Contemporary Neurology

2025

Update in Neuroimmunology

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Duke Neurology

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Clinical Neurological Society of America

Disclosures

Consulting Fee (e.g., Advisory Board)
TG Therapeutics

Contracted Research (Principal Investigators must provide information, even if received by the institution)
Novartis

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Objectives

To be familiar with disease state-based updates in the field of clinical neuroimmunology

- Describe new treatments for neuromyelitis spectrum disorder and their application

- Review the diagnostic criteria for myelin oligodendrocyte glycoprotein associated disorders
- Review Duke-specific outcome data for myelin oligodendrocyte glycoprotein associated disorders

- Recognize updated antibody based clinical syndromes for autoimmune encephalitis

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Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Previously named Devic's disease and believed to be an MS variant.
- First described by Eugene Devic in 1894
- Novel syndrome characterized by acute myelitis and optic neuritis

M. E. Devic, de Lyon. — **Myélite aiguë dorso-lombaire avec névrite optique. — Autopsie.**

Femme de 45 ans, migraineuse et nerveuse, ayant eu plusieurs crises d'hystérie pendant sa jeunesse. Ni maladies infectieuses récentes, ni intoxication professionnelle, pas d'alcoolisme, pas de syphilis. En juin 1890, son mari tombe gravement malade, elle le soigne pendant six mois avec un grand dévouement, passant la plus grande partie des nuits. Il meurt en décembre de la même année. Profondément affectée de cette mort, ayant dépensé ses dernières économies, elle dut se remettre à un travail peu rémunérateur, autant du moins que le lui permit l'apparition de symptômes neurasthéniques bien caractérisés : insomnie, troubles digestifs, asthénie neuro-musculaire, palpitations et surtout céphalée. Ces symptômes augmentèrent peu à peu d'intensité et en septembre 1892 la malade dut cesser tout travail. En novembre 1892 la faiblesse générale et la céphalée subirent une recrudescence notable sous l'influence d'une vive frayeur.

Heading and first paragraph of Eugène Devic's famous abstract for the *Congrès Français de Médecine* in Lyon in 1894.

J Neuroinflammation **10**, 797 (2013)

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NMOSD

Discovery of the AQP-4-IgG in 2004 allowed its distinction from MS.

Identified at 80% of patients

- 20% are seronegative

Prevalence in the U.S.: 3.9 per 100,000

- Higher in Afro-Americans/African Americans: 10 per 100,000

9:1 female to male predominance

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Lancet. 2004 Dec 11-

Pathogenesis

- NMOSD targets **circumventricular organs** where AQP4 expression is highest.
- AQP4-IgG binds to AQP4, located on the end feet of **astrocytes.**
- It is an IgG1 and thus can activate complement and initiates a cascade of immune mediated inflammation (macrophages, T cells, B cells, neutrophils, eosinophils) resulting in secondary demyelination.

Cardinal Features of NMOSD

1. Longitudinally Extensive Transverse myelitis (≥3 vertebral segments)
2. Optic neuritis (often severe and may be bilateral)
3. Area postrema syndrome (intractable nausea/vomiting with or w/o hiccups)

- Co-existing autoimmunity, particularly with Sjogren syndrome, SLE, anti-phospholipid syndrome, and myasthenia gravis.

Features

- Longitudinally extensive transverse myelitis spanning 3 or more contiguous segments (85%)
  - Can be short in 15% of cases.
- Brain lacks typical MS lesions
- ON involvement often bilateral, involves posterior optic pathway including optic chiasm

MRI Features

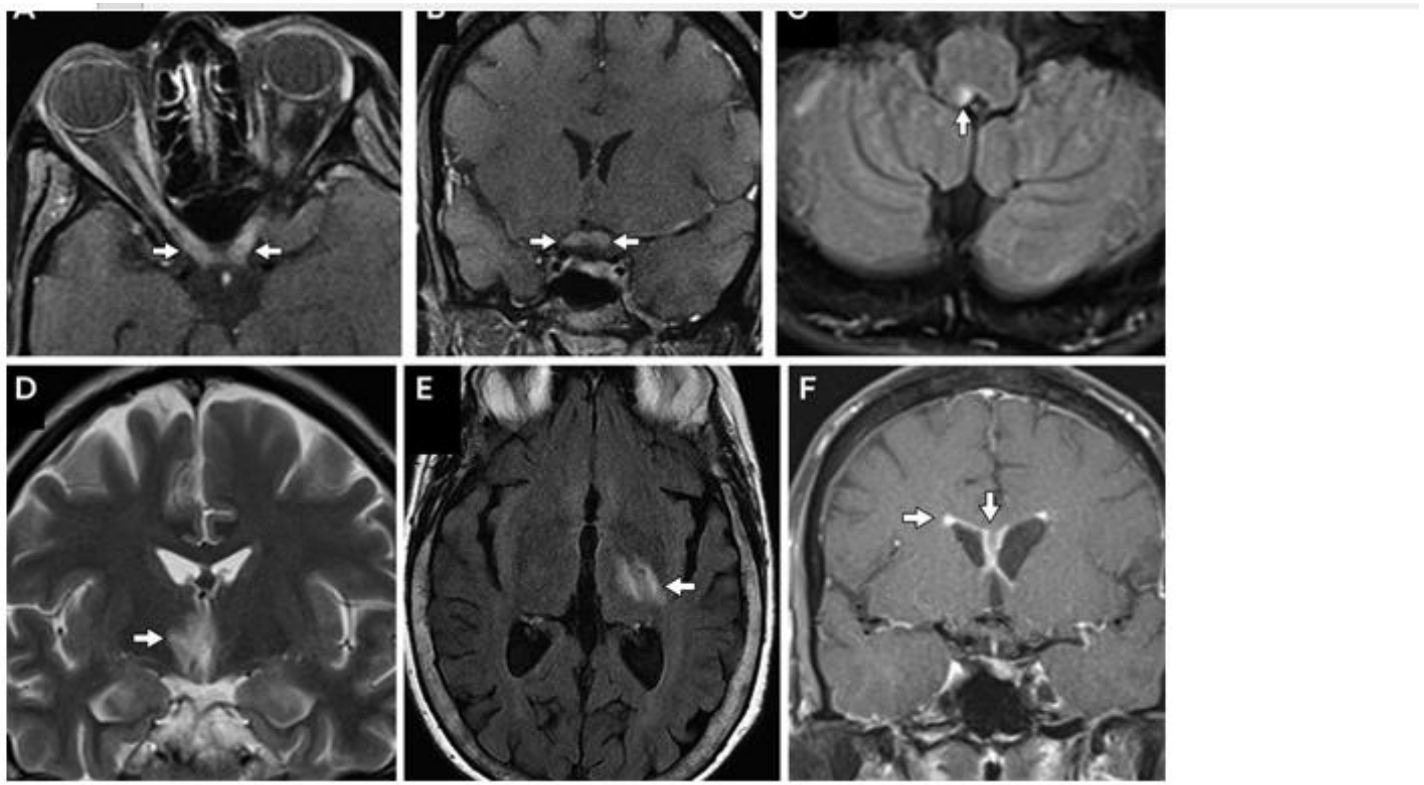
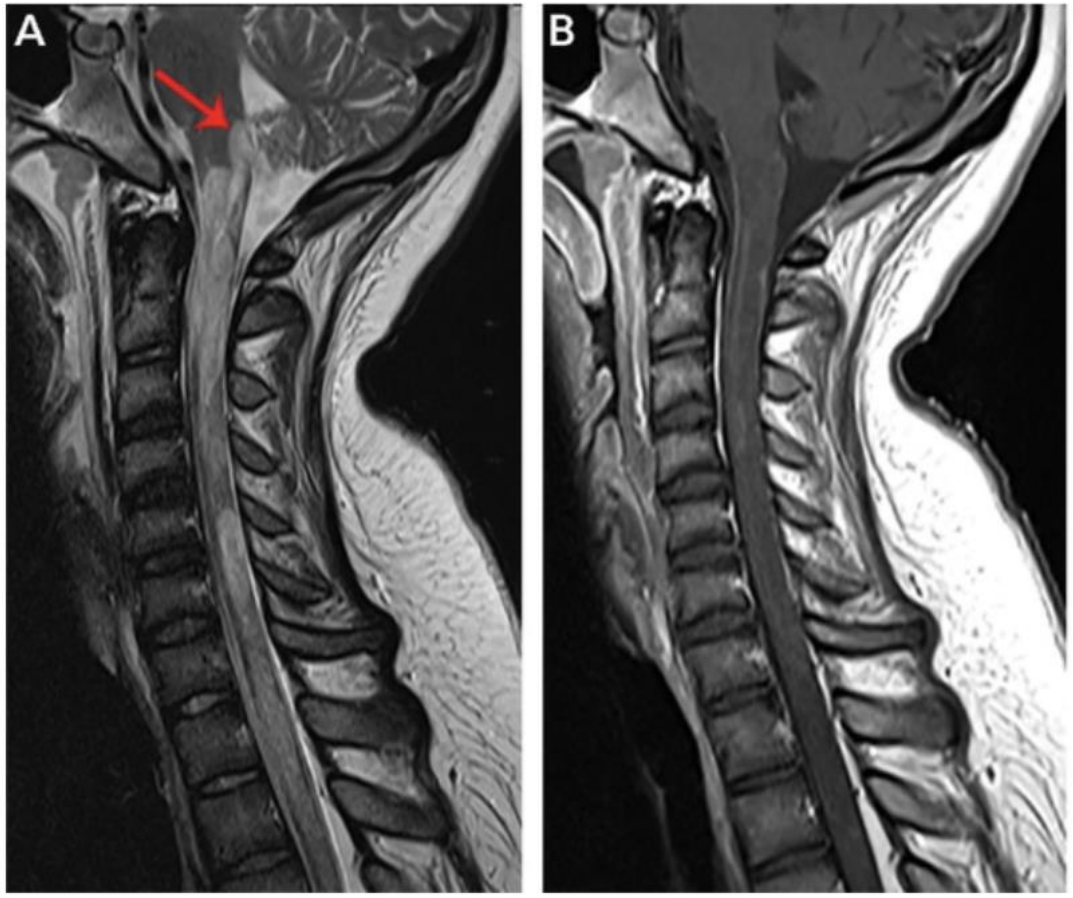


FIGURE 12-3. Typical brain and optic nerve lesions in patients with aquaporin-4 IgG–seropositive neuromyelitis optica spectrum disorder (NMOSD). Axial (*A*) and coronal (*B*) postcontrast T1-weighted images with fat suppression show bilateral posterior optic nerve enhancement extending to the optic chiasm (*arrows*). Axial fluid-attenuated inversion recovery (FLAIR) MRI shows a T2-hyperintense lesion in the region of the area postrema (*C, arrow*). Coronal T2-weighted MRI shows a characteristic lesion adjacent to the third ventricle (*D, arrow*). Axial FLAIR MRI shows a left internal capsule NMOSD lesion (*E, arrow*). Coronal postcontrast T1-weighted MRI with fat suppression shows pencil-thin linear ependymal enhancement (*F, arrows*).



- LETM with involvement of dorsal medulla (arrow) and patchy enhancement of spinal cord.

Diagnostic Criteria

Diagnostic criteria for neuromyelitis optica (NMOSD) with aquaporin-4 (AQP4) IgG

1. At least one core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses

Diagnostic criteria for NMO without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least two core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least one core clinical characteristic must be optic neuritis, acute myelitis with longitudinally extensive transverse myelitis, or area postrema syndrome
   b. Dissemination in space (two or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses

Core clinical characteristics

1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions

Published by the International Panel for NMO Diagnosis in 2015

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status

1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, *OR* (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over more than half optic nerve length or involving optic chiasm
2. Acute myelitis: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (longitudinally extensive transverse myelitis) *OR* ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions
4. Acute brainstem syndrome: requires associated periependymal brainstem lesions

Acute and Maintenance Therapy

- IVMP 1000 mg daily x 5 days
- PLEX
- Previously: Azathioprine, Mycophenolate mofetil, Rituximab, IVIG
- Now have 4 FDA approved drugs
  - Eculizumab/ravulizumab
  - Inebilizumab
  - Sartralizumab

Eculizumab

- First approved by the FDA in 2007
  - Paroxysmal nocturnal hemoglobinuria (PNH)
  - Approved for NMO based on PREVENT trial, 2019
- Terminal complement inhibitor, C5
- By blocking the terminal complement system, eculizumab increases risk of meningococcal and encapsulated bacterial infection.

N Engl J Med 2019

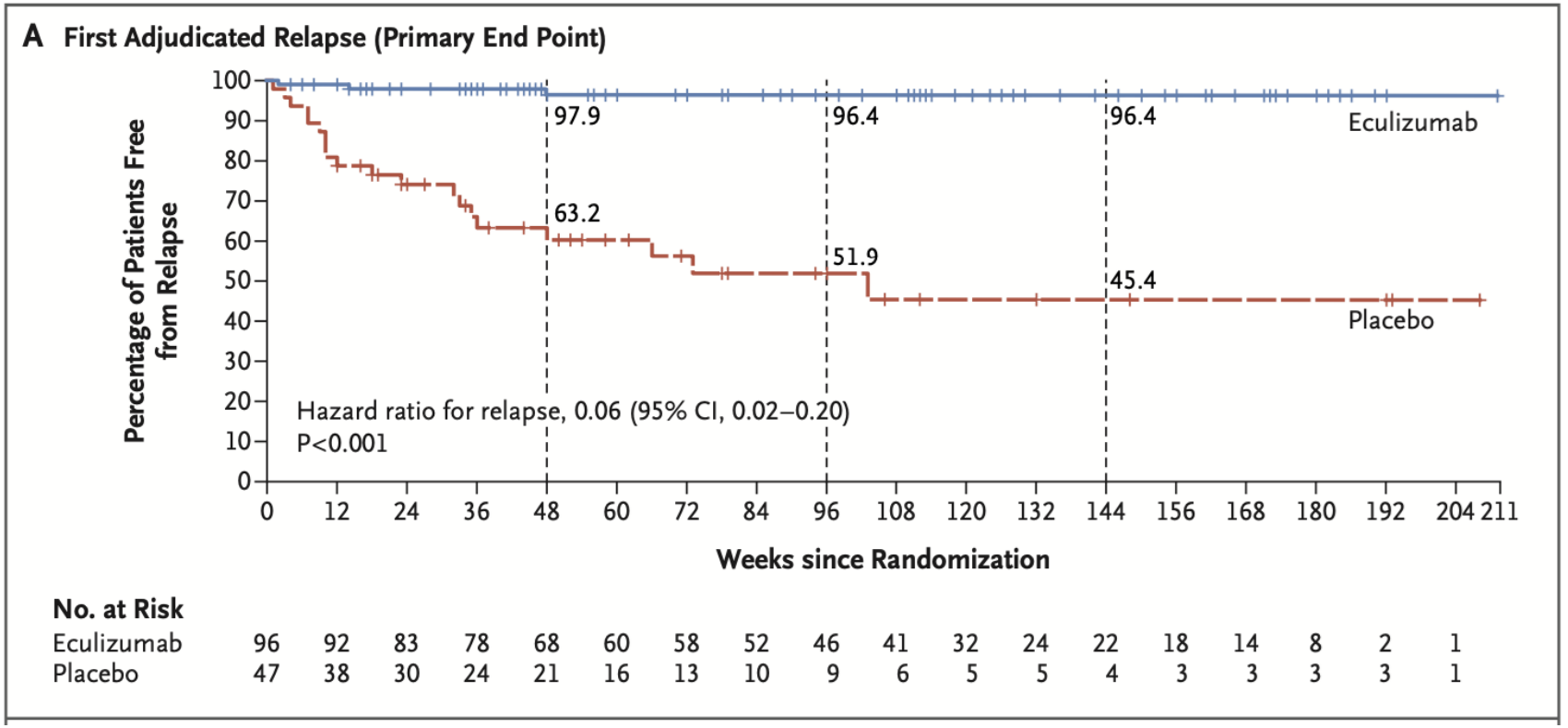
PREVENT Trial

- Randomized, double-blind, time-to-event trial
- 143 adults enrolled
- Randomized 2:1 ratio to receive IV Eculizumab (900 mg weekly x 4 doses, followed by 1200 mg q2W) or a matched placebo.
- Primary end point: first adjudicated relapse

PREVENT Trial Results

- 96 patients received Eculizumab and 47 received Placebo
- 91% of patients were women
- Of the total 143 patients, 46 (32% had received Rituximab but not within the 3 months before screening)
- 34 patients **(24%) did not receive any concomitant immunosuppressive** therapy during the trial
- The median time until the first adjudicated relapse was not reached in the eculizumab group and was reached at 103 weeks in the placebo group.
- Most relapses were myelitis.

Results


A First Adjudicated Relapse (Primary End Point)
Percentage of Patients Free from Relapse
100
90
80
70
60
50
40
30
20
10
0
97.9
96.4
96.4
Eculizumab
63.2
51.9
45.4
Placebo
Hazard ratio for relapse, 0.06 (95% CI, 0.02–0.20)
P<0.001
0 12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192 204 211
Weeks since Randomization
No. at Risk
Eculizumab 96 92 83 78 68 60 58 52 46 41 32 24 22 18 14 8 2 1
Placebo 47 38 30 24 21 16 13 10 9 6 5 5 4 3 3 3 3 1

Adverse Reactions

- Upper respiratory tract infections and headaches were more common in the eculizumab group

- One patient in the eculizumab group who was receiving concomitant azathioprine died from pulmonary empyema after 108 weeks in the trial.

- No cases of meningococcal infection were reported during the trial.

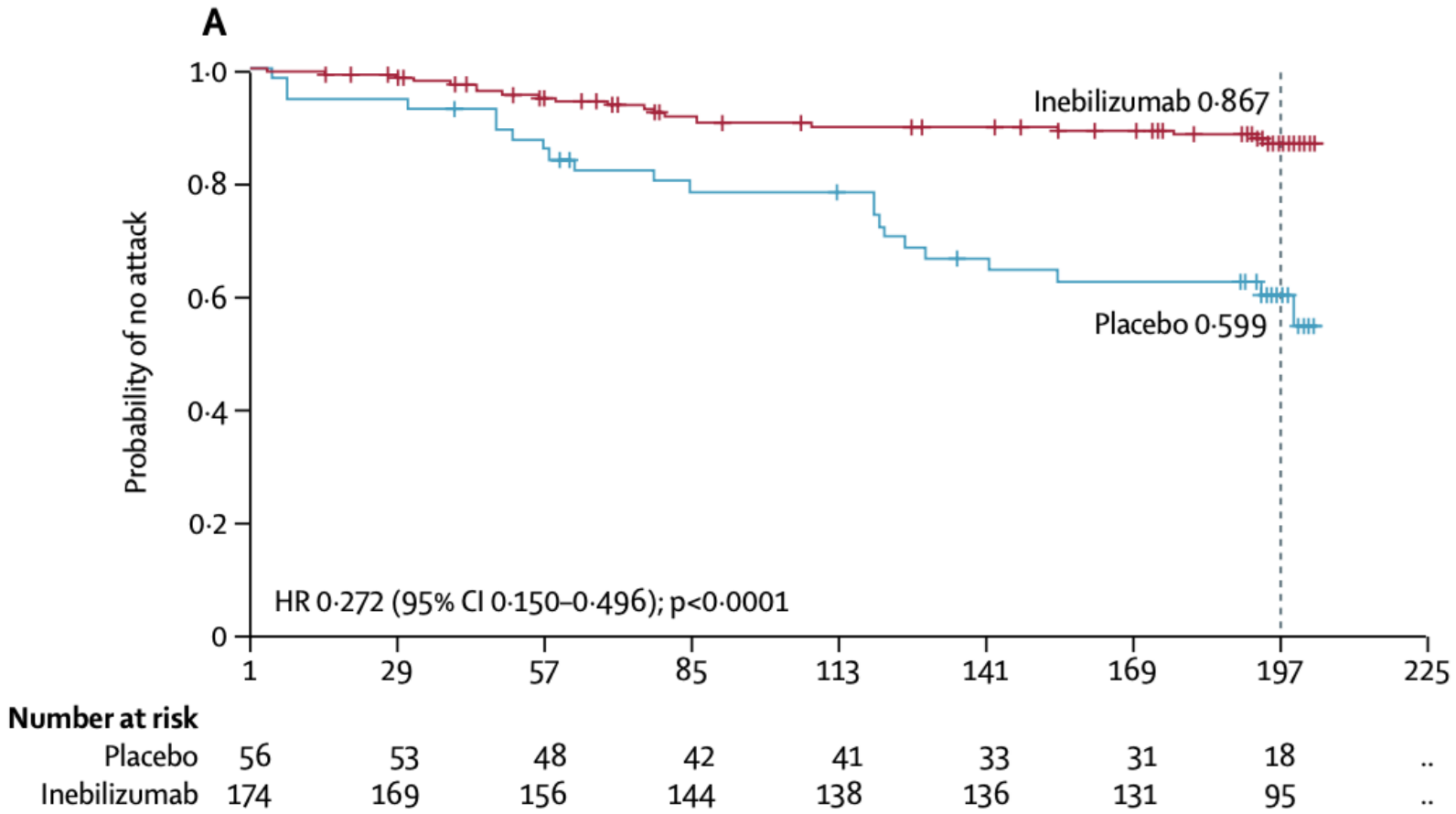
Inebilizumab

- FDA approved June 2020
- Humanized anti-CD19 monoclonal antibody
- Compared with anti-CD20 monoclonal antibodies that recognize and deplete a small subset of CD20-expressing T lymphocytes (in addition to B lymphocytes), **anti-CD19 antibodies recognize and deplete a wider range of lymphocytes exclusively from the B cell lineage**.

Lancet 2019; 394:1352-63

N-Momentum Trial

- Multicenter, double-blind, randomized placebo-controlled trial
- Efficacy and safety of Inebilizumab as monotherapy.
- 230 total participants were randomly allocated (3:1)
  - 174 received Inebilizumab (300 mg IV on days 1 and 15, total 600 mg), 56 received placebo
  - **93% were seropositive, 7% seronegative**
- All participants received **oral** corticosteroids x 21 days
- No other immunosuppressants were used.
- Primary endpoint was time to an NMO attack, or or before day 197.



21 (12%) of 174 participants receiving Inebilizumab had an attack versus 22 (39%) of 56 participants receiving placebo

Adverse Reactions

- Most common side effect was infusion related reaction.
- Infection rate was not higher than placebo.
- Grade 3 neutropenia occurred in 3 patients (2%), transient.
- Three deaths in the open label extension

Sartralizumab

- FDA approved August 2020
- Targets membrane bound and soluble Interleukin 6 receptor (IL-6)
- IL-6 promotes differentiation of naïve T cells into proinflammatory type 17 helper cells, which along with IL-6, promote differentiation of B cells into AQP-4 IgG producing plasmablasts.
- IL-6 also increases permeability of the BBB
- Levels of interleukin 6 are elevated in the CSF of patients with NMOSD, as compared with patients who have MS or noninflammatory neuro disorders

N Engl J Med 2019;381:2114-24.

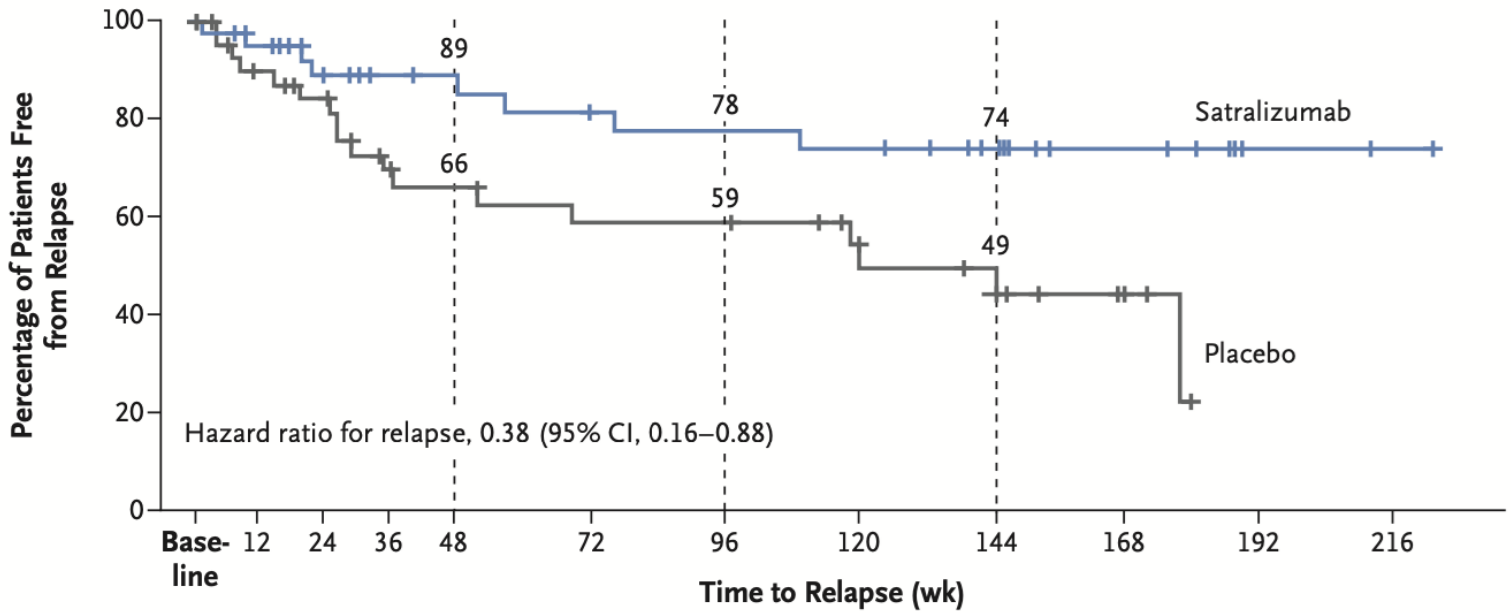
SAkuraSky Study

- Phase 3, randomized, double-blind, placebo controlled trial
- Total of 83 patient were enrolled, Randomized 1:1
- 42 assigned to Satralizumab + baseline drug, 42 to Placebo + baseline drug
- Seropositive or seronegative for AQP-4 IgG
- Satralizumab 120 mg or placebo administer subQ at weeks 0, 2, 4 and every 4 weeks thereafter, added to stable immunosuppressant treatment (Azathioprine 3 mg/kg/day, mycophenolate mofetil max 3000 mg/day, oral glucocorticoids)
  - Use of anti-CD20 including Rituximab was not permitted
- End point was relapse in a time to event analysis
- Median treatment duration was 107 weeks

Results

- Relapse occurred in 8 (20%) receiving satralizumab and in 18 (43%) receiving placebo.
- Among 55 AQP4-IgG–seropositive patients, relapse occurred in 11% of those in the satralizumab group and in 43% of those in the placebo group; among 28 AQP4-IgG–seronegative patients, relapse occurred in 36% and 43%, respectively.

A **Freedom from Relapse in Overall Population**



No. at Risk												
Satralizumab	41	37	29	25	24	22	20	19	14	9	2	1
Placebo	42	34	30	22	19	16	16	12	9	4	0	—

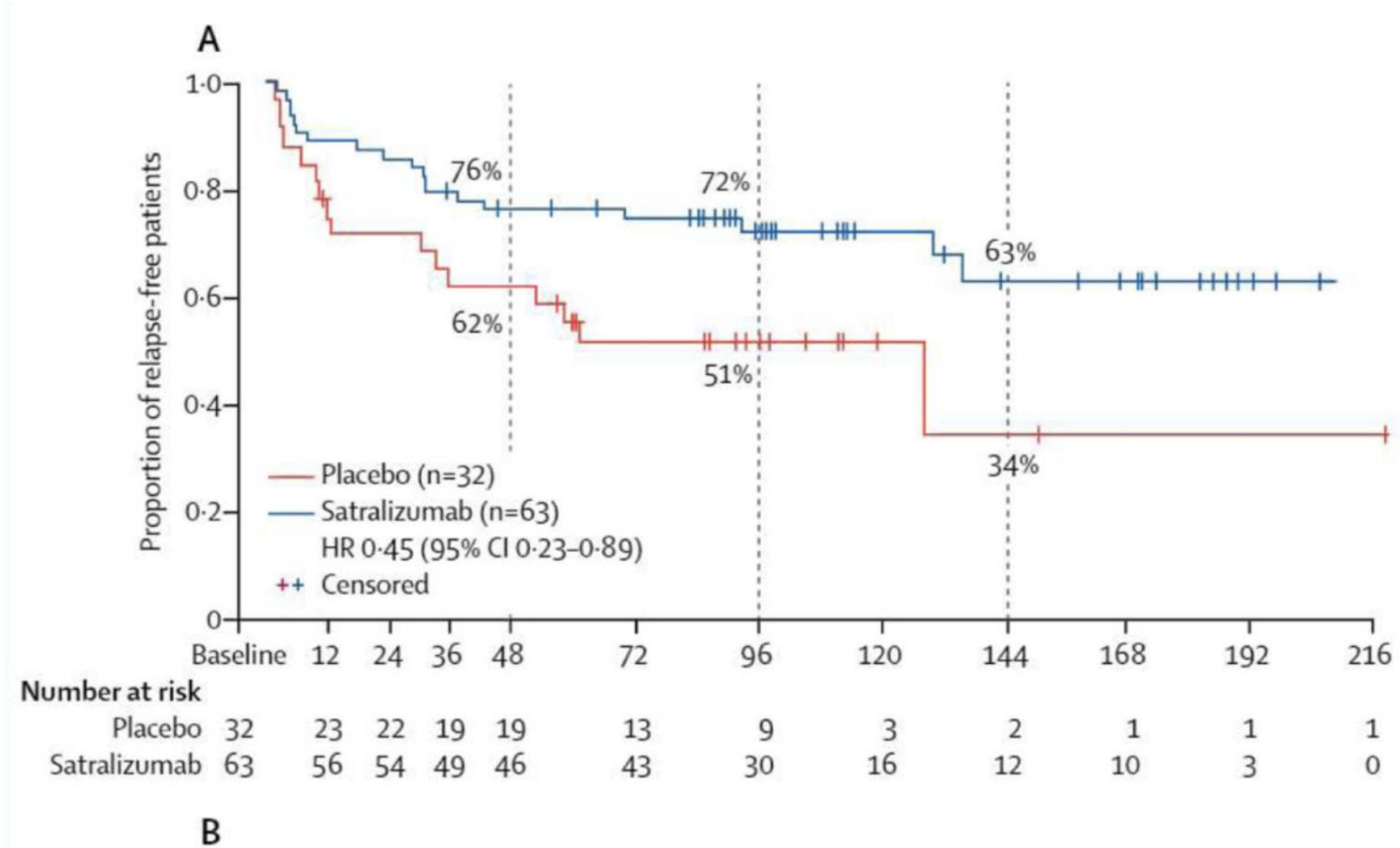
Adverse Events

- Injection site reactions
- No more frequent infections than placebo
  - Nasopharyngitis
  - Headache

SAkuraStar Study

- Second trial to assess safety and efficacy of Satralizumab monotherapy Phase 3, double-blind, placebo-controlled
- Participants were randomly assigned 2:1 to receive satralizumab 120 mg or placebo
- AQP4 IgG seropositive AND seronegative
- 95 (57%) of 168 screened participants were randomly assigned to treatment (63 to satralizumab; 32 to placebo)
- Protocol-defined relapses occurred in 19 (30%) patients receiving satralizumab and 16 (50%) receiving placebo

Lancet Neurology. 2020 May; 19(5): 402-412


A
1·0
0·8
0·6
0·4
0·2
0
Proportion of relapse-free patients
76%
72%
63%
62%
51%
34%
Placebo (n=32)
Satralizumab (n=63)
HR 0·45 (95% CI 0·23–0·89)
Censored
Baseline 12 24 36 48 72 96 120 144 168 192 216
Number at risk
Placebo 32 23 22 19 19 13 9 3 2 1 1 1
Satralizumab 63 56 54 49 46 43 30 16 12 10 3 0
B

When to consider which therapy?

Seronegative vs seropositive

Prior immunosuppression and need for alternative mechanism of action

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Myelin Oligodendrocyte Glycoprotein Associated Disorder (MOG-AD)

- MOG Antibody Associated Disease

- Distinct clinical entity
  - Phenotypically heterogeneous
  - Pathogenicity of antibody unclear

What is MOG?

- Myelin Oligodendrocyte Glycoprotein
  - One of several proteins produced by oligodendrocytes (the myelin-forming cells of the CNS)
  - Present on oligodendrocyte surface membranes
    - Myelin basic protein
    - Proteolipid protein

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MOG Antibody testing

- Cell-based assays
  - Allow for accurate detection of MOG antibody
  - If using cell-based assays, excellent agreement for high positive and negative samples
  - If borderline value, more discordance
- Methods used in the initial and former studies might have insufficient specificity and sensitivity; immunoblotting and ELISA techniques do not precisely discriminate between denatured and folded proteins

Reindl M, Schanda K, Woodhall M, et al. International multicenter examination of MOG antibody assays. *Neurol Neuroimmunol Neuroinflamm* 2020; **7:** e674.

Antibody titer specificity

- Anti-MOG antibodies are rarely found in patients with multiple sclerosis when measured using cell-based assays
  - 1 in 244 in a multicenter study
  - Two cross sectional multicenter studies
    - None in 200 patients with progressive MS
    - 2 in 685 patients with any form of MS from two tertiary centers

Polyreactivity

- Rare for patients to have coexistent MOG and AQP4
  - Clinical data from 197 MOG-Ab-positive patients ≥18 years of age

Cobo-Calvo A, Ruiz A, Maillart E, et al. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: The MOGADOR study. *Neurology* 2018; **90:** e1858–69.

In case of positivity…

- If clinical and lab features are not consistent with MOG-AD typical findings, closely monitor clinically

Neuropathologic findings

Diagnosis		
MOG-AD	Inflammatory demyelination	Perivascular infiltrated MOG-laden macrophages and CD4+ T-cell infiltration
Neuromyelitis Optica	Astrocytopathy	
Multiple Sclerosis	Perivascular deposits of activated complement proteins and immunogloblins	CD8+ T-cell infiltration

Epidemiology/Risks

- No racial groups with increased likelihood of diagnosis
  - Contrast to AQP4-NMOSD

- Equal number of males:females among children
- In postpubertal children and adults, slight female predominance

Clinical Features

- No significant HLA association
- Age dependent phenotype
  - Younger children = brain involvement
  - More severe in children
  - More complete and faster recovery in children
  - Risk of relapse is lower in children

A patient story

- 2004: First developed **right eye blurry vision** that progressed to near complete vision loss (age 19). Had associated eye pain with movement. She was treated with IV steroids and had significant improvement in her symptoms.

- Over the next several years, she had recurrent right eye optic neuritis.
- She was started on glatiramer acetate and continued to have episodes of optic neuritis whilst taking this.

2019

- She presented with new **left-sided** optic neuritis in April.
- Still taking glatiramer acetate.

MRI Brain and Orbits w/wo contrast

04/2019
1. Left optic neuritis.
2. Small nonspecific signal abnormalities in the pons, possibly representing demyelinating lesions given the clinical history.

Clinical Course

- She was treated with 5 days of IV steroids.
- She was found to have antibodies to MOG, **titer 1:1000**.
- Started on B cell depleting therapy

2020

- Established care with me on May, 23 weeks pregnant
- Delivered September 2020, resumed infusion therapy
- May 2021, pregnant with second child
- Due Dec 2021 with planned infusion in Jan 2022

Clinical Presentation

- Optic neuritis
  - Optic nerve head swelling
  - Less damaging than AQP4 associated ON
- Brainstem involvement
- [Longitudinally extensive] transverse myelitis
  - Conus medullaris involvement
- Encephalitis
  - ADEM
- Aseptic meningitis/leptomeningeal enhancement

CSF Biomarkers

- 50% have pleocytosis
  - Lymphocytic or monocytic
- Cell counts higher than Multiple Sclerosis
- OCBs and positive IgG index in <15%
- CSF cytokines elevated
- Utility of MOG-Ab in CSF is T.B.D

Imaging

- Brain
  - Poorly demarcated
  - Fewer brain parenchymal lesions
  - Less frequent “Dawson’s fingers”
  - Both white and gray matter involvement
- Spine
  - Confined to gray matter (sagittal line, ‘H’ sign) or nerve roots
  - Minimal enhancement
- Optic nerves
  - Anterior involvement
  - Perineural edema

Disease course

- Varied

- Estimated that 40% adults and 30% children have a second clinical attack within 5 years
  - Monophasic in children

Table 1. Comparison of typical characteristics of optic neuritis in MS, AQP4-seropositive NMOSD, and MOG-AD

Characteristic	MS	AQP4	MOG
Mean age at presentation	Rare in children, mostly adults in 20s	Rare in children, mostly adults in 40s	Children + adults with broad age of presentation
Sex predominance	Female > male (3:1)	Female >>> male (9:1)	Female ~ male
Ethnicity	Predominantly Caucasian	Over-represented in people of Asian or African origin	None identified so far
Disease course	Relapsing, primary progressive, secondary progressive	Relapsing with accumulating severe disability	Monophasic, but some are relapsing with mild–moderate disability progression
CSF analysis	Low nucleated cells, and OCB present in majority	Elevated nucleated cells (neutrophils or eosinophils), and OCB present in minority	50% can have elevated nucleated cells, and OCB present in minority
Characteristics related to optic neuritis			
Pain	+++	++	+++
Bilateral optic neuritis	+	++	+++
Severe vision loss at nadir of attack	++	+++	+++
Risk of recurrence	++	+++	+++
Steroid dependence	Rare	Rare	+++
Risk of vision loss (<20/200)	+	+++	++
Imaging findings			
Length	Short	Long	Long
Location	Variable	Canalicular and more posterior	Retroorbital and more anterior
Perineural enhancement	Rare	Rare	++
Optic chiasm involvement	Rare	+++	+

OCB oligoclonal bands. Rare less than 5%; + infrequent; ++ frequent; +++ very frequent

Diagnostic Criteria

Recommended indications for MOG-IgG testing in patients presenting with acute CNS demyelination of putative autoimmune etiology

1. Monophasic or relapsing acute optic neuritis, myelitis, brainstem encephalitis, encephalitis, or any combination thereof,

and

2. radiological or, only in patients with a history of optic neuritis, electrophysiological (VEP) findings compatible with CNS demyelination,

and

3. at least one of the following findings:

MRI

a. Longitudinally extensive spinal cord lesion (≥3 VS, contiguous) on MRI (so-called LE

b. Longitudinally extensive spinal cord atrophy (≥3 VS, contiguous) on MRI in patients

c. Conus medullaris lesions, especially if present at onset[c]

d. Longitudinally extensive optic nerve lesion (e.g., >1/2 of the length of the pre-chiasma

e. Perioptic Gd enhancement during acute ON[e]

f. Normal supratentorial MRI in patients with acute ON, myelitis and/or brainstem encep

g. Brain MRI abnormal but no lesion adjacent to a lateral ventricle that is ovoid/round or juxtacortical U fiber lesion (Matthews-Jurynczyk criteria[f])

h. Large, confluent T2 brain lesions suggestive of ADEM

Fundoscopy

i. Prominent papilledema/papillitis/optic disc swelling during acute ON

CSF

j. Neutrophilic CSF pleocytosis[g] or CSF WCC > 50/µl[h]

k. No CSF-restricted OCB as detected by IEF at first or any follow-up examination[i] (applies to continental European patients only)

Histopathology

l. Primary demyelination with intralesional complement and IgG deposits

m. Previous diagnosis of "pattern II MS"[j]

Clinical findings

n. Simultaneous bilateral acute ON

o. Unusually high ON frequency or disease mainly characterized by recurrent ON

p. Particularly severe visual deficit/blindness in one or both eyes during or after acute ON

q. Particularly severe or frequent episodes of acute myelitis or brainstem encephalitis

r. Permanent sphincter and/or erectile disorder after myelitis

s. Patients diagnosed with "ADEM", "recurrent ADEM", "multiphasic ADEM" or "ADEM-ON"

t. Acute respiratory insufficiency, disturbance of consciousness, behavioral changes, or epileptic seizures (radiological signs of demyelination required)

u. Disease started within 4 days to ~ 4 weeks after vaccination

v. Otherwise unexplained intractable nausea and vomiting or intractable hiccups (compatible with area postrema syndrome)[a]

w. Co-existing teratoma or NMDAR encephalitis (low evidence[k])

Treatment response

x. Frequent flare-ups after IVMP, or steroid-dependent symptoms[l] (including CRION)

y. Clear increase in relapse rate following treatment with IFN-beta or natalizumab in patients diagnosed with MS (low evidence)

Jarius S, Paul F, Aktas O, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. *J Neuroinflammation*. 2018;15(1):134. Published 2018 May 3. doi:10.1186/s12974-018-1144-2

Prognostic indicators

- MOG-antibody titers
  - Seropositivity does not correlate with clinical activity:
    - Sustained seropositivity does not predict relapse
    - Patients who become seronegative can still relapse
    - Titers do not clearly correlate with disability outcomes
    - At relapse, titers are higher than in remission
    - False positive in ~30%
    - Higher titers may have more positive predictive value

Sechi E, Buciuc M, Pittock SJ, et al. Positive Predictive Value of Myelin Oligodendrocyte Glycoprotein Autoantibody Testing. *JAMA Neurol.* 2021;78(6):741–746. doi:10.1001/jamaneurol.2021.0912

The Duke Experience

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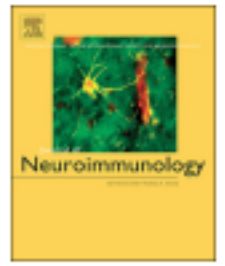

Review Article

The clinical presentation and treatment of MOG antibody disease at a single academic center: A case series

Petra Brayo, F. Lee Hartsell III, Mark Skeen, Joel Morgenlander, Christopher Eckstein, Suma Shah*

Department of Neurology, Duke University, Durham, NC, United States

The Duke Experience

Table 1
Demographics of patients presenting with MOG-AD.

Patient characteristics	
Sex, N (%)	
Male	6 (54.5)
Female	5 (45.5)
Age at initial presentation, year	
Mean (SD)	41.5 (13.6)
Range	25–69
MOG antibody titer	
Mean (SD)	1:240 (1:377)
Range	1:20–1:1000
Initial presentation, N (%)	
Optic neuritis	9 (81.8)
Bilateral	3
Unilateral	6
Longitudinally Extensive Transverse myelitis (LETM)	2 (18.2)
Disease course, N (%)	
Monophasic	5 (45.5)
Recurrent	6 (64.5)

- **Objectives:** To describe the clinical presentation of MOG antibody disease (MOG-AD) in a series of patients at a single academic center.
- **Methods:** We performed a retrospective review of patients with MOG antibodies. Results: We review the clinical presentation of 11 patients with MOG antibodies. In patients seen at Duke University Health System with MOG antibodies, the most common presentation was optic neuritis. Rituximab was the most used treatment for long-term management.
- **Conclusions:** Our case series highlights the common presentation of MOG antibody disease (MOG-AD) at a single academic medical center

Duke Neuroimmunology Case Series

Table 2
Acute and disease modifying treatments for MOG-AD patient with disease course.

Patient	Acute treatment	Oral steroid taper	Disease modifying treatment	Recurrences and outcomes
1	IVMP 1000 mg for 5 days	Prednisone 80 mg with slow wean over three months	None	Clinically and radiographically stable
2	IVMP 500 mg twice a day for 5 days	Prednisone 60 mg with a very prolonged taper given multiple recurrences	Rituximab	Multiple relapses prior to DMT initiation. Clinically and radiographically stable since.
3	None, presented for evaluation after acute setting.	None	Rituximab	Relapses prior to DMT initiation
4	IVMP 1000 mg for 5 days	Prednisone 60 mg over 12 days	Rituximab	N/A*
5	IVMP 1000 mg for 2 days, then oral dexamethasone 80 mg for 1 day	Prednisone 60 mg for 18 days	Mycophenolate mofetil	N/A*
6	IVMP 1000 mg for 3 days	Deferred due to severe hyperglycemia	Rituximab	N/A*
7	IVMP 1000 mg for 3 days	Multiple prednisone tapers for prior relapses	Rituximab	Multiple relapses prior to DMT initiation. Now, clinically and radiographically stable
8	IVMP 1000 mg for 3 days	None	Deferred- watchful waiting	N/A*
9	IVMP 1000 mg for 3 days	Prednisone 60 mg for 6 days	Rituximab	Relapse prior to DMT initiation. Now, clinically and radiographically stable
10	IVMP 1000 mg for 3 days, followed by IVIg 2 g	Prednisone 40 mg over 4 weeks	Rituximab	Relapse prior to DMT initiation.
11	IVMP 1000 mg for 3 days	Prolonged prednisone taper over weeks	Rituximab	N/A*, Patient with coexistent AQP-4 antibodies.

* These patient were identified as having MOG-AD in the acute setting and information regarding outcome is not available at the time of writing.

Treatment Options

- No randomized controlled trials for either acute treatment or relapse prevention
- Clinical trial outcomes pending: sartralizumab

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Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease: Presentation and outcomes of adults at a single center

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A B S T R A C T

Updated demographics

Table 1
Patient demographics including sex, race, age and disease characteristics.

Demographics of patients presenting with MOGAD	
Patient Characteristics	
Sex, N (%)	
Male	13 (39.4)
Female	20 (60.6)
Race, N (%)	
Caucasian/white	22 (66.7)
African American/black	8 (24.2)
Hispanic	2 (6.1)
Not reported	1 (3.0)
Age at first symptoms in years, N (%)	
18–29	9 (27.3)
30–39	7 (21.2)
40–49	8 (24.2)
50–59	7 (21.2)
$\geq$ 60	2 (6.1)
Median	40.0
MOG antibody titer, N (%)	
1:20	4 (12.1)
1:32 or 1:40	8 (24.2)
1:100	14 (42.4)
1:1000	6 (18.2)
1:10000	1 (3.0)
Initial presentation, N (%)	
Optic neuritis only	23 (69.7)
Optic neuritis plus other	3 (9.1)
Transverse myelitis	4 (12.1)
Brainstem symptoms	3 (9.1)
Disease course, N (%)	
Monophasic	14 (42.4)
Relapsing	18 (54.55)
Unknown	1 (3.0)

Acute treatment

- IV methylprednisolone 1g/day for 3-5 days
- Don’t wait on antibody testing
- If severe, escalate:
  - Plasma exchange
  - IVIg

Weaning steroids

- To be determined
- Factors to consider:
  - Attack severity
  - Risk of flare up
  - Timing/plan for maintenance therapy
    - Risk for relapse?

Chronic immunomodulation

- Considerations
  - Response to acute treatment
  - Severity of initial attack
  - Risk of short-term disability
  - Risks of immunosuppression/age
- Not recommended in children
- In adults, debated.
  - Wait until a second event?
  - METEOROID Study

Outcomes

- Proposed predictors:
  - Time to initiation of acute treatment
  - More relapses = more disability

- Overall disability appears to be less than that seen in NMOSD

Outcomes at ~9-16 mos

Treatment	Number of relapse free patients
IVIg	20/29 (69%)
Mycophenolate mofetil	30/63 (47%)
Azathioprine	21/55 (39%)
Rituximab	47/94 (50%)

Autoimmune Encephalitis, Updates

- Diagnostic history
- Recognition of NMDA Syndrome

- Recent updates:
  - LGI-1
  - IGLON5
  - GFAP
  - KLH11

Varley, J.A., Strippel, C., Handel, A. *et al.* Autoimmune encephalitis: recent clinical and biological advances. *J Neurol* **270**, 4118–4131 (2023). https://doi.org/10.1007/s00415-023-11685-3

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LGI-1

- Most common
- Underrecognized
- Subtle focal seizures
  - Faciobrachial dystonic seizures
- Elderly males
- Progressive course
  - Memory disturbance
  - Psychiatric disturbance
  - Hyponatremia

- ~25% exhibit adverse reactions toward certain first generation ASMs
- carbamazepine and phenytoin, including life-threatening Stevens–Johnson spectrum reactions

IGLON5

- Overlap between neurodegernative and immune mediated
- Clinical time course is slower on
- wide variety of clinical phenomenologies:
  - gait instability, chorea, bradykinesia, dystonia, tremor, myoclonus, hyperekplexia, and cramps/fasciculations
- Clinical cues
  - early prominent sleep disorders in REM and non-REM stages with dream re-enactment, stridor
  - a complex set of movement disorders
  - Dysautonomia
  - bulbar involvement
- Temporary initial response to IMT, subsequent waning
- Sudden death

GFAP

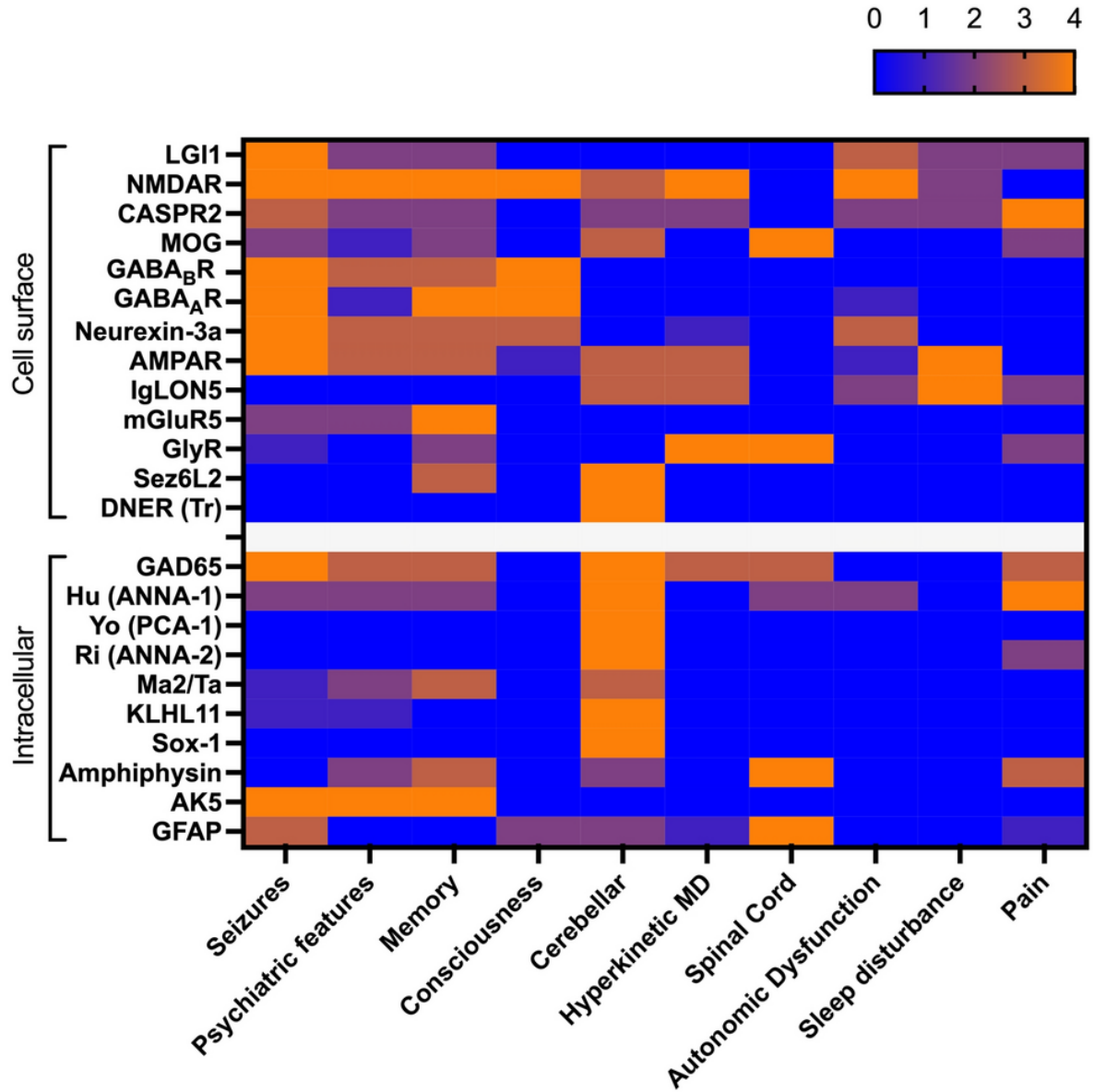
- Immunotherapy responsive
- Meningoencephalomyelitis
- Characteristic brain MRI pattern

- In the largest series to date (*n* = 102):
  - a viral prodrome was seen in the majority
  - 94% had either meningitis, encephalitis or myelitis
  - around 30% had concurrent AQP4- or NMDAR-antibodies
  - around 30% had an underlying neoplasia

KLH 11

- Neurological syndrome precedes the neoplasia (testicular seminoma)
- Rhombencephalitis
- Responds well to immunotherapy +/- cancer treatment

- Clinical cues:
  - Brainstem syndrome
  - Ataxia
  - Men >>Women


0 1 2 3 4
Cell surface
LGI1
NMDAR
CASPR2
MOG
GABA$_B$R
GABA$_A$R
Neurexin-3a
AMPAR
IgLON5
mGluR5
GlyR
Sez6L2
DNER (Tr)
Intracellular
GAD65
Hu (ANNA-1)
Yo (PCA-1)
Ri (ANNA-2)
Ma2/Ta
KLHL11
Sox-1
Amphiphysin
AK5
GFAP
Seizures
Psychiatric features
Memory
Consciousness
Cerebellar
Hyperkinetic MD
Spinal Cord
Autonomic Dysfunction
Sleep disturbance
Pain

Key takeaways

Many new updates in disease recognition and treatment options for antibody mediated CNS disease

Consider mechanisms of action and side effect profile when selecting best disease modifying therapy

MOG Antibody positivity is high, correlate clinically

Several novel autoimmune encephalitides being described and likely still underrepresented

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Questions