

Original Research Paper

Intravenous immunoglobulin treatment for acute attacks in myelin oligodendrocyte glycoprotein antibody disease

Lotan et al. 2023



Rescue therapies for MOGAD attack

- Data from case reports mostly:
- IL-6R inhibitors (*e.g.*, tocilizumab)
- Cyclophosphamide
- aHSCT
- Other? (*e.g.*, RTX)

Dramatic Response to Anti-IL-6 Receptor Therapy in Children With Life-Threatening Myelin Oligodendrocyte Glycoprotein-Associated Disease

Loren A. McLendon, MD, Claudia Gambrah-lyles, MD, Angela Viaene, MD, Nina A. Fainberg, MD, Elizabeth I. Landzberg, MD, Alexander M. Tucker, MD, Peter J. Madsen, MD, Jimmy Huh, MD, Maya R. Silver, MD, John D. Arena, MD, Martha F. Kienzle, MD, and Brenda Banwell, MD

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Neurol Neuroimmunol Neuroinflamm 2023;10:e200150. doi:10.1212/NXI.0000000000200150

Restricted access | Case report | First published online November 24, 2023

An aggressive form of MOGAD treated with aHSCT: A case report

Elvira Sbragia, Giacomo Boffa, [...], and Matilde Inglese +6 View all authors and affiliations

OnlineFirst | https://doi.org/10.1177/13524585231213792

Post-attack steroid taper?

- MOGAD patients may show a steroid-dependent course
- Early relapses associated with long-term relapsing disease
- Steroid taper may reduce the risk of relapses Jurynczyk et al. Brain 2017; Nosadini et al. N2 2023

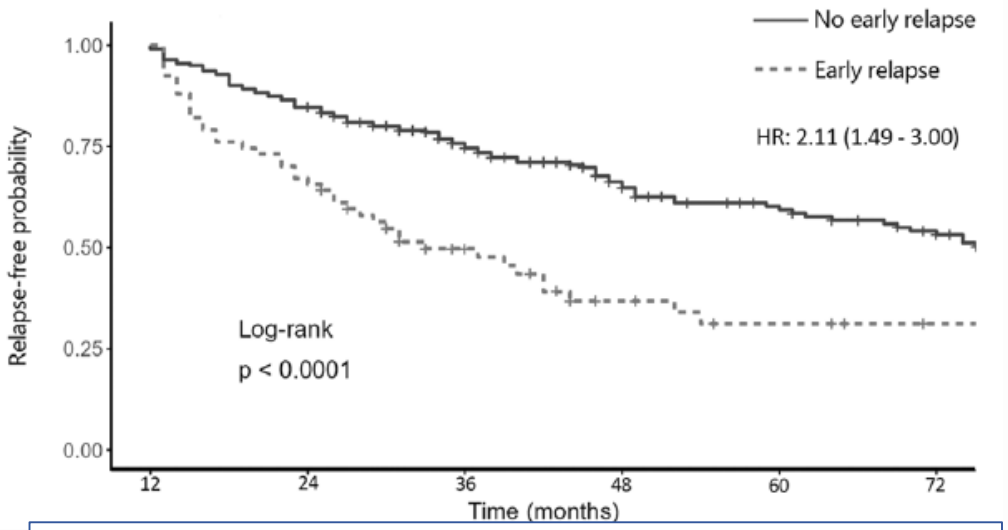
BUT

- Early relapses are less common:
  - Relapses within 1 year in 23%
  - Relapses within 3 months in 10%

Do Early Relapses Predict the Risk of Long-Term Relapsing Disease in an Adult and Paediatric Cohort with MOGAD?

Chen et al. Ann Neurol 2023

- Steroid taper in 25%
- Median duration, 13 mo (range, 1 we – 49 mo)



Use of steroids and steroid treatment duration did not reduce the risk of relapses; *p*=0.96

Post-attack long-term immunosuppression?

Just treat everyone and don't mind it!

OR

Choice based on:

- Recovery from the initial attack
- Highly relapsing course from onset
- Patient's preference/opinion

OR

Try to predict relapses with:

- Longitudinal MOG-IgG serostatus
- MRI (new/enlarging lesions in <5%!)

Neuro-inflammation
Original research

PDF

Prognostic relevance of quantitative and longitudinal MOG antibody testing in patients with MOGAD: a multicentre retrospective study

Matteo Gastaldi [1], Thomas Foiadelli [2], Giacomo Greco [3, 4], Silvia Scaranzin [1], Eleonora Rigoni [4], Stefano Masciocchi [1, 3], Sergio Ferrari [5], Chiara Mancinelli [6], Laura Brambilla [7], Margherita Mancardi [8], Thea Giacomini [8], Diana Ferraro [9], Marida Della Corte [10], Antonio Gallo [11], Massimiliano Di Filippo [12], Luana Benedetti [13], Giovanni Novi [14], Maurizio Versino [15], Paola Banfi [16], Raffaele Iorio [17], Lucia Moiola [18], Emanuela Turco [19], Stefano Sartori [20], Margherita Nosadini [20], Martino Ruggieri [21], Salvatore Savasta [2], Elena Colombo [4], Elena Ballante [22, 23], Sven Jarius [24], Sara Mariotto [5], Diego Franciotta [1] on behalf of the NINA study group

Correspondence to Dr Matteo Gastaldi, Laboratory of neuroimmunology, IRCCS Mondino Foundation, Pavia, Lombardia, Italy;

CLINICAL/SCIENTIFIC NOTE OPEN ACCESS

Frequency of New or Enlarging Lesions on MRI Outside of Clinical Attacks in Patients With MOG-Antibody–Associated Disease

Stephanie B. Syc-Mazurek, MD, PhD, John J. Chen, MD, PhD, Pearse Morris, MBBCh, Elia Sechi, MD, Jaywant Mandrekar, PhD, Jan-Mendelt Tillema, MD, A. Sebastian Lopez-Chiriboga, MD, Claudia Francesca Lucchinetti, MD, Nicholas Zalewski, MD, Laura Cacciaguerra, MD, Marina Buciuc, MD, Karl N. Krecke, MD, Steven Anthony Messina, MD, M. Tariq Bhatti, MD, Sean J. Pittock, MD, and Eoin P. Flanagan, MBBCh

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Observational Study › Neurology. 2023 Sep 26;101(13):e1376-e1381.
doi: 10.1212/WNL.0000000000207478. Epub 2023 Jun 19.

Timing and Predictors of T2-Lesion Resolution in Patients With Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

Laura Cacciaguerra [1], Vyanka Redenbaugh [1], John J Chen [1], Pearse Morris [1], Elia Sechi [1], Stephanie B Syc-Mazurek [1], A Sebastian Lopez-Chiriboga [1], Jan-Mendelt Tillema [1], Maria A Rocca [1], Massimo Filippi [1], Sean J Pittock [1], Eoin P Flanagan [2]

Long-term treatment options

- Rituximab less effective compared to NMOSD, but potentially better with highly relapsing course

Long-term Effectiveness and Safety of Rituximab in Neuromyelitis Optica Spectrum Disorder and MOG Antibody Disease

Paula Barreras, MD,* Eleni S. Vasileiou, MD,* Angeliki G. Filippatou, MD, Kathryn C. Fitzgerald, ScD, Michael Levy, MD, PhD, Carlos A. Pardo, MD, Scott D. Newsome, DO, Ellen M. Mowry, MD, MCR, Peter A. Calabresi, MD, and Elias S. Sotirchos, MD

Annals of NEUROLOGY
An Official Journal of the American Neurological Association and the Child Neurology Society
ANA AMERICAN NEUROLOGICAL ASSOCIATION

Research Article

Comparison of the Response to Rituximab between Myelin Oligodendrocyte Glycoprotein and Aquaporin-4 Antibody Diseases

Pierre Durozard MD, Audrey Rico MD, PhD, Clémence Boutiere M
Romaric Lacroix MD, PhD, Sylvie Cointe MD, PhD, Shirley Fritz MD
Jean Pelletier MD, PhD, Romain Marignier MD, PhD, Bertrand Aud

Efficacy and safety of rituximab in myelin oligodendrocyte glycoprotein antibody-associated disorders compared with neuromyelitis optica spectrum disorder: a systematic review and meta-analysis

Gregorio Spagni [1, 2], Bo Sun [3], Gabriele Monte [1, 4], Elia Sechi [5], Raffaele Iorio [2], Amelia Evoli [1, 2], Valentina Damato [1, 6]

Long-term treatment options

- Rituximab less effective compared to NMOSD, but potentially better with highly relapsing course
- Classic immunosuppressant (*e.g.*, AZA, MYC) only showed moderate efficacy
- Ongoing trials for IL-6R and FcRn
- Periodic IVIg are a good option, especially in children

Characteristic	Total MOGAD cohort (n = 59)	Relapsing while receiving IVIG (n = 20)	No relapses while receiving IVIG (n = 39)
<0.4 g/kg Every 4 wk	6 (10)	4 (20)	2 (5)
0.4 g/kg Every 4 wk[b]	21 (36)	8 (40)	13 (33)
>1 g/kg But less frequent than 4 wk	6 (10)	3 (15)	3 (8)
1 g/kg Every 4 wk	15 (25)	5 (25)	10 (26)
2 g/kg Every 4 wk[b]	11 (19)	0	11 (28)

April 4, 2022

Association of Maintenance Intravenous Immunoglobulin With Prevention of Relapse in Adult Myelin Oligodendrocyte Glycoprotein Antibody–Associated Disease

John J. Chen, MD, PhD[1,2]; Saif Huda, MD, DPhil[3]; Yael Hacohen, MD, DPhil[4,5]; et al

Treatment of myelin oligodendrocyte glycoprotein antibody associated disease with subcutaneous immune globulin

Elias S. Sotirchos • Eleni S. Vasileiou • Rebecca Salky • ... Sara Mariotto • John J. Chen • Michael Levy • Show all authors

Conclusions

- MOGAD differs from NMOSD and MS in disease course and attack recovery, and requires a different approach
- MOGAD attacks should be treated promptly and aggressively (even when MOG-IgG test result is not readily available)
- Patients with highly relapsing disease from onset or poor recovery after the presenting attack are reasonable candidate for long-term immunosuppressive therapy
- The optimal treatment strategy in MOGAD needs to be clarified but some drugs are promising (*e.g.*, anti-IL-6R, anti-FcRn, IVIg)

Thank you for your attention!

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