



MASSACHUSETTS
GENERAL HOSPITAL

NEUROLOGY



HARVARD
MEDICAL SCHOOL

NMOSD and MOGAD Clinical Trials

Michael Levy, MD, PhD

Associate Professor

**Research Director, Division of Neuroimmunology
& Neuroinfectious Disease**

Acute vs. Preventive Treatment



Regenerative



Symptomatic

Trials - Overview

NMOSD

- Satralizumab dosing for people > 100 kg
- Nabiximols (launching soon!)
- CAR-T cells (future)

MOGAD

- cosMOG (rozanolixizumab)
- METEOROID (satralizumab)
- Dairy free diet

ADEM

- TRE-515

Restorative

- Stem cell trial

Acute

- Efgartigimod (ON)
- PLEX (ON/TM)

Rozanolixizumab Study MOG001



Serum
pH 7.4

Endothelial cell

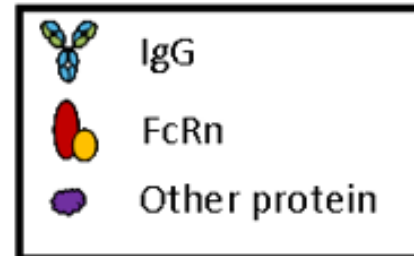
Uptake

Release at
neutral pH

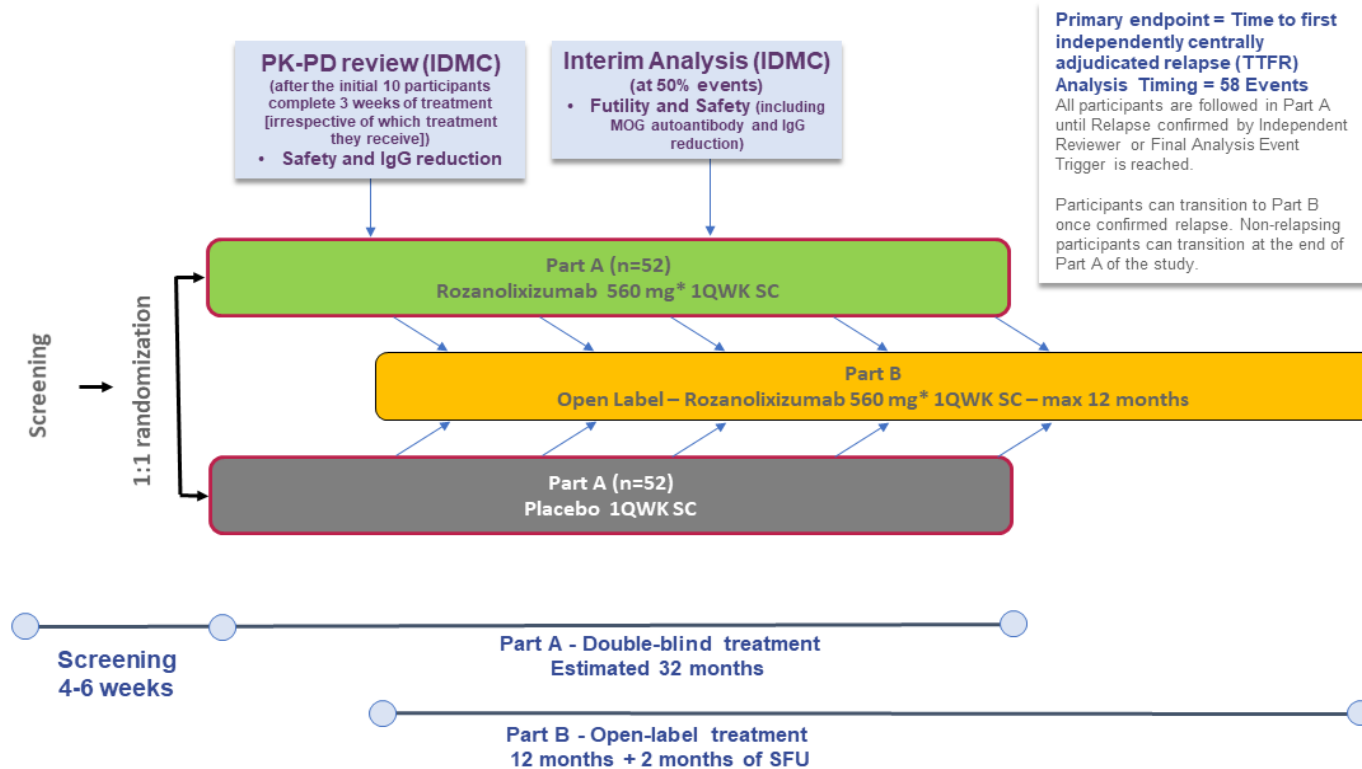
Endosome, pH 6.0
IgG binds FcRn

Recycling of
bound IgG

Unbound
proteins
degraded in
lysosome



Study Design



*May be increased to 840 mg 1QWK SC following PK-PD review

IDMC: Independent Data Monitoring Committee, IgG: immunoglobulin G; IMP: Investigational Medicinal Product; OLE: Open Label Extension; PD: Pharmacodynamic; PK: Pharmacokinetic, SC: subcutaneous, SFU: Safety Follow-Up



MASSACHUSETTS
GENERAL HOSPITAL

NEUROLOGY



HARVARD
MEDICAL SCHOOL



***Pivotal randomized,
phase 3, double-blind,
placebo-controlled
study of satralizumab
in adults and
adolescents with
MOGAD***

Clinical rationale for IL-6 inhibition in MOGAD

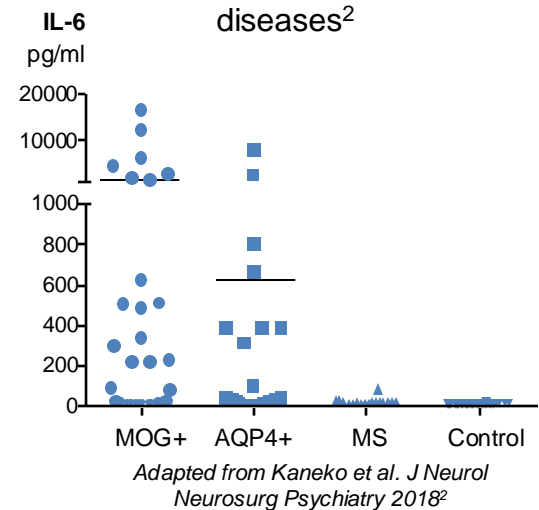
Pre-clinical evidence

- IL-6 levels are increased in the CSF and possibly serum of MOGAD patients (**Figure 1**)¹⁻⁴
- Peripheral Th17-cell subset increases during MOGAD attacks and decreases in the remission phase⁵

Clinical evidence

- The IL-6 receptor (IL-6R) antagonist tocilizumab, used off-label, was shown to be effective in >20 patients with MOGAD⁶⁻¹³
- Satralizumab significantly reduced relapse risk in AQP4-IgG+ NMOSD, an autoantibody-driven disease that is clinically similar to MOGAD^{14,15}
- Satralizumab was investigated in both adolescents and adults with NMOSD, with up to 7 years of exposure^{16,17}

Figure 1. CSF IL-6 levels in patients with demyelinating diseases²



AQP4-IgG+, aquaporin-4 immunoglobulin G seropositive; CSF, cerebrospinal fluid; IL-6, interleukin 6; MOG, myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder.

1. Kohur K et al. *PLoS One* 2016;11:e0149411. 2. Kaneko et al. *J Neurol Neurosurg Psychiatry* 2018;89:927-936. 3. Serguera C et al. *J Neuroinflammation* 2019;16:244. 4. Hder LS et al. *Mult Scler J Exp Transl Clin* 2019;5:2055217319848463. 5. Liu J et al. *J Neurol Neurosurg Psychiatry*. 2020;91:132-139. 6. Hayward-Koennecke H et al. *Neurology* 2019;92:765-767. 7. Novi G et al. *Mult Scler Relat Disord* 2019;27:312-314. 8. Lotan I et al. *Mult Scler Relat Disord* 2019;39:101920. 9. Jelcic et al. *J Neuroophthalmol* 2019;39(1):3-7. 10. Rigal J et al. *Mult Scler Relat Disord* 2020;46:102483. 11. Elsbend PM et al. *Mult Scler Relat Disord*. 2021;48:102696. 12. Masocco FG, et al. *Mult Scler Relat Disord* 2020;46:102592. 13. Ringelstein M, et al. *Neurol Neuroimmunol Neuroinflamm* 2022;9:e1100. 14. Yamamura T et al. *N Engl J Med* 2019;381:2114-2124. 15. Trabousee A, et al. *Lancet Neurol* 2020;19(5):402-12. 16. Yamamura T, et al. *Mult Scler Relat Disord* 2022;66:104025. 17. Kleiter I, et al. *Neurol Neuroimmunol Neuroinflamm* 2022 (under review).

METEOROID: Phase 3, double-blind study of satralizumab (\pm IST)

Event-driven DB treatment period:

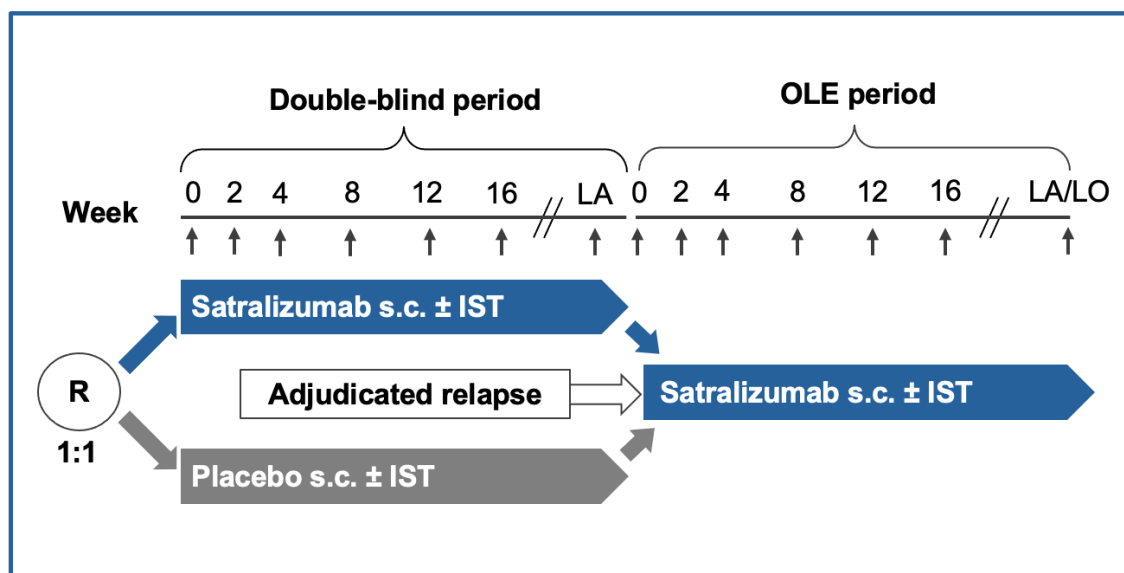
- Ends when 28 adjudicated MOGAD relapses are observed (expected 44 months after FPI)

OLE period:

- Approximately 24 months

Safety follow up:

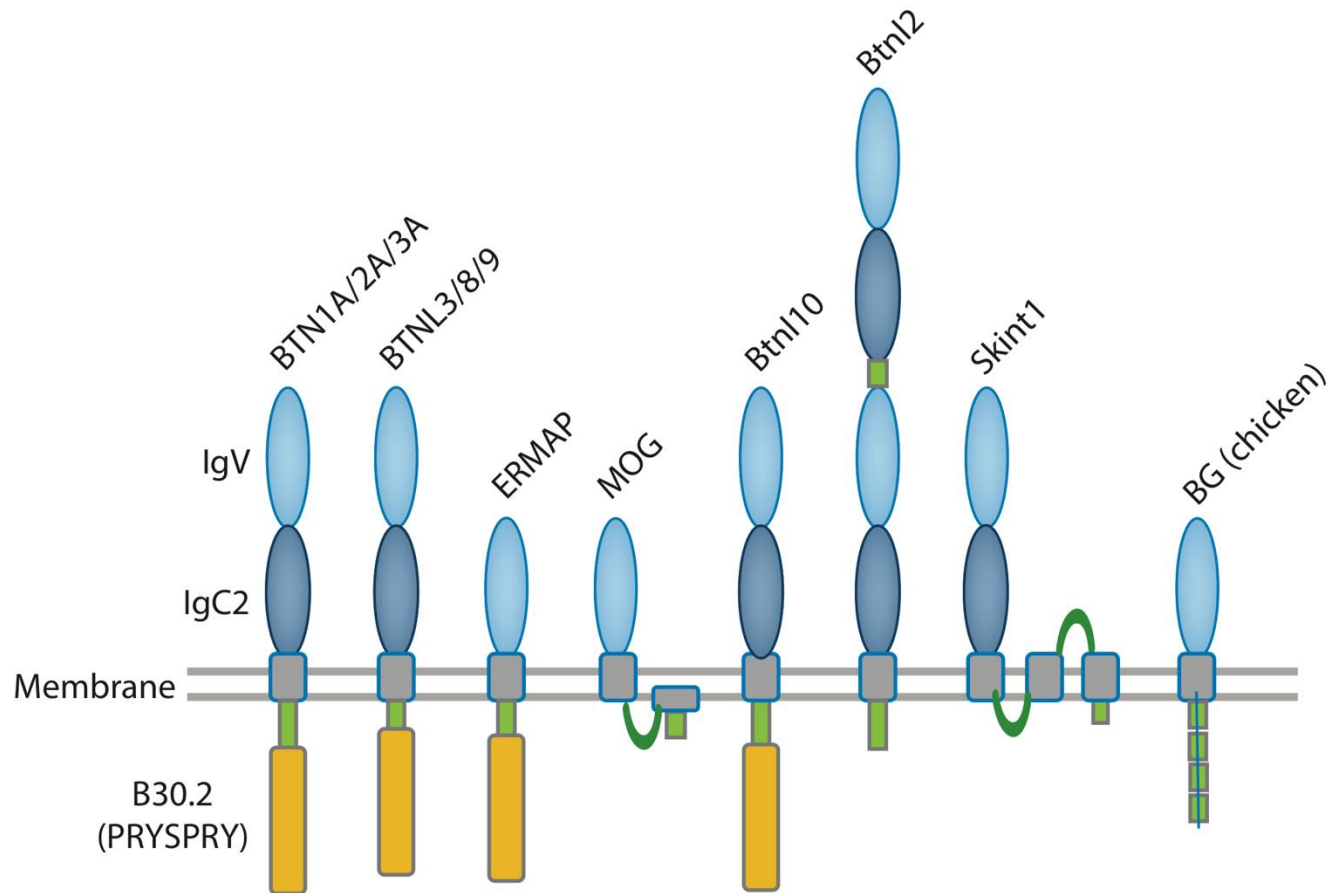
- 12 weeks for adults and 24 weeks for adolescents



DB, double-blind; CEC, Clinical Endpoint Committee; FPI, first patient in; IST, baseline/background immunosuppressive therapy; LA/LO, last administration/observation; OLE, open-label extension.



MOG is a Butyrophilin-Like Molecule



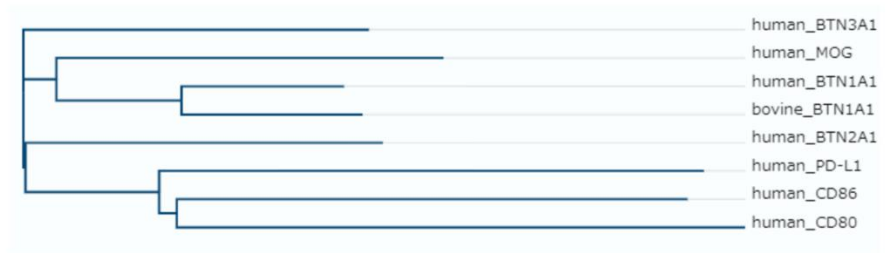
Rhodes, David & Reith, Walter & Trowsdale, John. (2016). Regulation of Immunity by Butyrophilins. Annual Review of Immunology. 34. 10.1146/annurev-immunol-041015-055435.

Cross-Reactivity with Cow Butyrophilin

A

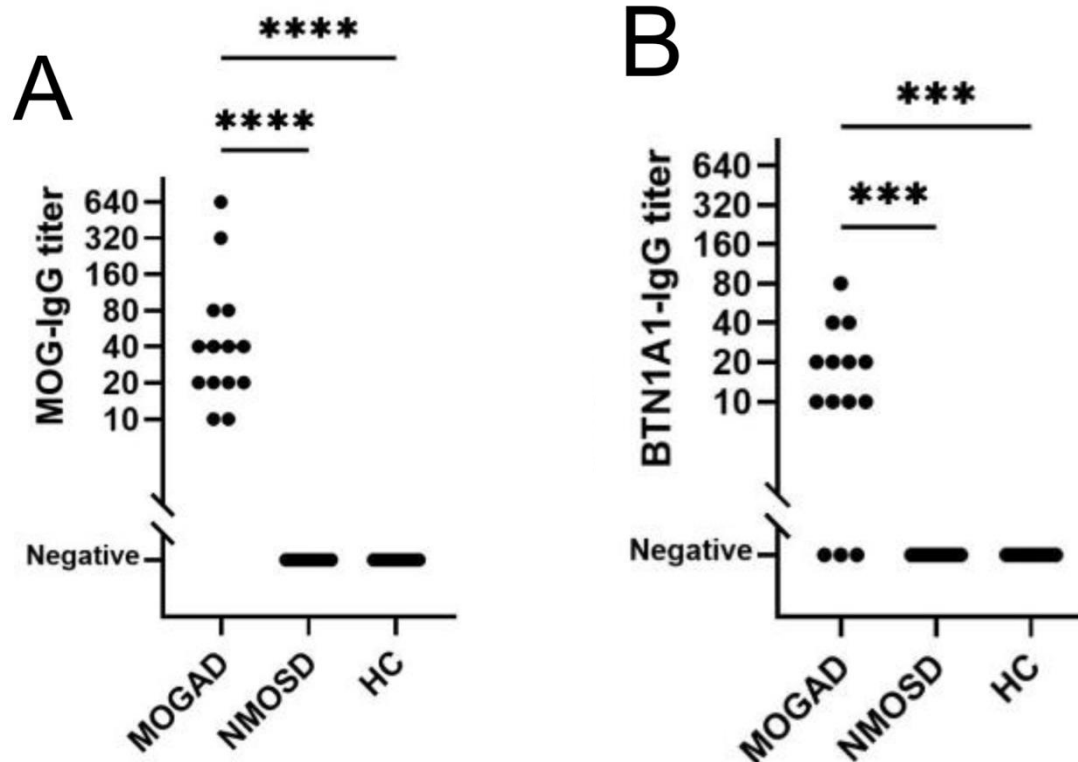


B



Unpublished data. Levy Lab.

Cross-Reactivity with Cow Butyrophilin



Unpublished data. Levy Lab.



Trials - Overview

NMOSD

- Satralizumab dosing for people > 100 kg
- Nabiximols (launching soon!)
- CAR-T cells (future)

MOGAD

- cosMOG (rozanolixizumab)
- METEOROID (satralizumab)
- Dairy free diet

ADEM

- TRE-515

Restorative

- Stem cell trial

Acute

- Efgartigimod (ON)
- PLEX (ON/TM)

Efgartigimod in NEW Optic Neuritis

Understanding Optic Neuritis

Causes, Diagnosis,
& Treatment



VYVGART[™]
(efgartigimod alfa-fcab)

Plasma Exchange in ON and TM

**Understanding
Optic Neuritis**
Causes, Diagnosis,
& Treatment



Nabiximols in NMOSD



- Spasms
- Neuropathic pain
- Sleep
- Anxiety
- Fatigue