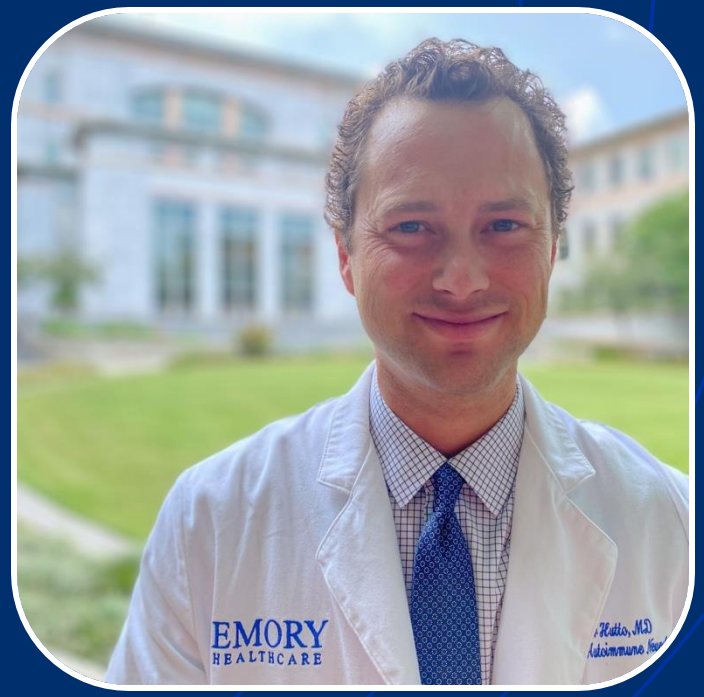
SRNA Rare Neuroimmune Disorders Symposium | Atlanta

Treatment of NMOSD



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Disclosures

- May discuss off-label use of medications
- Today's activities are all volunteer-based with no financial relationships

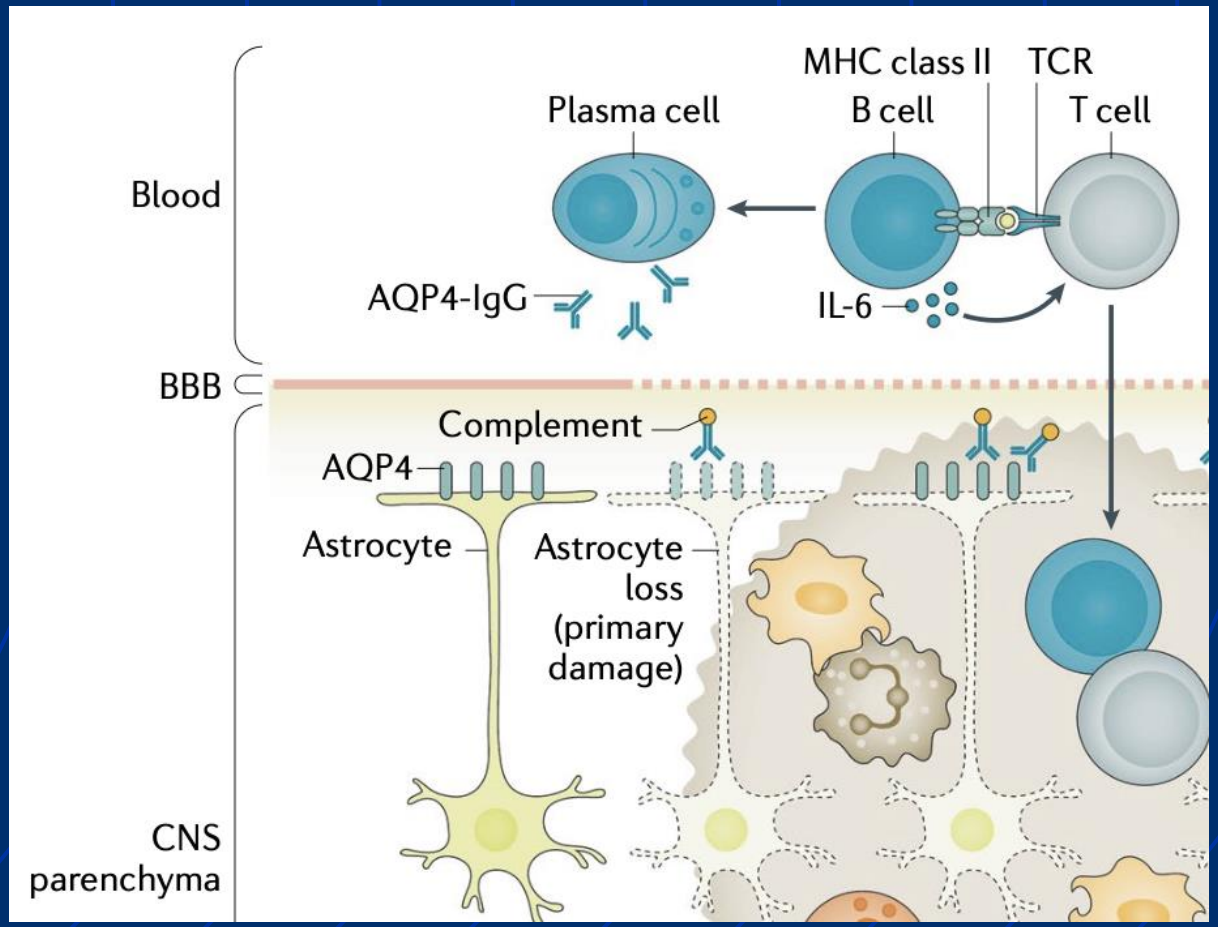
Objectives

- Treatment targets
- Treatments in the hospital
- Long-term treatments

What Happens in NMO

PATHOPHYSIOLOGY

- B cells are activated, sometimes by a molecule called IL-6
- Some of these produce the AQP4 antibody of NMO
- These antibodies damage the nervous system via complement fixation



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Jarius et al. Nat Rev Dis Primers 2020.

Treatments in the Hospital

- Intravenous methylprednisolone (IV steroids)
  - Eliminates multiple immune cells
  - 3-5 days, depending on symptom evolution
- Plasmapheresis (PLEX)
  - Removes antibodies, signaling molecules, and complements
  - 1 session every other day for 5 sessions

Maintenance Treatment Considerations

- Average 0.7 attacks/patient/year (range: 0.1-3)
- Disability is cumulative and attack-related
  - No progressive phase
- An individual attack can be severe

Cabre et al. JNNP 2009.
Merle et al. Ophthalmology 2007.

DMT Selection

EFFICACY
LOGISTICS
POTENTIAL RISKS
VACCINATIONS

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B Cell Depletion

Rituximab

- Developed in 1997, targets CD20 on B cells
- Intravenous
- Loading doses of 1000 mg twice two weeks apart
- Maintenance dose once every 6 months
- Screening for HBV and TB
- Risk for HBV reactivation and infections

B Cell Depletion

Inebilizumab

- Approved in 2020, targets CD19 on B cells
- Intravenous
- Loading doses of 300 mg twice two weeks apart
- Maintenance dose of 300 mg every 6 months
- Screening for HBV and TB
- Risk for HBV reactivation and infections

IL-6 Antagonism

Satralizumab

- Approved in 2020
- Subcutaneous
- Loading doses of 120 mg at weeks 0, 2, and 4
- Maintenance dose of 120 mg every 4 weeks
- Headache, upper respiratory tract infections, nausea, and joint pain most common side effects
- Screening for HBV and TB
- Regularly checking liver function

Pediatrics patients age > 12 yo

Complement Inhibition

Eculizumab

- Approved in 2019
- Intravenous
- Weekly loading doses of 900 mg for 4 weeks
- Maintenance dosing of 1200 mg every 2 weeks
- Headache, diarrhea, and upper respiratory tract infections most common side effects
- Risk for meningococcal meningitis
- Meningococcal vaccination and potentially prophylactic antibiotics

Complement Inhibition

Ravilizumab

- Approved in 2024
- Extended-dosing complement inhibitor (every 8 weeks)
- Headache, diarrhea, and upper respiratory tract infections most common side effects
- Risk for meningococcal meningitis

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Clinical Trials

SLIDE SUBHEAD

Eculizumab for Pediatric NMO

Clinicaltrials.gov ID: NCT04155424
Sponsor: Alexion Pharmaceuticals
US Sites: Terminated early, only 5 enrolled

- Purpose: Safey and efficacy of eculizumab in patients between 2 and 18 years old
- Type: open-label, all patients receive eculizumab
- Dosing: weight-based, weekly during the induction phase, every two weeks thereafter
- Timeframe: 52-53 weeks, may extend to 104 weeks

Eligibility

- Between 2 and 17 years old
- At least 10 kg, two relapses in the last two years
- Vaccinated
- Stable dosing of supportive immunosuppressing medications

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Clinicaltrials.gov

Satralizumab for Pediatric NMO

Clinicaltrials.gov ID: NCT05199688
Sponsor: Hoffmann-La Roche
US Sites: Children's Hospital Colorado

- Purpose: Pharmacodynamics of satralizumab in patients between 2 and 11 years old
- Type: open-label, all patients receive satralizumab
- Dosing: weight-based, every 2 weeks during the induction phase, every four weeks thereafter
- Timeframe: 48 weeks, option to extend

Eligibility

- AQP4 positive
- Between 2 and 11 years old
- At least 10 kg
- One attack in the preceding year
- Stable dosing of supportive immunosuppressing medications

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Clinicaltrials.gov

Inebilizumab for Pediatric NMO

Clinicaltrials.gov ID: NCT05549258
Sponsor: Amgen
US Sites: Loma Linda, UCSD, Mass Gen

- Purpose: Pharmacodynamics, pharmacokinetics, and safety of inebilizumab in patients between 2 and <18 years old
- Type: open-label, all patients receive satralizumab
- Dosing: administered IV over 28 weeks
- Timeframe: 80 weeks maximum

Eligibility

- AQP4 positive
- Between 2 and 18 years old
- At least 15 kg
- Two attacks in last two years
- Receipt of certain meds previously may exclude

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Clinicaltrials.gov

Ravulizumab for Pediatric NMO

Clinicaltrials.gov ID: NCT05346354
Sponsor: Alexion Pharmaceuticals
US Sites: Worldwide (Miami, Durham, DC)

- Purpose: Efficacy and safety of ravulizumab in pediatric patients
- Type: open-label, all patients receive ravulizumab
- Dosing: weight-based, two initial loading doses two weeks apart followed by maintenance doses every 4 or 8 weeks depending on weight
- Timeframe: 50 weeks, with a follow-up extension period of up to 104 weeks

Eligibility

- AQP4 positive
- Age not precisely defined
- One attack in the preceding year
- Stable supportive immunosuppressing drugs
- Vaccinated against meningitis
- Excluded if recently receiving certain treatments

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Pediatric Observational NMO Studies

- Longitudinal Study of NMO and Transverse Myelitis: UTSW in Dallas. Children ages > 6 previously with NMO, TM, or ON. Blood and DNA samples. Must be able to go to UTSW.
- Neuroimaging and Neurobehavioral Outcomes: Johns Hopkins. Children between 13-18 years old. Neuropsychological testing and MRI of the brain.
- Pediatric Observational NMO Study: Mayo Clinic in Rochester. Any pediatric patient with positive AQP4 antibodies. Determination of clinical course over multiple visits during one year (times 0, 3, 6, 9, and 12 months).

Rituximab vs FDA Medications in Adults

Clinicaltrials.gov ID: NCT07010302
Sponsor: Massachusetts General Hospital
US Sites: Boston

- Purpose: compare relapse prevention in the 5 commonly-used treatments
- Type: randomized, double-blind
- Dosing: medication dependent, at usual doses
- Timeframe: 30-48 months

Eligibility

- AQP4 positive
- Age > 18
- Excluded if certain co-morbid infections (hepatitis, TB) or immunodeficiencies (HIV or otherwise)

Efgartigimod for Adult Acute Optic Neuritis

Clinicaltrials.gov ID: NCT06453694
Sponsor: Massachusetts General Hospital
US Sites: Boston

- Purpose: determining whether or not efgartigimod in addition to steroids is better than steroids alone
- Type: randomized, placebo-controlled trial, with option for PLEX rescue, pilot study of 20 patients
- Dosing: 2,016 mg of drug or placebo on days 0 and 3
- Timeframe: 6 months (not yet enrolling, estimated completion 7/2027)

Eligibility

- First episode of optic neuritis
- Clinically symptomatic with visual acuity 20/60 or worse
- Age > 18
- Treatment can be administered within 10 days of symptom onset

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Clinicaltrials.gov

Ravulizumab Safety in Pregnancy

Clinicaltrials.gov ID: NCT06312644
Sponsor: Alexion Pharmaceuticals
US Sites: Boston

- Purpose: to determine frequency and characteristics of maternal and fetal complications in those receiving ravulizumab during pregnancy
- Type: observational patient registry
- Dosing: any
- Timeframe: now through July 2034

Eligibility

- Medically-confirmed pregnancy
- Receipt of ravulizumab up to 40 weeks prior to conception and up to 52 weeks after birth

DMTs Under Study in Adults Internationally

- Bruton's tyrosine kinase inhibitors: zanubrutinib
- B-cell activating factor antibodies: belimumab
- JAK inhibitors: baricitinib
- Neonatal Fc receptor antibodies: batoclimab
- CD38 antibodies: daratumumab
- CD20 antibodies: ofatumumab, MIL62, divozilimab
- CAR-T: BAFF-R CAR-T

Anderson, Levy. J Cent Nerv Syst Dis 2024.
Clinicaltrials.gov

Acute Treatments Under Study in China

- Efgartigimod
- Eculizumab
- Immunoadsorption vs PLEX

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Clinicaltrials.gov

Thank you for listening!

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