Welcome

2022 Pre-ECTRIMS NMOSD Symposium

Amsterdam – The Netherlands

October 25, 2022

Year In Review

2022 Pre-ECTRIMS NMOSD Symposium

Amsterdam – The Netherlands

October 25, 2022

GUTHY JACKSON®
Charitable Foundation

GUTHY JACKSON® Charitable Foundation

Recognition

“2019-2020 is the Year of NMO”

Scientific Committee – American Academy of Neurology

GUTHY JACKSON® Charitable Foundation

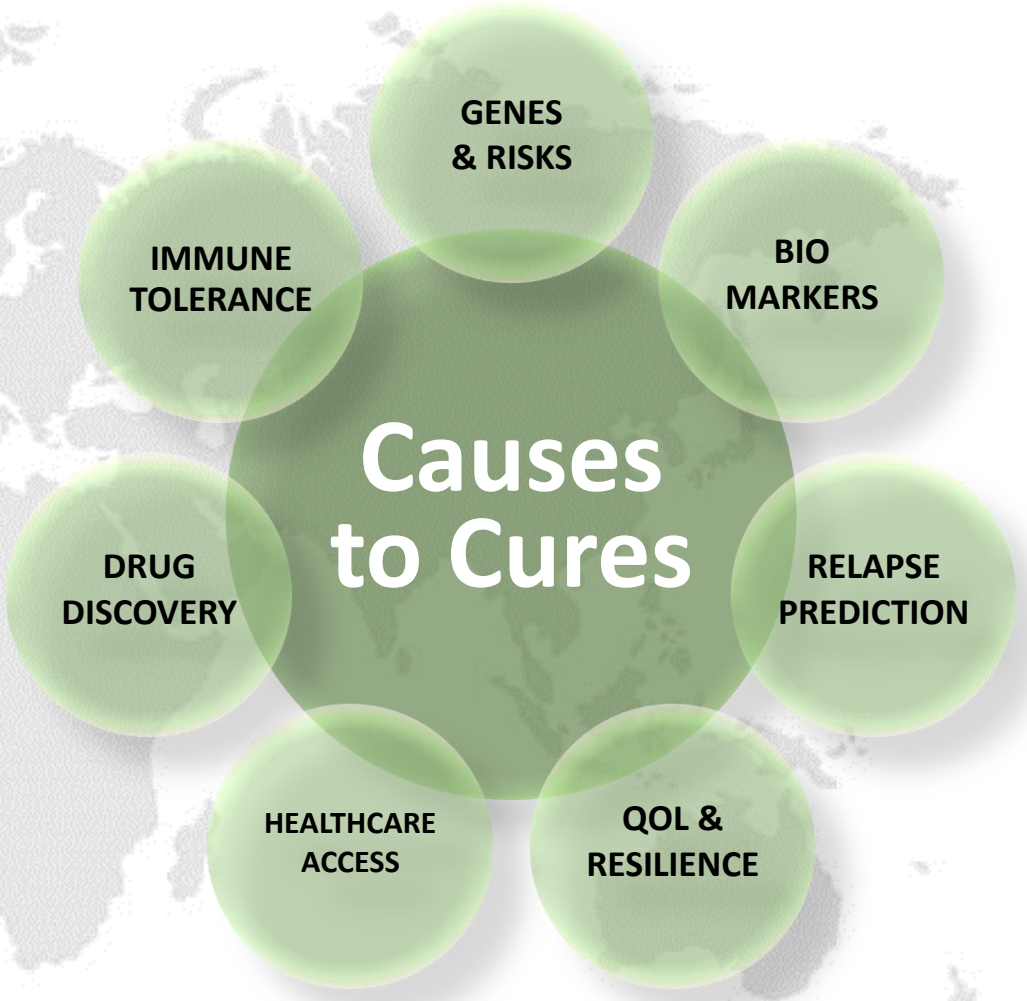
Collaboration

117 Members

33 Countries

100 Projects

25+ Partners



Source: ***GJCF ICC & CIRCLES Biorepository*** [as of October 2022]

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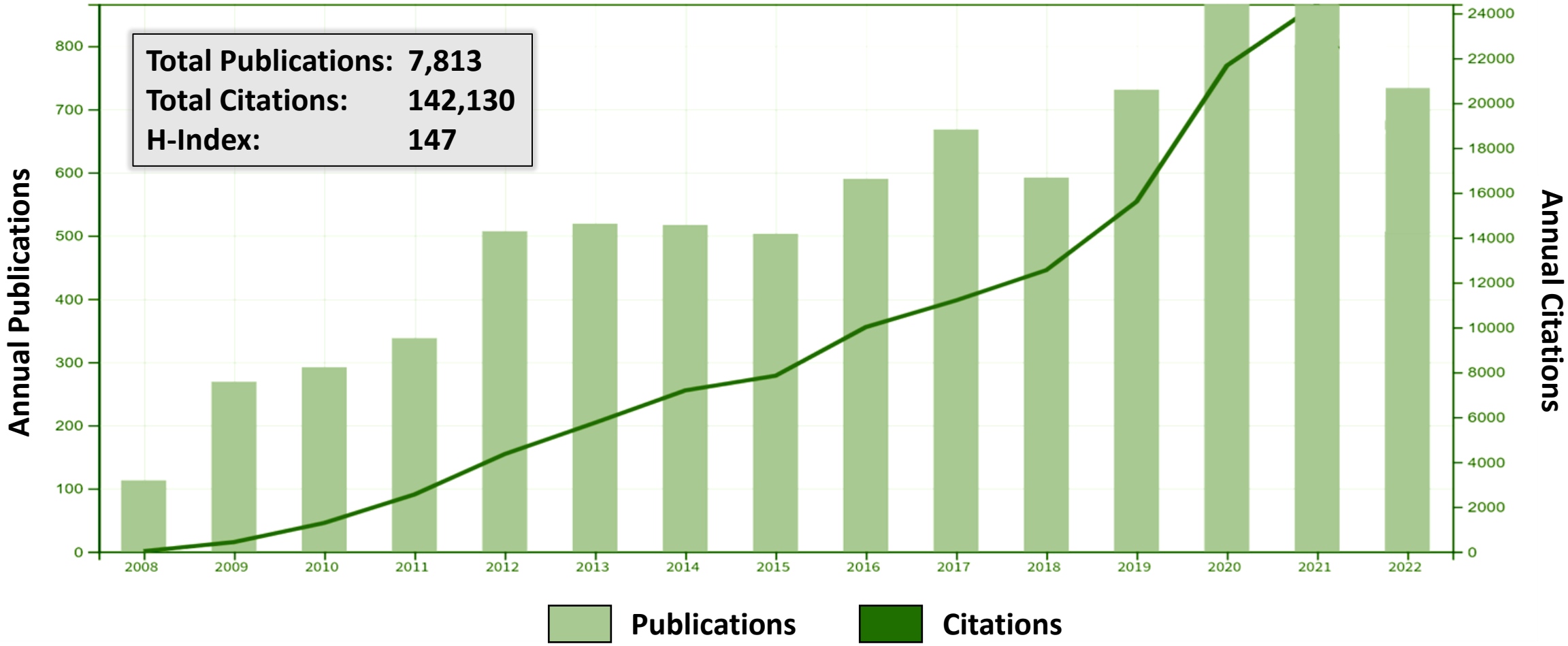
Transformation



Source: Clarivate Analytics [2022] ***Web of Science*** (accessed 10-23-2022)

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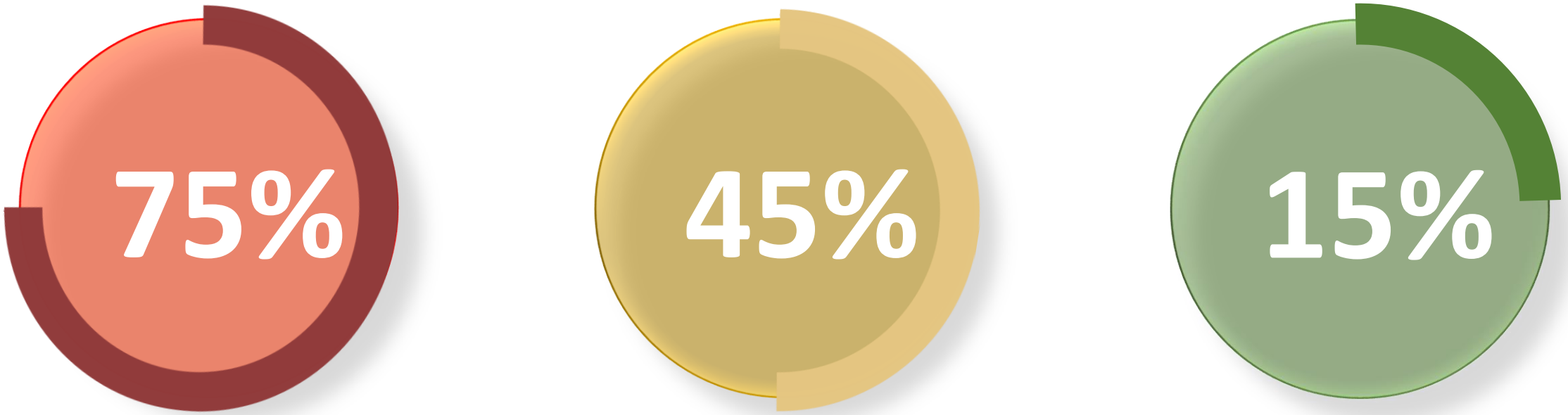
Detection



2008 **2015** **2022**

NMOSD Misdiagnosis Rate

Source: estimated from Knapp *et al.* [2022] ***Neurol Therapy*** 11:247-263

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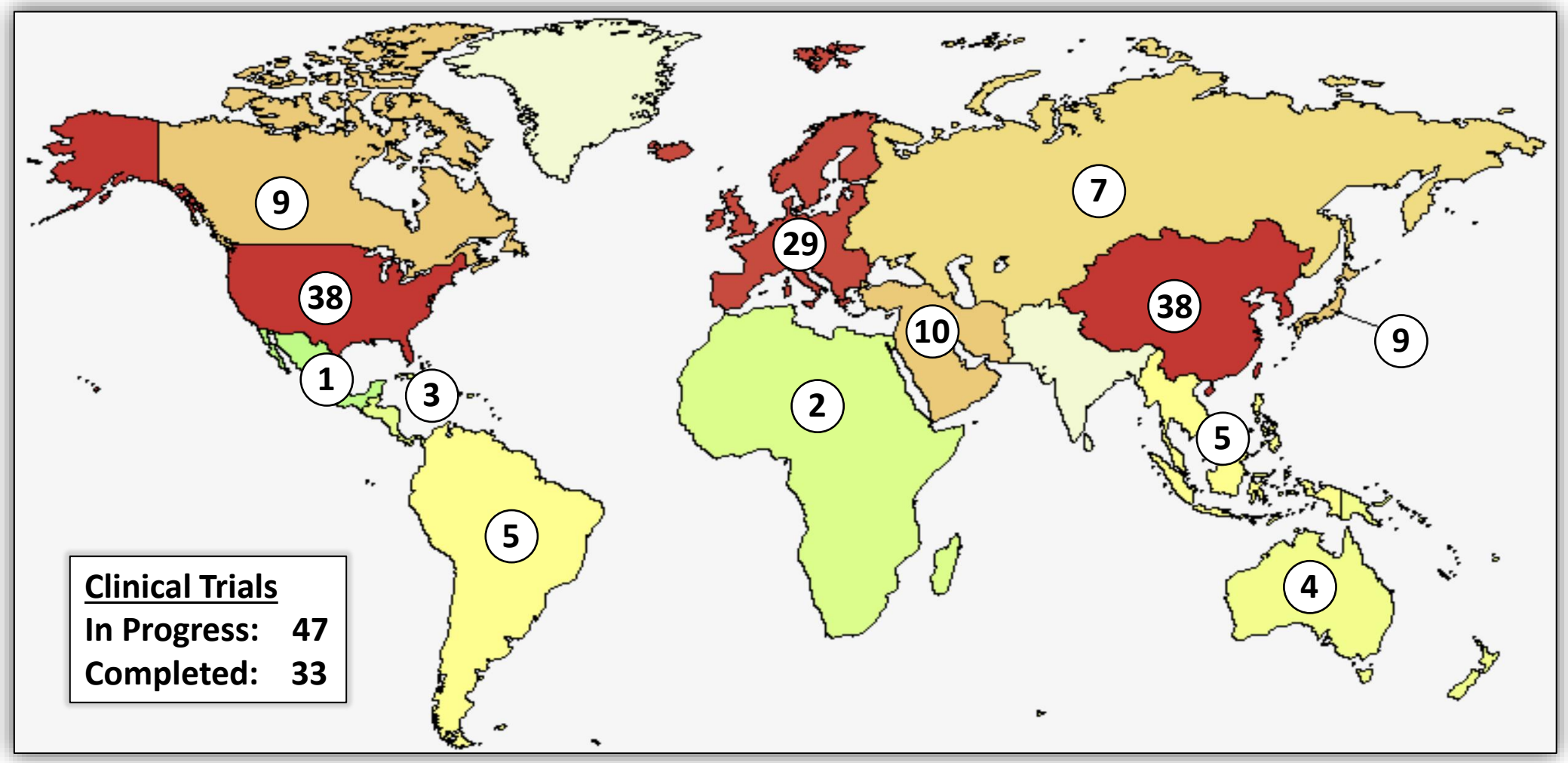
Globalization



Source: U.S. National Library of Medicine [2022] ***ClinicalTrials.gov*** (accessed 10-23-2022)

Application

Interactive Pocket Guide to NMOSD Therapeutics†

Healthcare Provider Edition / Version 7.1.22 / © 2019-2022 Guthy-Jackson Charitable Foundation

Approved Therapeutics | Non-Approved (Off-Label) Therapeutics

Feature	Soliris®	Uplizna®	Enspryng®	Rituxan®	Actemra®	Ultomiris®	CellCept®	Imuran®
Medical Name	Eculizumab	Inebilizumab	Satralizumab	Rituximab	Tocilizumab	Ravulizumab	Mycophenolate	Azathioprine
Disease Target	Complement Protein C5	CD19+ B Cells	IL-6 Receptor	CD20+ B Cells	IL-6 Receptor	Complement Protein C5	T and B Cell IMPDH Enzyme	DNA & RNA Synthesis
Clinical Trial Name	PREVENT	NMOmentum	SAkura Sky SAkura Star	RIN-1	TANGO	CHAMPION	MONICA	TANGO
Trial / Study Publication	NEJM 2019	Lancet 2019	NEJM 2019 Lancet 2020	Clinical Study Lancet 2020	Clinical Study Lancet 2020	Trial Results Pending	Clinical Study Front Imm 2018	Clinical Study Lancet 2020
Clinical Trial Efficacy †	Yes; See Data (Mono/Poly)	Yes; See Data (Mono Tx)	Yes; See Data (Mono/Poly)	Non-Trial Data (Mono/Poly)	Non-Trial Data (Mono/Poly)	Trial Results Pending	Non-Trial Data (+ Steroid)	Non-Trial Data (Mono/Poly)
U.S. FDA Status	Approved Jun 27, 2019	Approved Jun 11, 2020	Approved Aug 17, 2020	Not Approved	Not Approved	Not Approved	Not Approved	Not Approved
Package Insert	Soliris® FDA Label	Uplizna® FDA Label	Enspryng® FDA Label	Rituxan® FDA Label	Actemra® FDA Label	Ultomiris® FDA Label	CellCept® FDA Label	Imuran® FDA Label
Approved Indication	Anti-AQP4+ Age 18+ Yrs	Anti-AQP4+ Age 18+ Yrs	Anti-AQP4+ Age 18+ Yrs	Not Approved	Not Approved	Not Approved	Not Approved	Not Approved
Medication Guide Summary	Soliris® Medication Guide	Uplizna® Medication Guide	Enspryng® Medication Guide	Rituxan® Medication Guide	Actemra® Medication Guide	Ultomiris® Medication Guide	CellCept® Medication Guide	Imuran® Medication Guide
Status in < 18 Yrs	Not Approved; Clinical Trial; Used in HUS	Not Approved; Consult Peds Neurologist	Not Approved; Outcomes in Adolescents	Approved for NHL, RA, GPA; MOGAD Data	Approved for SJIA and PJIA	Approved for HUS, PNH, MG	> 3 months old; Consult Peds	Peds Data; Consult Peds
Status in Pregnancy	Data Available; Consult Neuro	Data Pending; Consult Neuro	Data Pending; Consult Neuro	Data Available; Consult Neuro	Data Available; Consult Neuro	Data Available; Consult Neuro	***Avoid Use*** (Fetal Harm)	***Avoid Use*** (Fetal Harm)
Status in Comorbidity	Consult Neurologist	Consult Neurologist	Consult Neurologist	Consult Neurologist	Efficacy Intact [see TANGO]	Consult Neurologist	Consult Neurologist	Consult Neurologist
Safety Warning*	***Label Box:*** Nm Infection	No Specific Warning	No Specific Warning	***Label Box:*** IRxn; TLS; PML	***Label Box:*** TB & Opp Infxn	***Label Box:*** Nm Infection	***Label Box:*** Preg; Infxn; CA	***Label Box:*** Cancer; Infxn
Safety Precaution*	IRx; Infection; Nm Infection	IRx; Infection Ab; PMN	Liver Function; Cho; PLT; WBC	IRx; Infection Ab; PMN	Liver Function; Cho; PLT; WBC	IRx; Infection; Nm Infection	Infection; Tox; Malignancy	Infection; Tox; Malignancy
U.S. FDA REMS	REMS Required	REMS Not Required	REMS Not Required	REMS Not Required	REMS Not Required	REMS Required	REMS Not Required	REMS Not Required
Pre-Use Screening	None Required	HBV; JCV [PML]; TB Serum IgG	HBV; TB; Liver Function	HBV; JCV; TB Serum IgG	HBV; TB; Liver Function	Hepatitis B; Tuberculosis	Liver Function; Blood Cell Cnt	TPMT Enzyme Level
Required* Vaccines Δ	MenACWY + B* ACIP Guidance	Standard ACIP Guidance	Standard ACIP Guidance	Standard ACIP Guidance	Standard ACIP Guidance	MenACWY + B* ACIP Guidance	Standard ACIP Guidance	Standard ACIP Guidance
Laboratory Monitoring	None Specifically Required	B Cell Count; Ig Levels; Neutrophils	Liver Function; Neutrophils; Lipid/LDL; PLT	Infection; B Cell Counts; Ig Levels; PMN	Liver Function; Chol & Lipids; WBC / PLT Cnt	PLT count; Liver & Kidney Function	Routinely Blood Cell Cnt; Bleeding Issues	Routinely WBC Count; Infxn; Cancer
Maintenance Dosing	Uniform Dose (1,200 mg)	Uniform Dose (300 mg)	Uniform Dose (120 mg)	Per Body m^2 (~375mg/m^2)	Uniform Dose (8mg/kg; 4wk)	Per Body Mass (3g/60-100kg)	Uniform Dosing (up to 2 g/d)	Per Body Mass (2-3 mg/kg/d)
Mode of Dosing	Intravenous Infusion	Intravenous Infusion	Subcutaneous Injection	Intravenous Infusion	Intravenous Infusion	Intravenous Infusion	Oral Tablet	Oral Tablet
Mono or Poly Tx	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro	± Add On; Consult Neuro
Induction Regimen	Every Week First 4 Doses	Every 2 Weeks First 2 Doses	Every 2 Weeks First 3 Doses	Every 2 Week Half-Doses	Every 2 Weeks First 3 Doses	Loading Dose for 2 Weeks	Loading Dose; Consult Neuro	Loading Dose; Consult Neuro
Routine Regimen	Every 2 Wks Infusion	Every 24 Wks Infusion	Every 4 wks Injection	Every 24 Wks Infusion	Every Wk Injection	Every 8 Wks Infusion	Usually Daily if Oral	Usually Daily if Oral
PLEX Re-Dosing	Re-Dose < 60 min Post-PLEX	Consult Neurologist	Consult Neurologist	Consult Neurologist	Consult Neurologist	Re-Dose < 60 min Post-PLEX	Consult Neurologist	Consult Neurologist
Company Website	Soliris® Website	Uplizna® Website	Enspryng® Website	Rituxan® Website	Actemra® Website	Ultomiris® Website	CellCept® Website	Imuran® Website
Patient Support	OneSource® Website	Horizon BYS® Website	Access Solutions® Website	No NMOSD Aid Program	No NMOSD Aid Program	No NMOSD Aid Program	No NMOSD Aid Program	No NMOSD Aid Program

† *Important*: content is reference information only and subject to update; it neither expresses nor implies recommendations for therapy. Consult FDA-approved label.

* Label Box Warnings & Precautions per the U.S. FDA [2022] [www.accessdata.fda.gov/scripts/cder/daf/index.cfm]; see FDA label/package insert for specific therapies.

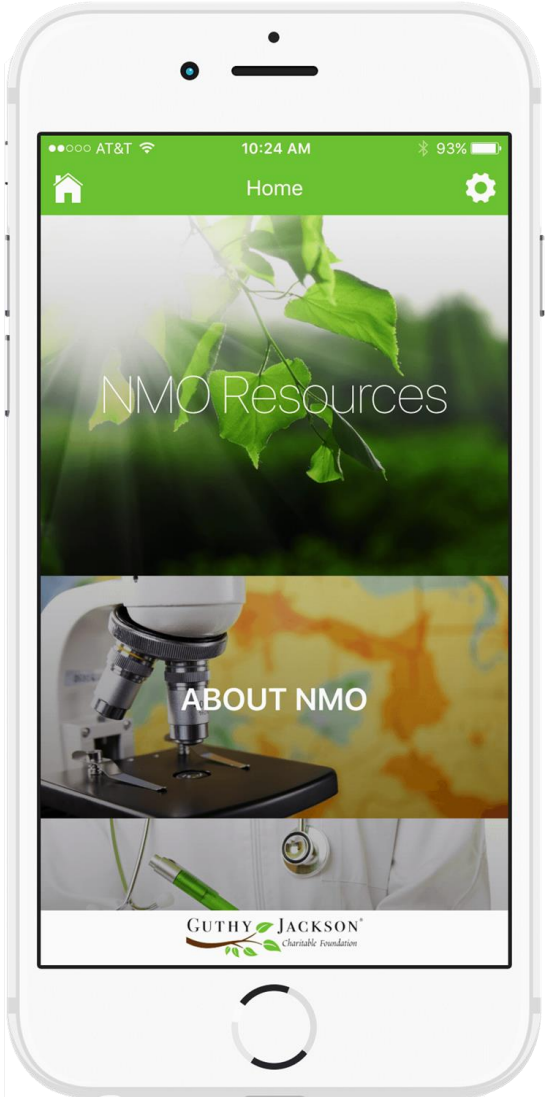
Δ U.S. CDC Advisory Committee on Immunization in Persons with Altered Immune Competence (ACIP) [2022] [access 7-1-22 via website: www.cdc.gov/vaccines/acip/].

Key: [Ab], antibody; [AQP4], aquaporin-4; [Cho], cholesterol; [HBV], hepatitis B virus; [IRx], infusion reaction; [JCV], JC virus; [MenACWY + B], conjugate + serogroup B meningococcal vaccines [Nm], *N. meningitidis*; [PLT], platelet; [PML], progressive multifocal leukoencephalopathy; [PMN], neutrophil; [REMS], Risk Evaluation & Mitigation Strategy; [Tx], therapy; [Tox], toxicity; [TB], tuberculosis; [TLS], tumor lysis syndrome; [WBC], total white blood cell

Molecule & Target
Clinical Trial Data
Regulatory Guides

Special Populations
Screening & Safety
Vaccines & Monitors

Dosing Information
Industry Websites
Patient Access



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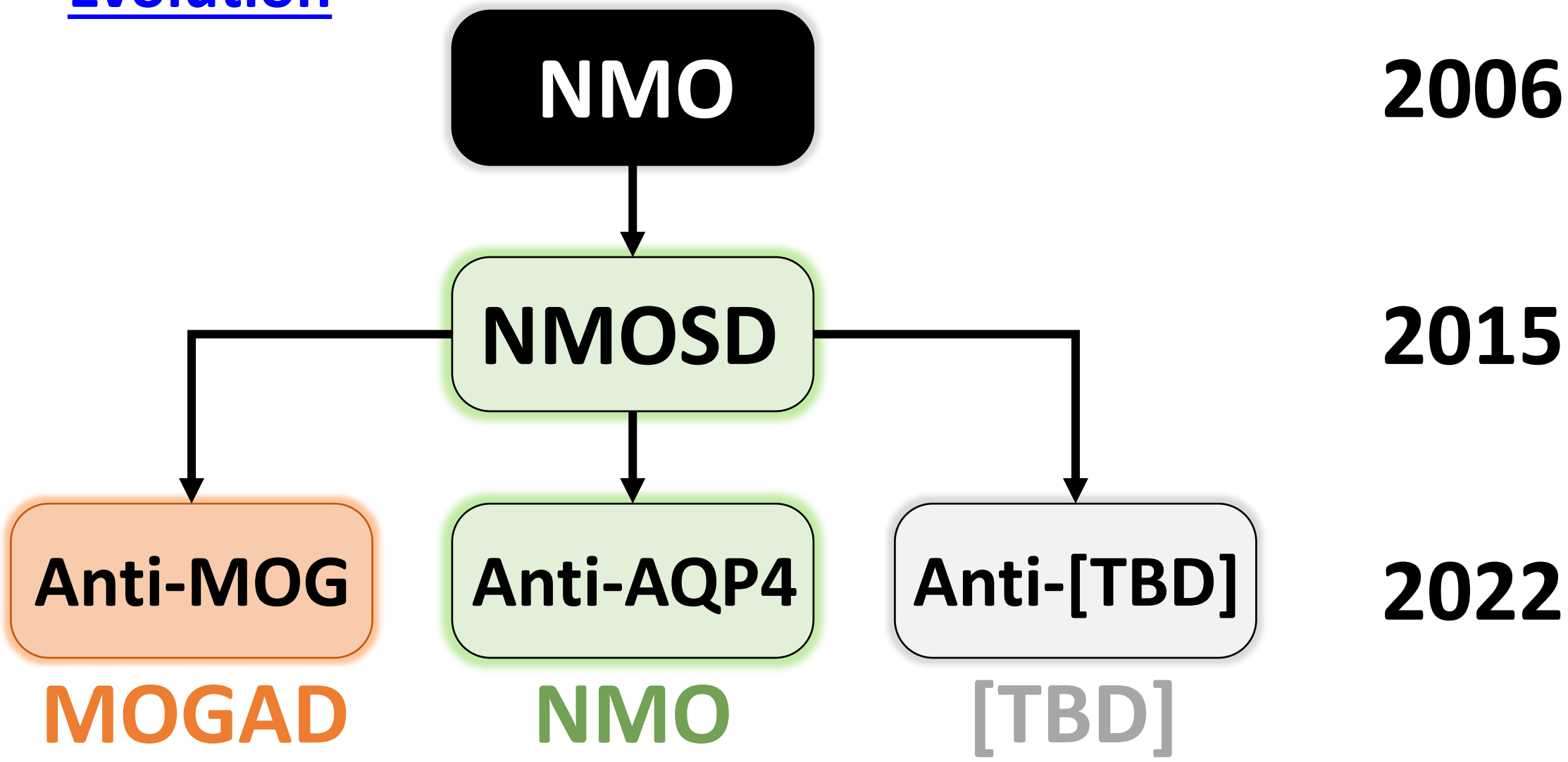
Evolution



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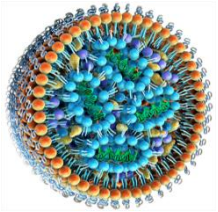
Innovation

RELAPSE NAVIGATOR™

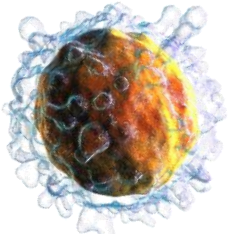
Consensus Guide to Uniform Relapse Adjudication

The Guthy-Jackson Charitable Foundation

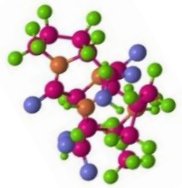
Tolerization



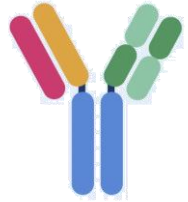
Auto-Ag Nanoparticles



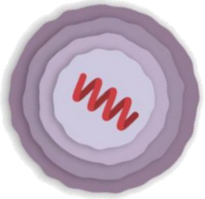
CAR/CAAR T Cells



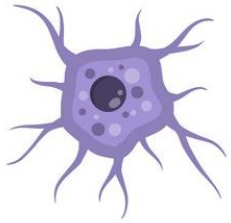
Imotopes Apotopes



Checkpoint Gating

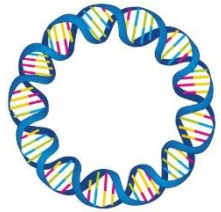


Inverse Vaccines



APC / Dc Vaccines

RBC Tolerance



Targeted PCD

Source: The Guthy-Jackson Charitable Foundation [2022] ***Pioneer Curative Therapies***

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Inspiration

We study Disability

Vision Loss
Immobile
Painful
Incontinent
Unemployed
Stigmatized
Loneliness
Depression
Uncertainty
Disease Burden

We promote Resilience

Vision Gain
Mobile
Pain Free
Continent
Employed
Included
Relationships
Optimism
Preparedness
Life Quality

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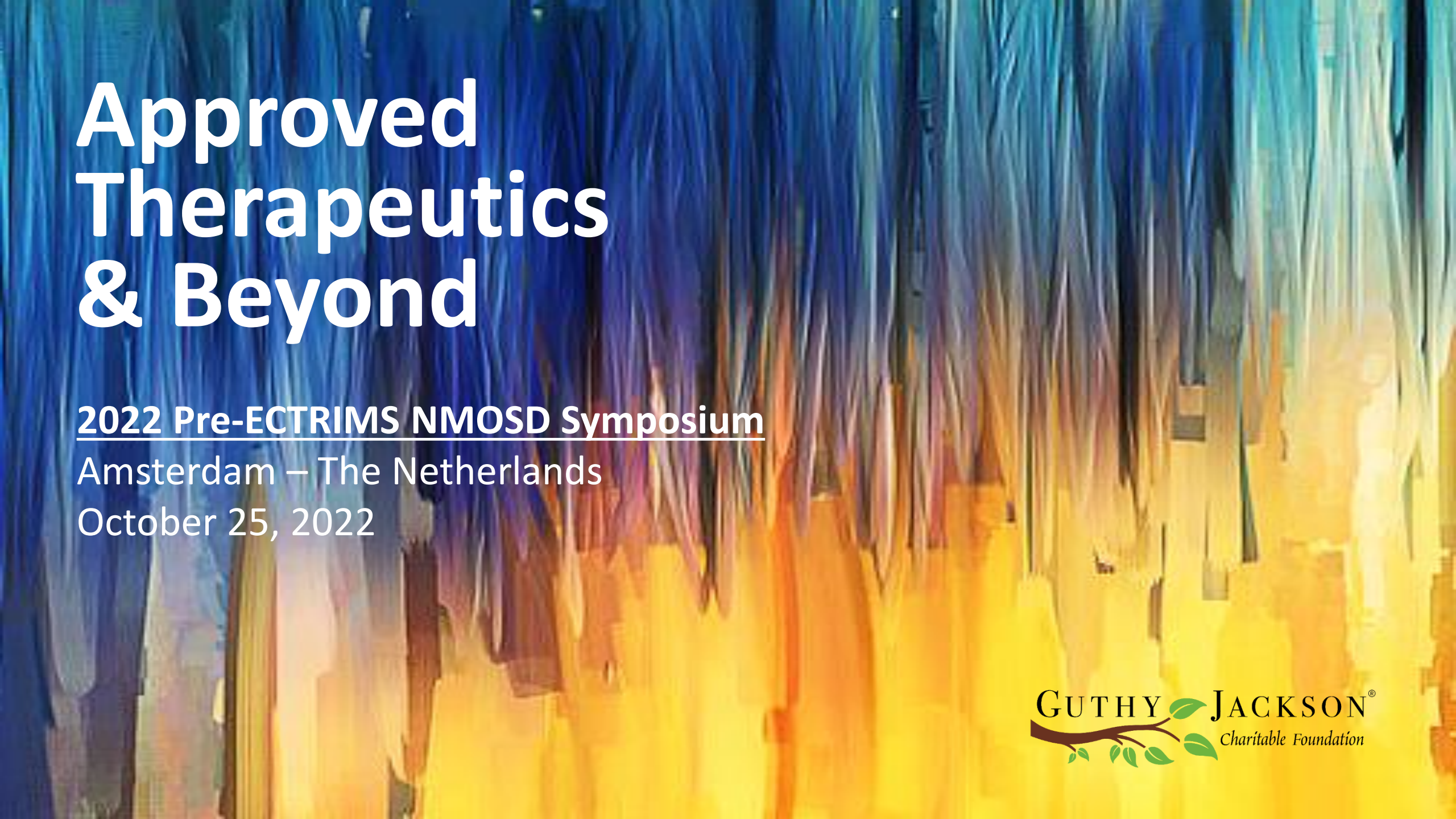
Charitable Foundation

Dedication



Approved Therapeutics & Beyond

2022 Pre-ECTRIMS NMOSD Symposium

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GUTHY JACKSON® Charitable Foundation

Guthy-Jackson Charitable Foundation Pre-ECTRIMS Symposium

Eculizumab in NMOSD Patients Who Are Anti-Aquaporin-4 Antibody-Positive

Yuriy Edwards
Medical Director, Neurology
Alexion AstraZeneca Rare Disease

ALEXION
AstraZeneca Rare Disease

M/INT/SOL-N/0020 October 2022

Speaker disclosures

- Research Funding for PREVENT and PREVENT OLE was provided by Alexion, AstraZeneca Rare Disease

- Yuriy Edwards is an employee of Alexion, AstraZeneca Rare Disease

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Presentation objectives

- Describe the significant **burden associated with NMOSD attacks** and the **importance of attack prevention** in clinical management
- Understand the **role of complement** in NMOSD
- Review eculizumab data from a phase 3 clinical trial and its open-label extension
- Demonstrate that real-world evidence supports eculizumab clinical trial results, using Japanese PMS study of safety and effectiveness of eculizumab

This presentation includes discussion on Alexion product eculizumab.
Eculizumab is indicated in the adults for the treatment of Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease.
The eculizumab Summary of Product Characteristics (SmPC) is available at: https://www.ema.europa.eu/en/documents/product-information/soliris-epar-product-information_en.pdf

NMOSD, neuromyelitis optica spectrum disorder

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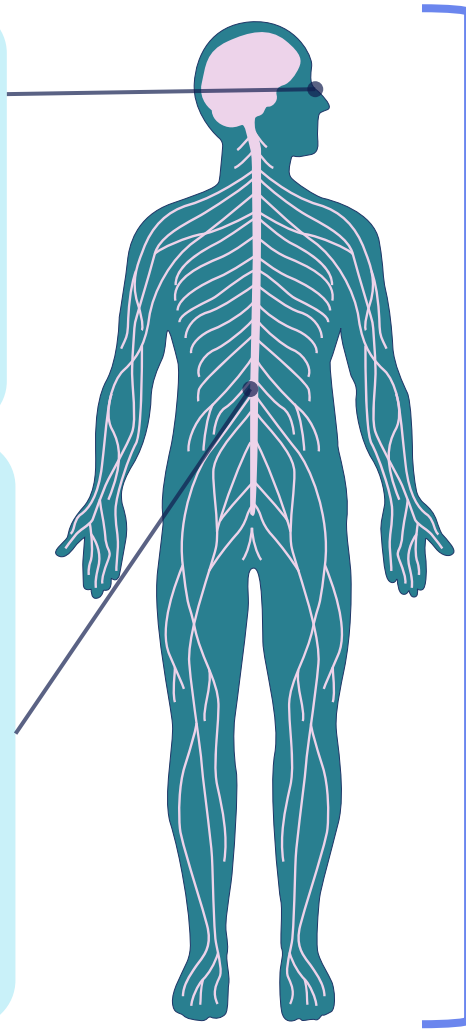
Neuronal damage from each attack results in cumulative permanent neurological disability[1-4]

Optic neuritis is linked to:[1,2]

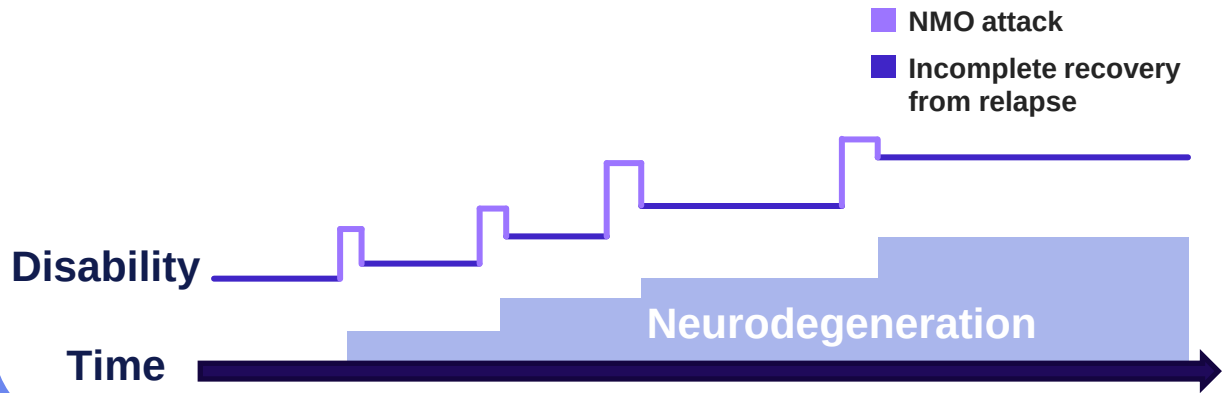
- blindness
- loss of color vision
- pain with eye movement
- scotoma (blind spots)

Longitudinally extensive transverse myelitis is linked to:[1–3]

- bilateral motor weakness
- impact on sensation
- tonic spasms
- neuropathic pain
- bladder/bowel dysfunction



Typical disease course[4]



1. Wingerchuk DM. *Neurologist* 2007;13:2–11; 2. Kim SM *et al. Ther Adv Neurol Disord* 2017;10:265–89; 3. Kessler RA *et al. Curr Treat Options Neurol* 2016;18:2;
4. Kawachi I, Lassmann H. *J Neurol Neurosurg Psychiatry* 2017;88:137–45

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Preventing attacks should be the primary treatment goal in NMOSD[1]

Among patients with AQP4+ NMOSD

41%

go blind in at least one eye within 5 years after diagnosis[a,2]

34%

experience permanent motor disability within 6 years after diagnosis[b,3]

23%

need a wheelchair within 6 years after diagnosis[b,3]

9%

die after a median disease duration of 6 years[b,3]

Over 90% of patients with NMOSD experience attacks that may lead to cumulative, irreversible neurological disability[c,4,5]

[a]The study collected data from 140 patients who tested AQP4+ at the Mayo Clinic in the USA and were diagnosed with NMO
[b]The study described the clinical outcomes of 106 patients with AQP4+ NMOSD from the UK and Japan
[c]Based on a retrospective review of medical records of 187 patients with NMO/NMOSD undergoing evaluation during 5-year period
AQP4+, aquaporin-4 antibody-positive; NMO, neuromyelitis optica; NMOSD, neuromyelitis optica spectrum disorder

1. Wingerchuk D *et al. Handb Clin Neurol* 2014;122:581-99; 2. Jiao Y *et al. Neurology* 2013;81:1197–204; 3. Kitley J *et al. Brain* 2012;135:1834–49; 4. Jarius S *et al. J Neuroinflammation* 2012;9:14; 5. Mealy MA *et al. Arch Neurol* 2012;69:1176–80

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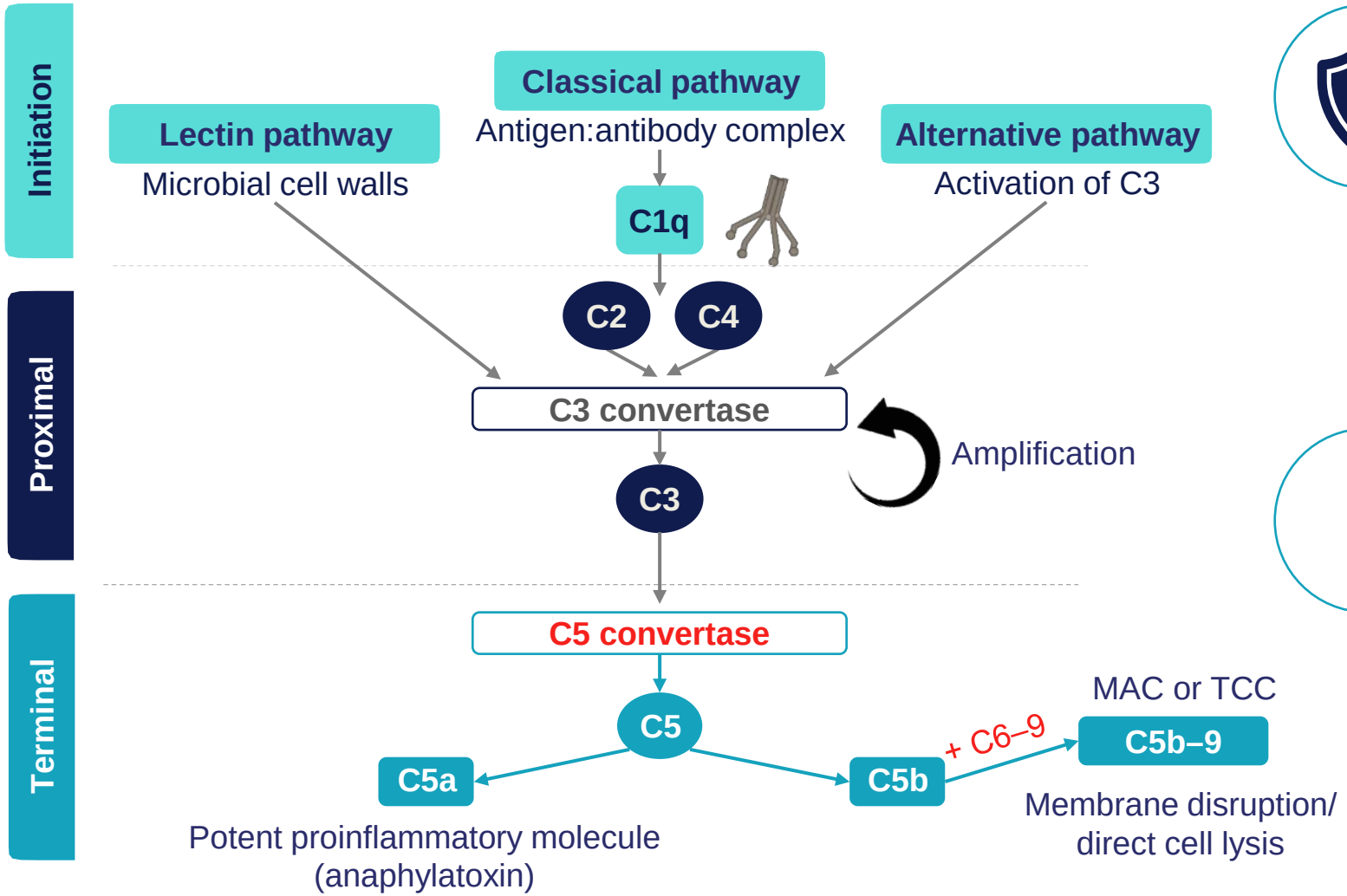
C5 is a key target for NMOSD precision medicine[1,2]



C5 inhibition prevents the formation of C5a and MAC while preserving the critical functions of upstream components, including C3b-mediated opsonization and immune complex clearance[1]

C5 inhibition is associated with increased risk of meningococcal infections

Using a tetravalent vaccine before treatment initiation is recommended[2]

Figure adapted from Pio R *et al. Front Immunol* 2019;10:744. doi: 10.3389/fimmu.2019.00774
C1q/2–5/3b/5a/5b, complement component 1q/2–5/3b/5a/5b; MAC, membrane attack complex; TCC, terminal complement complex
1. Rother RP *et al. Nat Biotechnol* 2007;25:1256–64; 2.Figueroa JE *et al. Clin Microbiol Rev* 1991;4:359–95.

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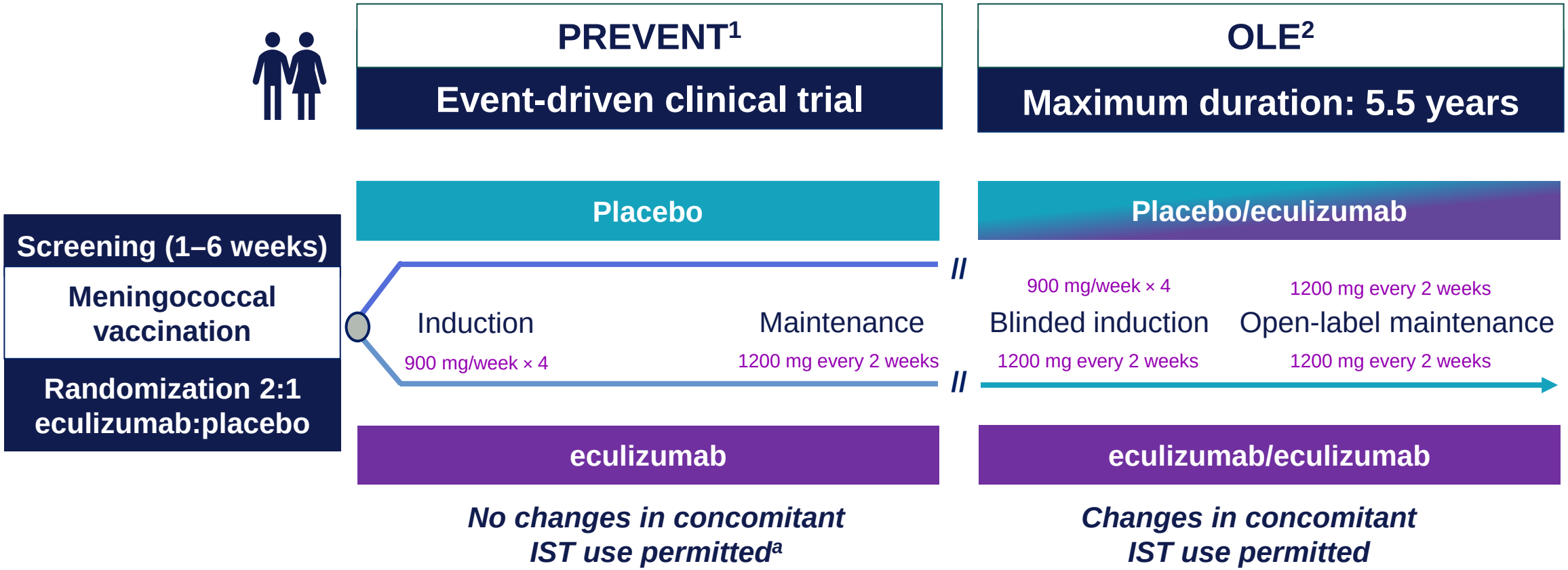
A phase 3 study assessed eculizumab's safety and efficacy in NMOSD: PREVENT and its OLE[1,2]



Eculizumab is indicated in adults for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease[3]

Adapted from Pittock SJ *et al*. 2019 and Wingerchuk DM *et al.* 2021

[a]Only changed if treating physician determined a relapse had occurred or had safety concerns. Changes to ISTs after relapses were unrestricted

IST, immunosuppressive therapy; NMOSD, neuromyelitis optica spectrum disorder; OLE, open-label extension

1. Pittock SJ *et al*. *N Engl J Med* 2019;381:614–25; 2. Wingerchuk DM *et al*. *Ann Neurol* 2021;89:1088–98; 3. SOLIRIS (eculizumab) EU; SmPC

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In the PREVENT study, eculizumab significantly reduced the risk of adjudicated NMOSD relapses compared with placebo (p<0.001)[a,1]

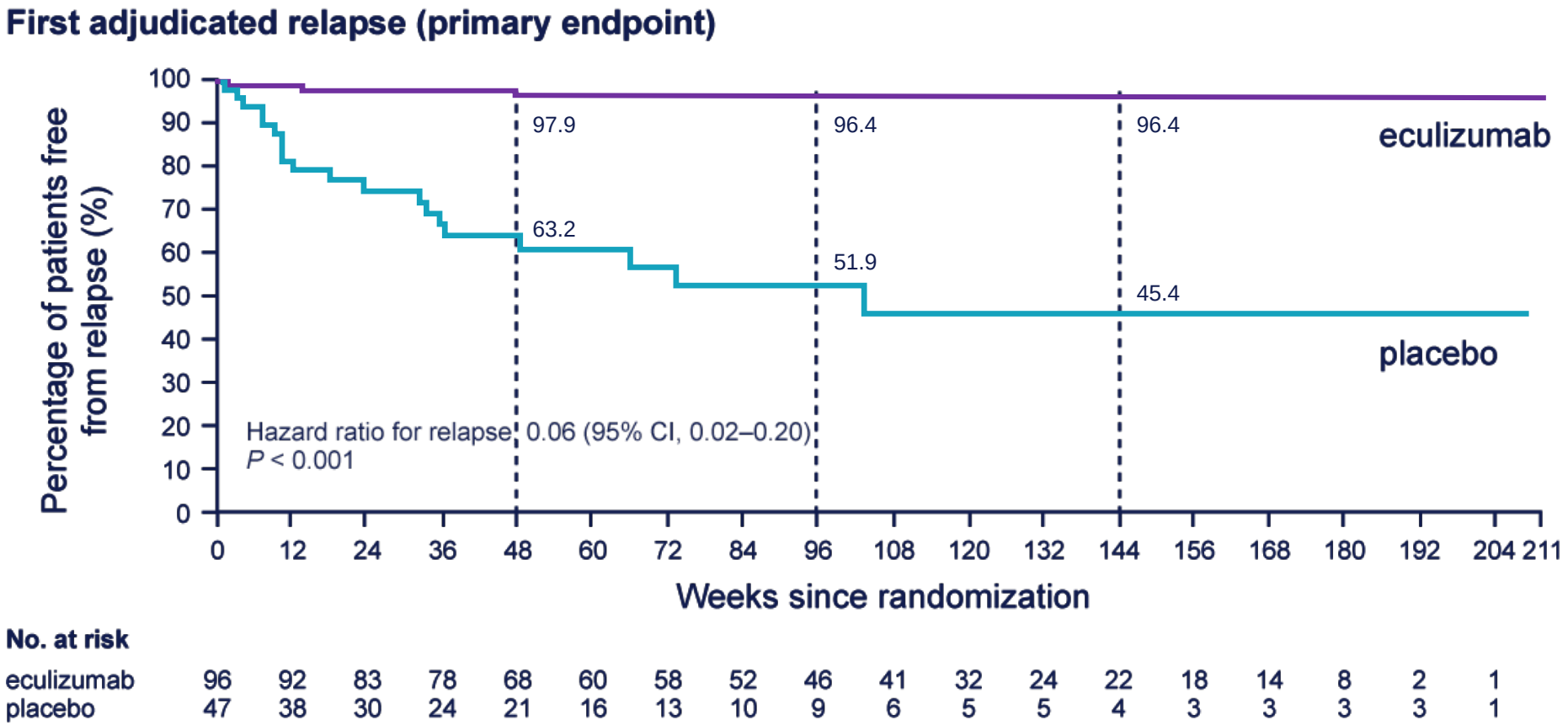

Figure reproduced from Pittock *SJ et al.* 2019

[a]In patients with AQP4+ NMOSD

AQP4+, anti-aquaporin-4 antibody-positive; CI, confidence interval; NMOSD, neuromyelitis optica spectrum disorder

1. Pittock SJ *et al. N Engl J Med* 2019;381:61

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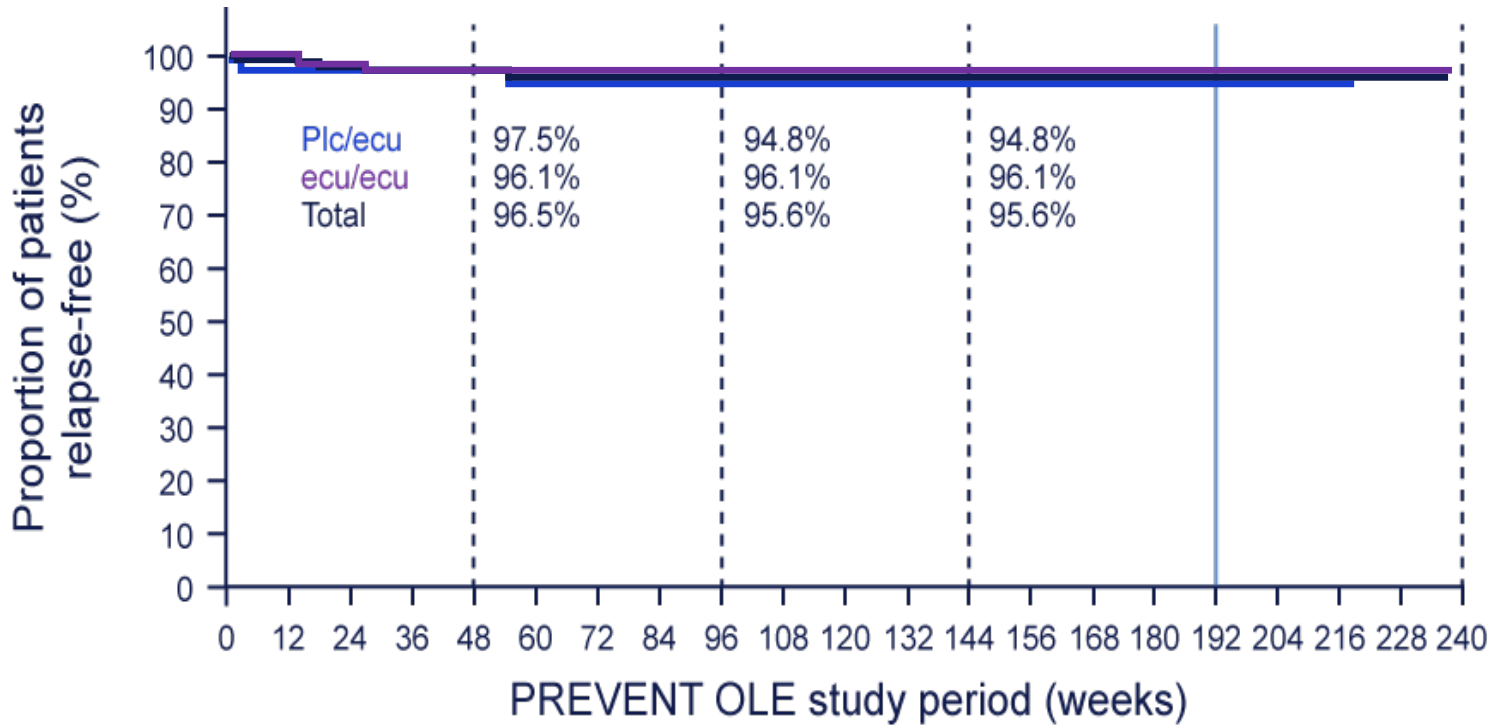
In PREVENT OLE, risk of relapses reduced for over 3.6 years in patients receiving eculizumab[1]



The study was carried out in 119 patients with 78 patients in ecu/ecu group and 41 patients in plc/ecu group

This was a secondary objective and an Open Label Extension study

ecu, eculizumab; OLE, open-label extension; plc, placebo

1. Wingerchuk DM *et al. Ann Neurol* 2021; 89:1088–98

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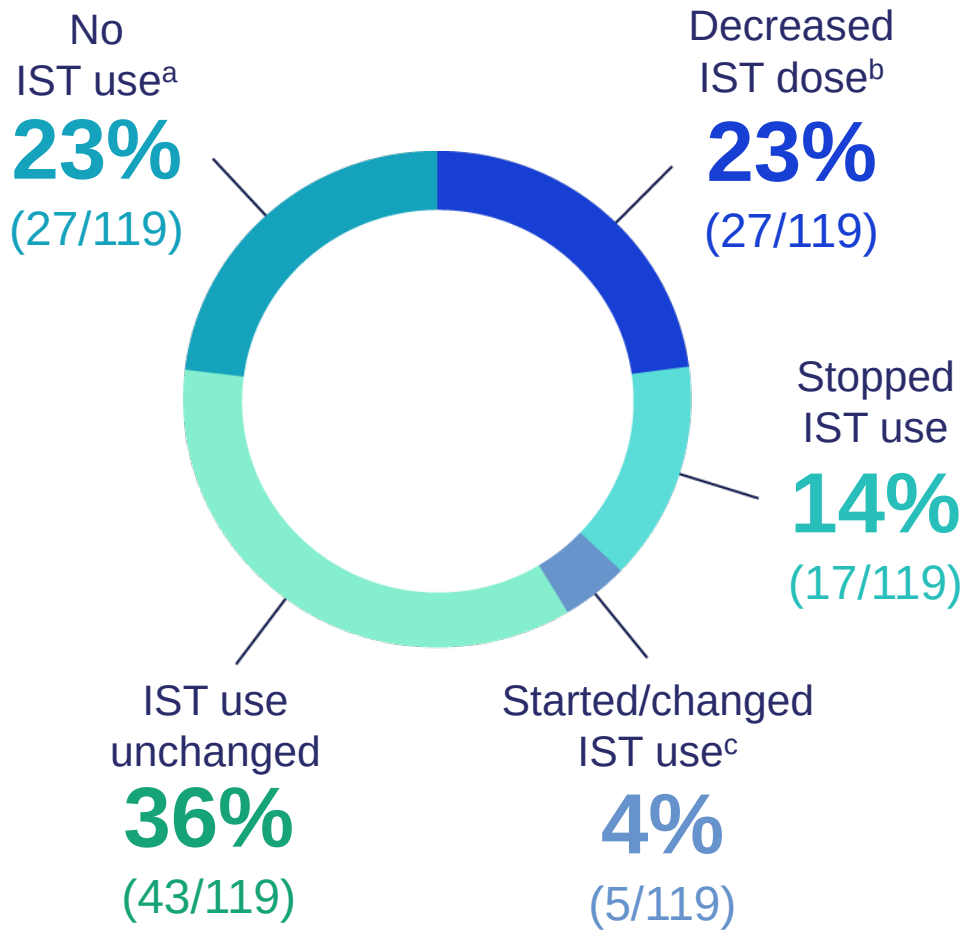
In all, 37% of PREVENT OLE participants stopped or reduced their dose of concomitant ISTs[a,1]



[a]Corticosteroids, azathioprine, mycophenolate mofetil or cyclophosphamide. [b]Decrease in IST dose, discontinuation of one or more ISTs with no change in other ISTs, or a combination of such changes.
[c]Multiple changes that do not reflect a clear increase or decrease, or changes in medication
IST, immunosuppressive therapy; OLE, open-label extension

1. Wingerchuk DM *et al. Ann Neurol* 2021; 89:1088–98

The PREVENT OLE confirmed the long-term safety and tolerability profile of eculizumab[1,2]

The **primary objective** of the OLE was to evaluate the long-term safety of eculizumab in patients with relapsing NMOSD, including the occurrence of AEs and SAEs

SAEs[a]

eculizumab (PREVENT + OLE) **29.8** **events/PY**

54.6 **events/PY** **placebo** (PREVENT)

1 death was reported

One death (pulmonary empyema) was reported as probably related to eculizumab treatment

0

meningococcal infections were reported[b]

AEs reported in at least 15% of patients	PREVENT placebo (n = 47, 53.1 PY)	PREVENT + OLE eculizumab (N = 137, 362.3 PY)
	Events/100 PY	Events/100 PY
Headache	39.5	57.7
Upper respiratory tract infection	18.8	25.7
Nasopharyngitis	28.2	27.6
Urinary tract infection	24.5	25.7
Arthralgia	18.8	8.8
Back pain	16.9	12.4
Diarrhoea	37.6	12.4
Nausea	35.7	13.2

[a]Excluding NMOSD relapses. [b]All patients must be vaccinated at least 2 weeks before receiving eculizumab. Patients who initiate treatment less than 2 weeks after receiving a tetravalent meningococcal vaccine must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. Please refer to the eculizumab EU summary of product characteristics, available from: https://www.ema.europa.eu/en/documents/product-information/soliris-epar-product-information_en.pdf (Accessed August 2022)

AE, adverse event; NMOSD, neuromyelitis optica spectrum disorder; OLE, open-label extension; PY, patient-years; SAE, serious adverse event

1. Wingerchuk DM *et al. Ann Neurol* 2021;89:1088–98; 2. Pittock SJ *et al. N Engl J Med* 2019;381:614–25

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Japanese PMS study assesses the long-term safety of eculizumab in NMOSD in patients who are anti-aquaporin-4 AQP4 antibody-positive[1]

This Japanese PMS is a 10-year long study[2]

PMS guidelines are set by the Japanese regulatory authority[2,3]

PMS is an observational safety study in real-life conditions[1]

All Japanese patients treated with eculizumab are included[1]

NMOSD, neuromyelitis optica spectrum disorder; PMS, post-marketing surveillance

1. Nakahara J *et al.* Abstract accepted for poster presentation at the Annual Meeting Pan-Asian Committee on Treatment and Research in Multiple Sclerosis (PACTRIMS), 24–26 November 2022, Singapore. Accepted abstract list available from: https://www.pactrims.org/assets/Abstracts-with-Poster-Numbers-for-Authors_20-Sep.xlsx (Accessed October 2022)
2. Ministry of Health Labour and Welfare. Pharmaceutical regulations in Japan, chapter 4, post-marketing surveillance of drugs. 2020. Available from: https://www.jpma.or.jp/english/about/parj/eki4g6000000784o-att/2020e_ch04.pdf (Accessed September 2022); 3. Ministry of Health, Labour and Welfare. MHLW ordinance related to standards for conducting post-marketing surveys and studies on drugs (MHLW ordinance no. 171) [in Japanese]. 2004. Available from: https://www.pmda.go.jp/files/000161574.pdf (Accessed 5 October 2022).

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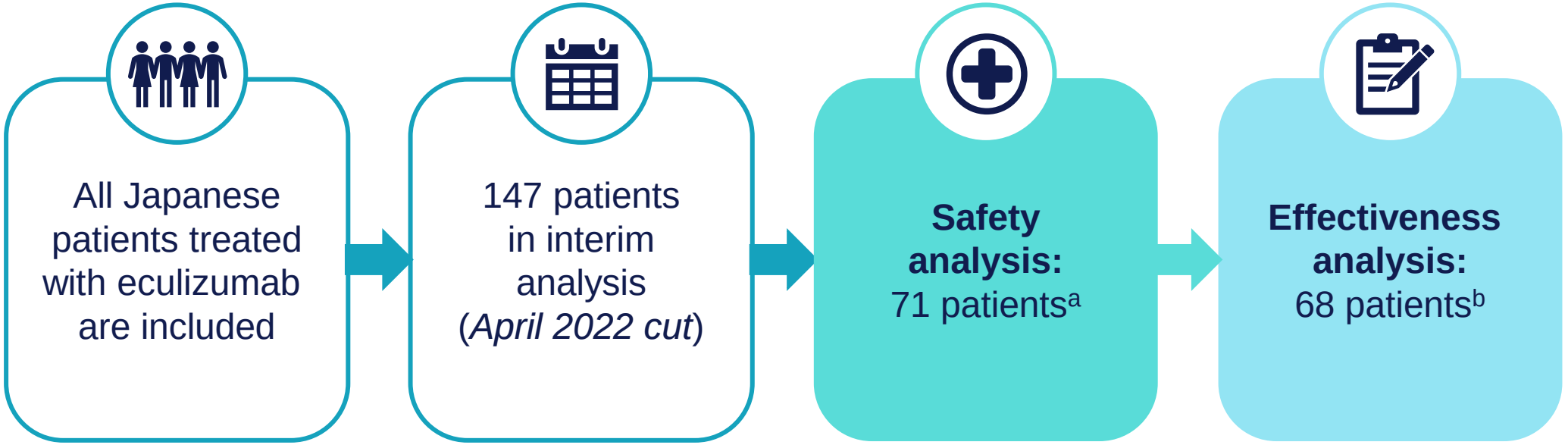
Patient disposition in the Japanese PMS[1]



The median (range) treatment duration was 52.1 (0.1–104.4) weeks

[a] Those patients consenting to publication
[b] Three patients were excluded owing to participation in PREVENT
PMS, post-marketing surveillance

1. Nakahara J *et al.* Abstract accepted for poster presentation at the Annual Meeting Pan-Asian Committee on Treatment and Research in Multiple Sclerosis (PACTRIMS), 24–26 November 2022, Singapore. Accepted abstract list available from: https://www.pactrims.org/assets/Abstracts-with-Poster-Numbers-for-Authors_20-Sep.xlsx (Accessed October 2022)

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Safety data were consistent with the eculizumab safety profile from PREVENT and its OLE[1–5]

26.8% had AEs

15.5% had SAEs

0 meningococcal infections

0 deaths

Ten patients (14.1%) had treatment-related AEs

Ten treatment-related SAEs occurred in seven patients (9.9%)

11.3% of patients had infections (non-meningococcal)

Safety set	
SAE	**n (%)**
Pneumonia	1 (1.4)
Cellulitis	1 (1.4)
Device-related infection	1 (1.4)
Pulmonary hypertension	1 (1.4)
Systemic lupus erythematosus	1 (1.4)
Renal impairment	1 (1.4)
Pyrexia	2 (2.8)
Meningitis, bacterial	1 (1.4)
Meningitis, herpes	1 (1.4)

AE, adverse event; OLE, open-label extension; SAE, serious adverse event

1. Alexion data on file. 2. Nakashima I *et al.* Oral presentation at the 2022 Annual Meeting of the American Academy of Neurology (AAN), 2–7 April 2022, Seattle, USA. Available from: https://www.aan.com/education/annual-meeting-on-demand (Accessed August 2022); 3. Nakashima I *et al. Neurology* 2022;98:1593; 4. Pittock SJ *et al. N Engl J Med* 2019;381:614–25; 5. Wingerchuk DM *et al. Ann Neurol* 2021;89:1088–98

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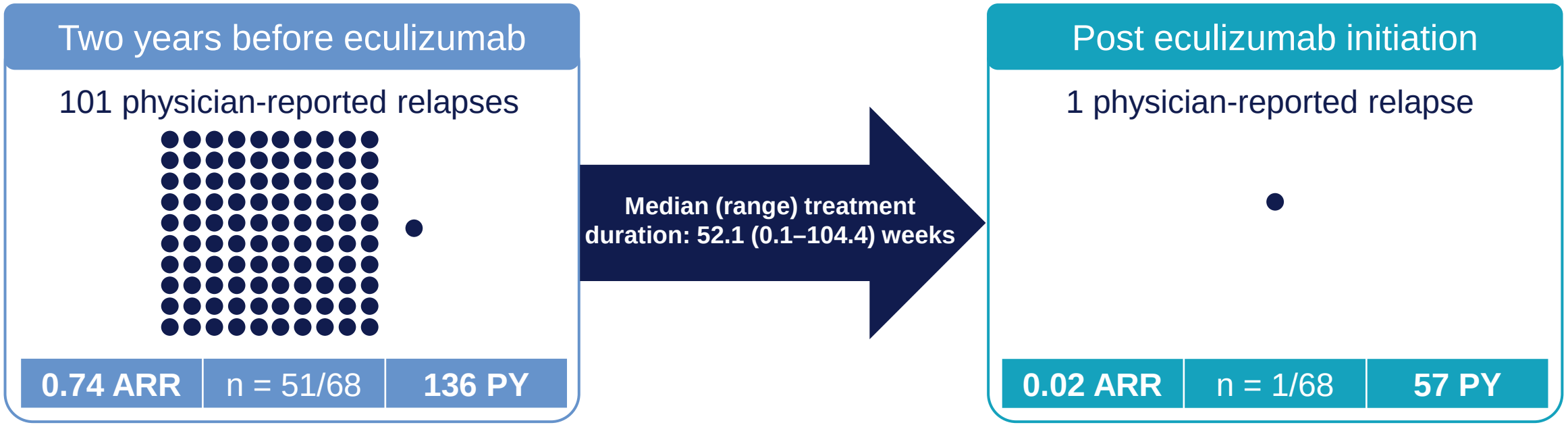
Efficacy outcome was consistent with that of PREVENT and its OLE[1–3]



These findings align with the PREVENT OLE,[3] which showed an **ARR decrease from 2.0 to 0.03**

ARR, annualized relapse rate; OLE, open-label extension; PY, patient-years

1. Nakahara J *et al.* Abstract accepted for poster presentation at the Annual Meeting Pan-Asian Committee on Treatment and Research in Multiple Sclerosis (PACTRIMS), 24–26 November 2022, Singapore. Accepted abstract list available from: https://www.pactrims.org/assets/Abstracts-with-Poster-Numbers-for-Authors_20-Sep.xlsx (Accessed October 2022);
2. Alexion data on file; 3. Wingerchuk DM *et al. Ann Neurol* 2021;89:1088–98

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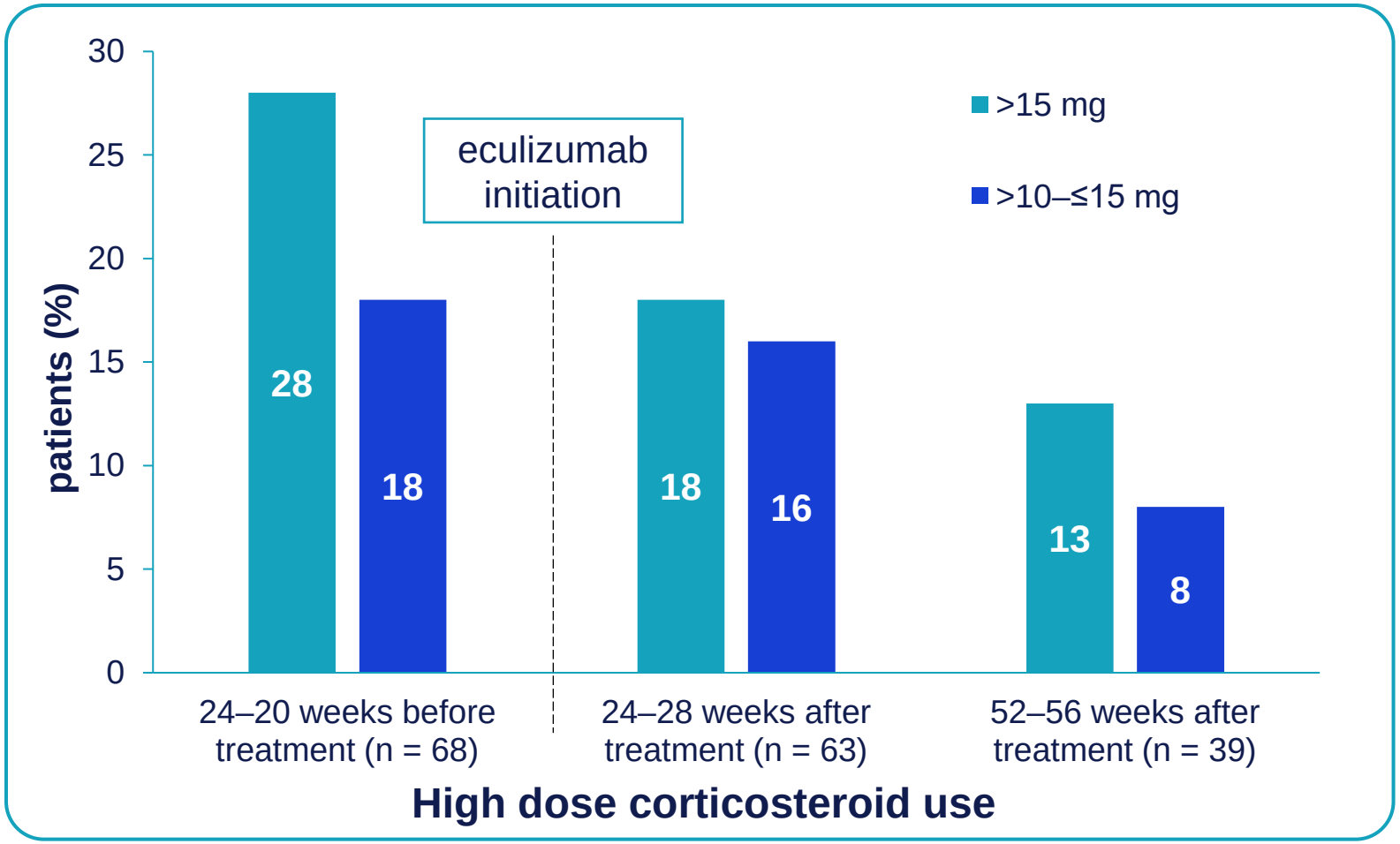
Treatment with eculizumab was associated with a decrease in high-dose[a] corticosteroid use[1]



Japan PMS:[1]
54% (37/68) of patients decreased high-dose[a] corticosteroid use

PREVENT OLE:[2]
37% (44/119) of patients stopped or decreased IST

[a]Total daily dosage over 10 mg/day
IST, immunosuppressive therapy; OLE, open-label extension; PMS, post-marketing surveillance
1. Alexion data on file; 2. Wingerchuk DM *et al. Ann Neurol* 2021; 89:1088–98

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Summary[1-9]

- Complement dysregulation is a key driver in the pathophysiology of NMOSD[1,2]
- **Preventing attacks should be the primary treatment goal** to avoid cumulative irreversible disability[3]
- In PREVENT, eculizumab was **well tolerated and effective** in preventing relapses, **irrespective of previous rituximab use and of concomitant IST use**[a,4,5]
- PREVENT OLE confirmed the eculizumab safety profile and established **long-term efficacy of eculizumab** in reducing the risk of a relapse, thereby **changing the disease course**[6,7]
- Long-term eculizumab treatment was linked to a **decrease in IST use**[5,7]
- **The safety and effectiveness of eculizumab** in the Japanese PMS **were consistent with** the safety and efficacy profiles of eculizumab in **PREVENT** and its **OLE**[6–9]
- Eculizumab treatment in Japanese PMS was associated with a **decrease in physician reported relapses** from 101 (ARR, 0.74) to 1 (ARR, 0.02)[8,9] and with **decreased use of concomitant corticosteroids**[9]

[a]Patients previously receiving rituximab could be included in the trial if they had not received rituximab in the 3 months before screening, rituximab is not currently approved in treatment of NMOSD

ARR, annualized relapse rate; IST, immunosuppressive therapy; NMOSD, neuromyelitis optica spectrum disorder; OLE, open-label extension; PMS, post-marketing surveillance

1. Saadoun S *et al. Brain* 2010;133:349–61; 2. Duan T *et al. J Neuroinflammation* 2018;15:294; 3. Wingerchuk D *et al. Handb Clin Neurol* 2014;122:581-99; 4. Palace J *et al. Mult Scler Relat Disord.* 2021;47:10264; SOLIRIS (eculizumab) EU; SmPC; 6. Pittock SJ *et al. N Engl J Med* 2019;381:614–25; 7. Wingerchuk DM *et al. Ann Neurol* 2021;89:1088–98; 8. Nakahara J *et al.* Abstract accepted for poster presentation at the Annual Meeting Pan-Asian Committee on Treatment and Research in Multiple Sclerosis (PACTRIMS), 24–26 November 2022, Singapore. Accepted abstract list available from: https://www.pactrims.org/assets/Abstracts-with-Poster-Numbers-for-Authors_20-Sep.xlsx (Accessed October 2022); 9. Alexion data on file

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Abbreviated Summary of Product Characteristics

Name of the medicinal product: Soliris® 300 mg concentrate for solution for infusion. **Pharmaceutical form and composition:** Soliris® 300 mg concentrate for solution for infusion containing eculizumab (10mg/mL), a humanized monoclonal ($IgG_{2/4k}$) antibody. One vial of 30 ml contains 300 mg of eculizumab (10 mg/ml). After dilution, the final concentration of the solution to be infused is 5 mg/ml. **Pharmacotherapeutic group:** Selective immunosuppressants, ATC code: L04AA25. **Therapeutic indication:** Soliris is indicated in adults and children for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) and atypical haemolytic uremic syndrome (aHUS). Soliris is also indicated in adults for the treatment of refractory generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor (AChR) antibody-positive and Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease. **Posology and method of administration:** Soliris must be administered by a healthcare professional and under the supervision of a physician experienced in the management of patients with haematological, renal, neuromuscular or neuro inflammatory disorders. Home infusion may be considered for patients who have tolerated infusions well in the clinic. The decision of a patient to receive home infusions should be made after evaluation and recommendation from the treating physician. Home infusions should be performed by a qualified healthcare professional. There is limited safety data supporting home-based infusions, additional precautions in the home setting such as availability of emergency treatment of infusion reactions or anaphylaxis are recommended. Posology Adult Patients: In Paroxysmal Nocturnal Haemoglobinuria (PNH): The PNH dosing regimen for adult patients (≥18 years of age) consists of a 4-week initial phase followed by a maintenance phase: Initial phase: 600 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every week for the first 4 weeks. Maintenance phase: 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion for the fifth week, followed by 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every 14 ± 2 days. In atypical Haemolytic Uremic Syndrome (aHUS), refractory generalized Myasthenia Gravis (gMG) and Neuromyelitis Optica Spectrum Disorder (NMOSD): The aHUS, refractory gMG and NMOSD dosing regimen for adult patients (≥18 years of age) consists of a 4 week initial phase followed by a maintenance phase: Initial phase: 900 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every week for the first 4 weeks. Maintenance phase: 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion for the fifth week, followed by 1,200 mg of Soliris administered via a 25 – 45 minute (35 minutes ± 10 minutes) intravenous infusion every 14 ± 2 days. Paediatric patients in PNH and aHUS: Paediatric PNH and aHUS patients with body weight ≥ 40 kg are treated with the adult dosing recommendations, respectively. In paediatric PNH and aHUS patients with body weight below 40 kg, the Soliris dosing regimen is available in the summary of product characteristics. For further details on posology, consult the summary of product characteristics. **Contraindications:** Hypersensitivity to eculizumab, murine proteins or to any of the excipients. Soliris therapy must not be initiated in patients with unresolved *Neisseria meningitidis* infection or patients who are not currently vaccinated against *Neisseria meningitidis* unless they receive prophylactic treatment with appropriate antibiotics until 2 weeks after vaccination. **Special warnings and precautions for use:** Due to its mechanism of action, the use of Soliris increases the patient's susceptibility to meningococcal infection (*Neisseria meningitidis*). To reduce the risk of meningococcal infection, all patients must be vaccinated at least 2 weeks prior to receiving Soliris unless the risk of delaying Soliris therapy outweighs the risks of developing a meningococcal infection. Patients who initiate Soliris treatment less than 2 weeks after receiving a tetravalent meningococcal vaccine must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination. Patients should be closely monitored for disease symptoms after recommended vaccination. All patients should be monitored for early signs of meningococcal infection. Physicians must discuss the benefits and risks of Soliris therapy with patients and provide them with a patient information brochure and a patient safety card. Soliris therapy should be administered with caution to patients with active systemic infections. Physicians should advise patients about gonorrhoea prevention. Administration of Soliris may result in infusion reactions or immunogenicity that could cause allergic or hypersensitivity reactions (including anaphylaxis). Patients less than 18 years of age must be vaccinated against *Haemophilus influenzae* and pneumococcal infections, and strictly need to adhere to the national vaccination recommendations. When immunosuppressant and anticholinesterase therapies are decreased or discontinued, patients should be monitored closely for signs of disease exacerbation. PNH patients receiving Soliris therapy should be monitored for intravascular haemolysis by measuring serum lactate dehydrogenase (LDH) levels, and may require dose adjustment within the recommended 14±2 day dosing schedule during the maintenance phase (up to every 12 days). If PNH patients discontinue treatment with Soliris they should be closely monitored for at least 8 weeks to detect signs and symptoms of serious intravascular haemolysis and other reactions. aHUS patients receiving Soliris therapy should be monitored for thrombotic microangiopathy by measuring platelet counts, serum LDH and serum creatinine, and may require dose adjustment within the recommended 14±2 day dosing schedule during the maintenance phase (up to every 12 days). Discontinuation of treatment should only be considered if medically justified. If aHUS patients discontinue treatment with Soliris, they should be monitored closely for signs and symptoms of severe thrombotic microangiopathy complications. Patients with refractory gMG that discontinue Soliris treatment should be carefully monitored for signs and symptoms of deterioration of disease. Soliris contains sodium, this should be taken into consideration with patients on a controlled sodium diet. For details on fertility, pregnancy and lactation, consult the summary of product characteristics. **Possible side effects:** Headache is a very common side effect, other common side effects are pneumonia, upper respiratory tract infection, bronchitis, nasopharyngitis, urinary tract infection, oral herpes, leukopenia, anaemia, insomnia, dizziness, dysgeusia, hypertension, cough, oropharyngeal pain, diarrhoea, vomiting, nausea, abdominal pain, rash, pruritus, alopecia, arthralgia, myalgia, pyrexia, fatigue and influenza like illness. The most serious possible side effect is meningococcal infection (including *Meningococcal sepsis, Meningococcal meningitis, Neisseria infection).* Other cases of *Neisseria species* have been reported including sepsis with *Neisseria gonorrhoeae*, *Neisseria sicca/subflava, Neisseria spp* unspecified. Uncommon side effects reported: sepsis, septic shock, peritonitis, lower respiratory tract infection, fungal infection, viral infection, abscess, cellulitis, influenza, gastrointestinal infection, cystitis, infection, sinusitis, thrombocytopenia, lymphopenia, anaphylactic reaction, hypersensitivity, decreased appetite, depression, anxiety, mood swings, paresthesia, tremor, vision blurred, tinnitus, vertigo, palpitation, accelerated hypertension, hypotension, hot flush, vein disorder, dyspnoea, epistaxis, throat irritation, nasal congestion, rhinorrhoea, constipation, dyspepsia, abdominal distension, urticaria, erythema, petechiae, hyperhidrosis, dry skin, muscle spasms, bone pain, back and neck pain, joint swelling, pain in extremity, renal impairment, dysuria, haematuria, spontaneous penile erection, edema, chest discomfort, asthenia, chest pain, infusion site pain, chills. Elevated alanine aminotransferase and aspartate aminotransferase levels, elevated gamma-glutamyltransferase, decreased haematocrit and decreased haemoglobin and also infusion related reactions are reported. Rare possible side effects are: Aspergillus infection, arthritis bacterial, genitourinary tract gonococcal infection, *Haemophilus influenzae* infection, impetigo, gingivitis, malignant melanoma, myelodysplastic syndrome, haemolysis, abnormal clotting factor, red blood cell agglutination, coagulopathy, Basedow's disease, abnormal dreams, sleep disorder, syncope, conjuctival irritation, haematoma, gastroesophageal reflux disease, gingival pain, jaundice, dermatitis, skin depigmentation, trismus, menstrual disorder, extravasation, infusion site paresthesia, feeling hot and positive Coombs test are reported. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Nederlands Bijwerkingen Centrum Lareb, Website: www.lareb.nl. **Marketing authorization holder:** Alexion Europe SAS, 103-105 rue Anatole France, 92300 Levallois-Perret, France. **Marketing authorization number:** EU/1/07/393/001. **Delivery status:** UR (Medicinal product subject to restricted medical prescription). **Reimbursement:** Orphan drug reimbursed under the applicable regulations and rules of the government and your healthcare insurer. **Date of revision of the text:** 05/2020.

Please reference the following link for the full SmPC. https://www.ema.europa.eu/en/medicines/human/EPAR/soliris

M/INT/SOL-N/0020 October 2022

Inebilizumab and NMOSD:

What's New in 2022

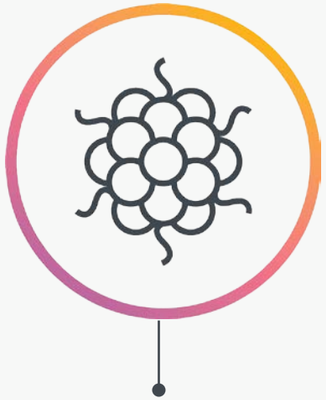
Kristina Patterson, MD, PhD
Medical Director-Neuroimmunology
Medical Affairs
Horizon Therapeutics

Guthy Jackson Charitable Foundation Symposium
October 25, 2022
Amsterdam, Netherlands

Horizon Therapeutics

We Are a Science-Based Organization Addressing Unmet Needs for Underserved Patients

When only five percent of the 7,000 known rare diseases have a treatment, we know we must think differently about research and development so we can deliver in new ways for the patients and communities we serve.



RARE DISEASE

- At Horizon, we believe science and compassion must work together to transform lives
- Our mission is to deliver medicines for rare, autoimmune, and severe inflammatory diseases

NOVEL NMOSD TREATMENT

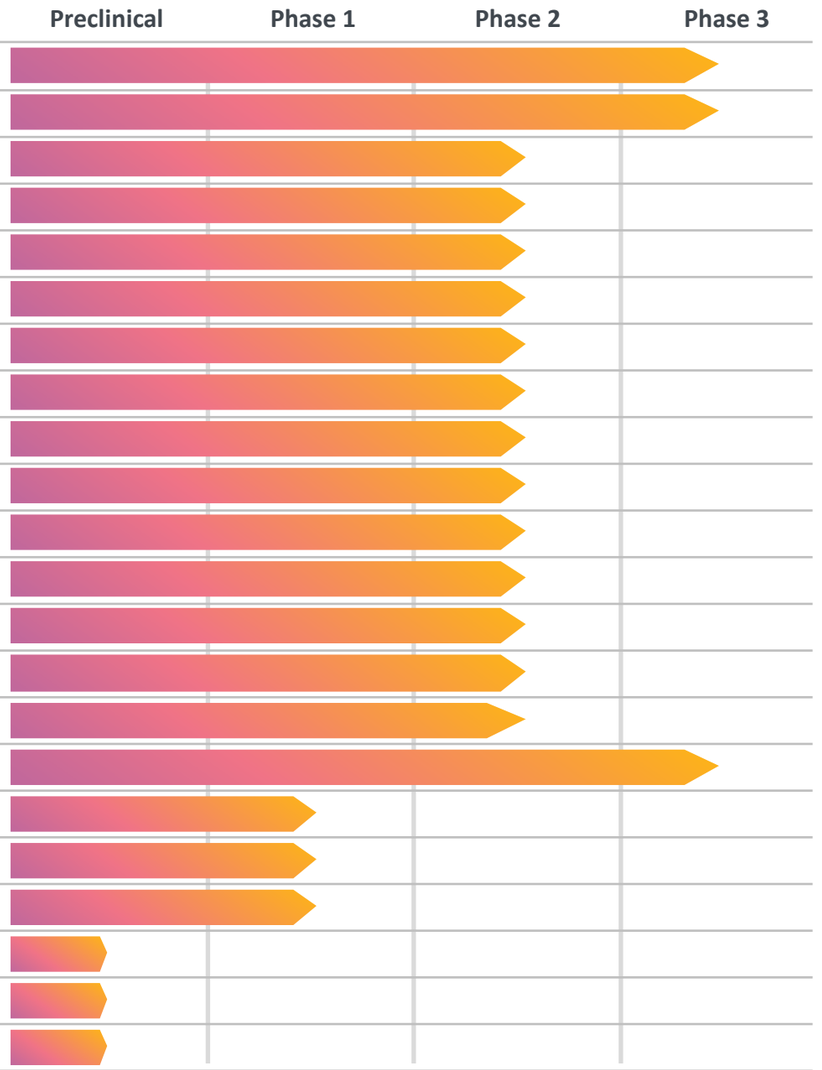
- UPLIZNA® (inebilizumab-cdon) is the first and only CD19+ B-cell–depleting monotherapy proven to reduce the risk of attacks in adult patients with AQP4-IgG+ NMOSD

NMOSD COMMITMENT

- Horizon continues to invest heavily in NMOSD awareness and education
- We are committed to advancing innovative NMOSD disease state, biomarker, and therapeutic research

Expanding Our Pipeline to Address Unmet Need

Medicine/Candidate	Program/Potential Indication
UPLIZNA	Myasthenia Gravis (MG)
	IgG4-Related Disease (IgG4-RD)
Daxdilimab	Systemic Lupus Erythematosus (SLE)
	Alopecia Areata (AA)
	Discoid Lupus Erythematosus (DLE)(1)
	Lupus Nephritis (LN)(1)
	Dermatomyositis (DM)(1)
Dazodalibep	Sjögren's Syndrome
	Rheumatoid Arthritis(2)
	Kidney Transplant Rejection
	Focal Segmental Glomerulosclerosis (FSGS)(1)
HZN-825	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
	Idiopathic Pulmonary Fibrosis (IPF)
ADX-914	Atopic Dermatitis(1,3)
	Additional Autoimmune Disease(1,3)
TEPEZZA	TED in Japan (OPTIC-J)
	Subcutaneous Administration
	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
HZN-1116	Autoimmune Diseases
Alpine	Autoimmune Diseases(4)
ARO-XDH	Next-Gen Uncontrolled Gout(4)
HemoShear	Novel Gout Targets(4)



- **>20 programs**
- **Initiated 3 clinical trials** year-to-date
- **10 potential approvals** in the second half of the decade
- **4 additional Phase 4 programs:**
  - TEPEZZA chronic/low-CAS TED
  - KRYSTEXXA shorter infusion duration
  - KRYSTEXXA monthly dosing
  - KRYSTEXXA retreatment

IgG4: Immunoglobulin G4. | TED: Thyroid eye disease.
CAS: Clinical activity score.
(1) Planned programs; not yet initiated.
(2) Trial complete. Announced positive topline results on May 3, 2022. The trial met the primary endpoint across all doses and was well tolerated.
(3) Horizon has an option to acquire ADX-914 from Q32 Bio on pre-negotiated terms through the completion of Phase 2 clinical trials. Phase 2 trials to be conducted by Q32.
(4) External collaborations.

Expanding Our Pipeline to Address Unmet Need

Medicine/Candidate	Program/Potential I
UPLIZNA	Myasthenia Gravis (M
	IgG4-Related Disease
Daxdilimab	
	Lupus
	Dermatomy
Dazodalibep	Sjögren's Syndro
	Rheumatoid Arthritis
	Kidney Transplant Rej
	Focal Segmental Glom
HZN-825	Diffuse Cutaneous Sys
	Idiopathic Pulmonary
ADX-914	Atopic Dermatitis[1,3]
	Additional Autoimmu
TEPEZZA	TED in Japan (OPTIC-J
	Subcutaneous Admini
	Diffuse Cutaneous Sys
HZN-1116	Autoimmune Disease
Alpine	Autoimmune Disease
ARO-XDH	Next-Gen Uncontrolle
HemoShear	Novel Gout Targets[4]

Clinical Trial In Recruitment

Study of Inebilizumab in Pediatric Subjects With Neuromyelitis Optica Spectrum Disorder

A Phase 2, open-label, multicenter study to evaluate the pharmacokinetics, pharmacodynamics, and safety of inebilizumab in eligible **pediatric** participants 2 to < 18 years of age with recently **active NMOSD** who are **seropositive** for autoantibodies against aquaporin-4 (AQP4-immunoglobulin [Ig]G)

Trial listing on Clinicaltrials.gov

Horizon Is Actively Building Partnerships in the NMOSD Community

SPHERES Registry

GJCF International NMO Patient Day

Learn NMOre Together Event

Sumaira Foundation Gala

NMOSD, neuromyelitis optica spectrum disorder.

Overview of N-MOmentum and Long-term Data

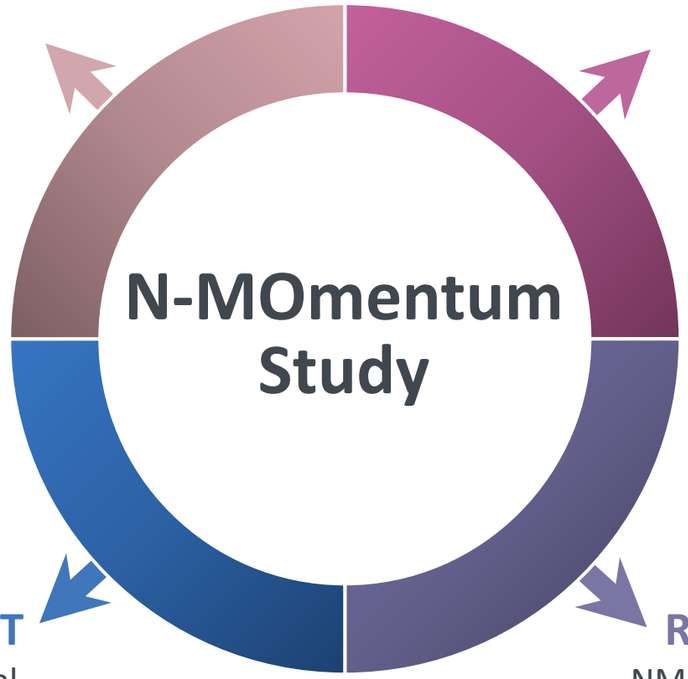
N-MOmentum Trial Highlights

DATA FROM DAY 1

Attacks were counted from day 1 in the N-MOmentum study and were not omitted if they occurred early in treatment[1]

MONOTHERAPY

N-MOmentum studied inebilizumab as monotherapy in patients with NMOSD[1]



DISABILITY ENDPOINT MET

N-MOmentum was the only pivotal NMOSD trial to meet its disability endpoint[1-4]

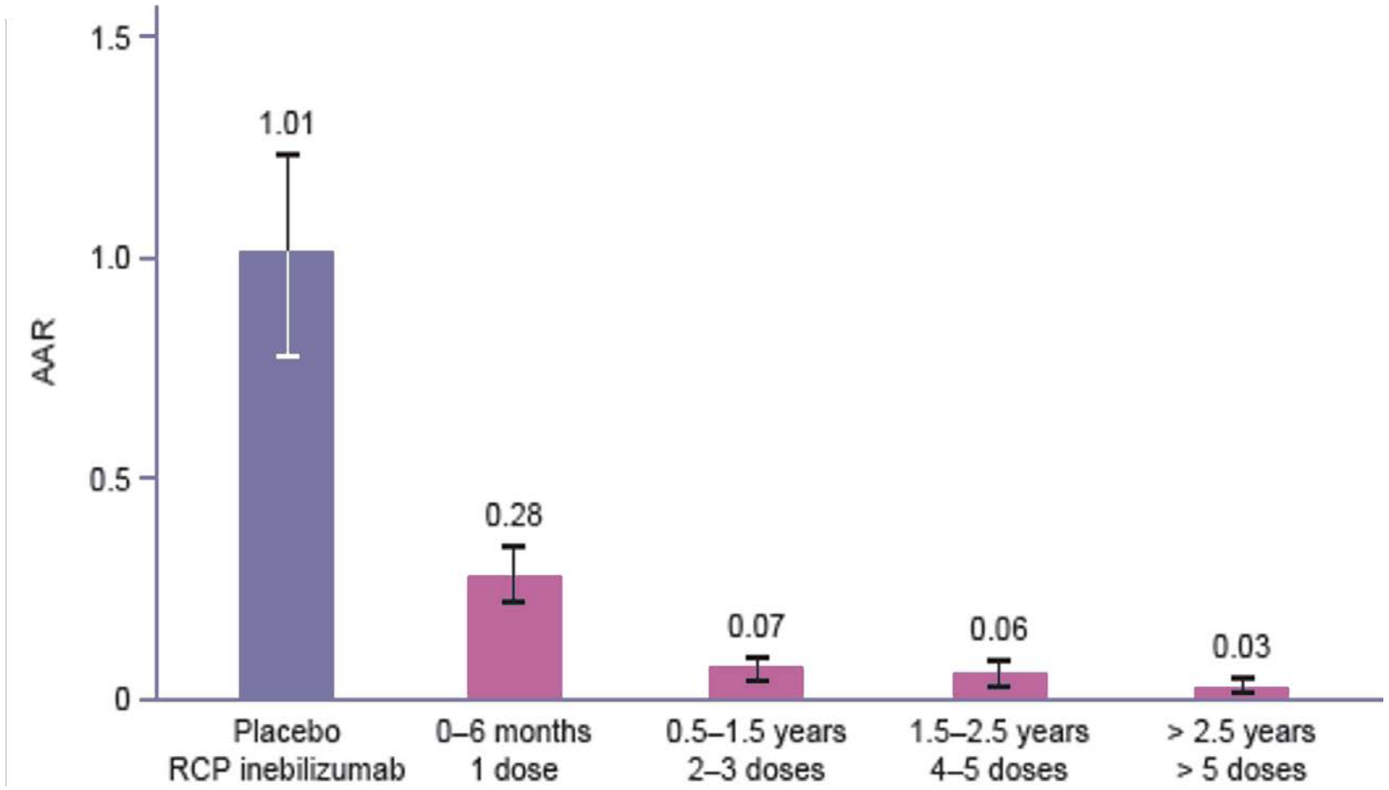
REAL-TIME ADJUDICATION

NMOSD attack adjudication occurred in real time with protocol-defined clinical and **MRI criteria**[1]

MRI, magnetic resonance imaging; NMOSD, neuromyelitis optica spectrum disorder.

1. Cree et al. *Lancet*. 2019;394:1352-1363. **2.** Yamamura et al. *N Engl J Med.* 2019;381:2114-2124. **3.** Pittock et al. *N Engl J Med*. 2019;381:614-625. **4.** Traboulsee et al. *Lancet Neurol.* 2020;19:402-412.

Long-term Inebilizumab Treatment Provided a Sustained Reduction in NMOSD Attack Risk From Baseline



Participants, n	**56**	**225**	**213**	**197**	**168**
Number of attacks	22	31	14	11	7
Years of observation	23	111	208	189	222

Annualized Attack Rate (AAR) Decreased by **97%** After 2.5 Years of Treatment With Inebilizumab

AAR (95% CI) at 4 years is 0.092 (0.067–0.127) in “any inebilizumab” patients

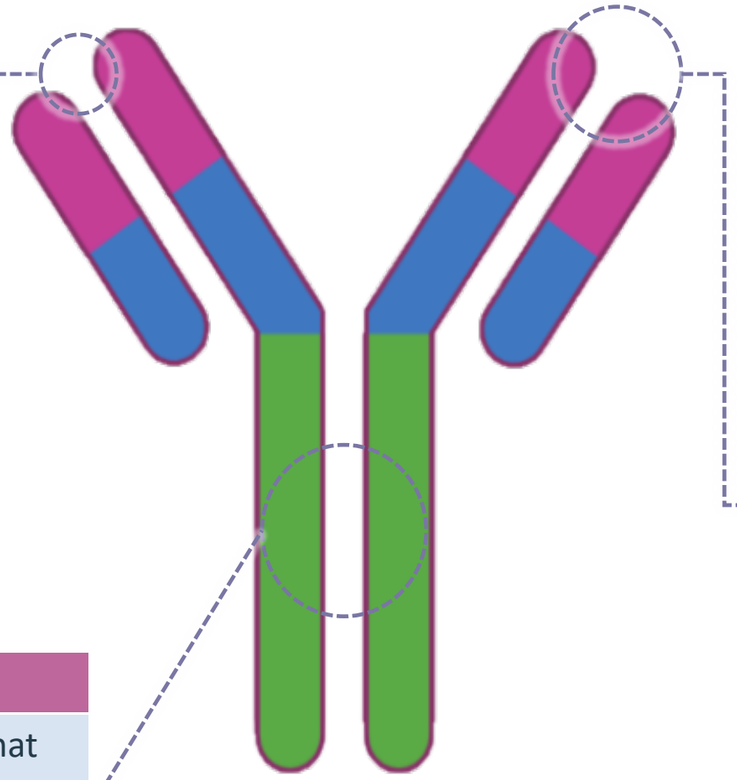
AC, adjudication committee; RIOI: Randomized to inebilizumab in RCP/OLP inebilizumab group; RPOI: Randomized to placebo in RCP/OLP inebilizumab group; any inebilizumab, participants who received inebilizumab at any point during the study
Adapted from Bennett et al. Poster presented at the European Committee for Treatment and Research in Multiple Sclerosis 2021 Annual Meeting, October 13-15, 2021. Cree et al. Presentation at the European Academy of Neurology 2021 Annual Meeting June 19-22, 2021

Advancing NMOSD Therapeutic Research

Inebilizumab Has a Unique Mechanism and Clinical Profile

Targeted for CD19 binding

Depletes B cells central to NMOSD pathogenesis, including plasmablasts and some plasma cells[1-4]



Humanized

Designed to improve tolerability and decrease infusion reactions[5,6]

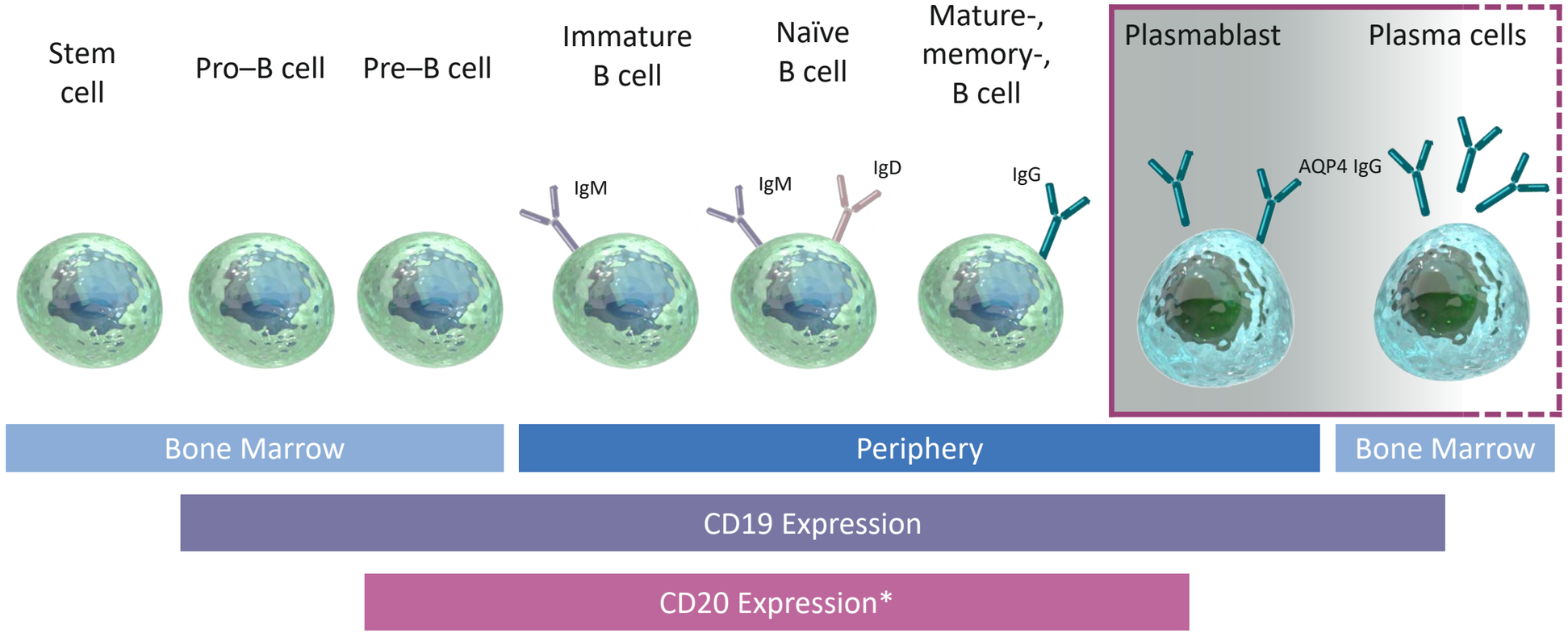
Glycoengineered Fc Region

To provide efficacy in those that may have diminished responses to other monoclonal antibody therapies[7]

1. UPLIZNA (inebilizumab-cdon) [Prescribing Information] Horizon. 2. Cree BAC, et al. *Lancet*. 2019;394:1352-1363. 3. Forsthuber TG et al. *Ther Adv Neurol Disord.* 2018;11:1-13. 4. Bennett JL, et al. *Neurol Neuroimmunol Neuroinflamm.* 2015;2(3):e104. 5. Hwang WYK, Foote J. *Methods*. 2005;36(1):3-10. 6. Harding FA, et al. *MAbs*. 2010;2(3):256-265. 7. Herbst R, et al. *J Pharmacol Exp Ther*. 2010;335(1):213-222.

B cell maturation

CD19 is expressed on the surfaces of B cells as they mature into plasmablasts



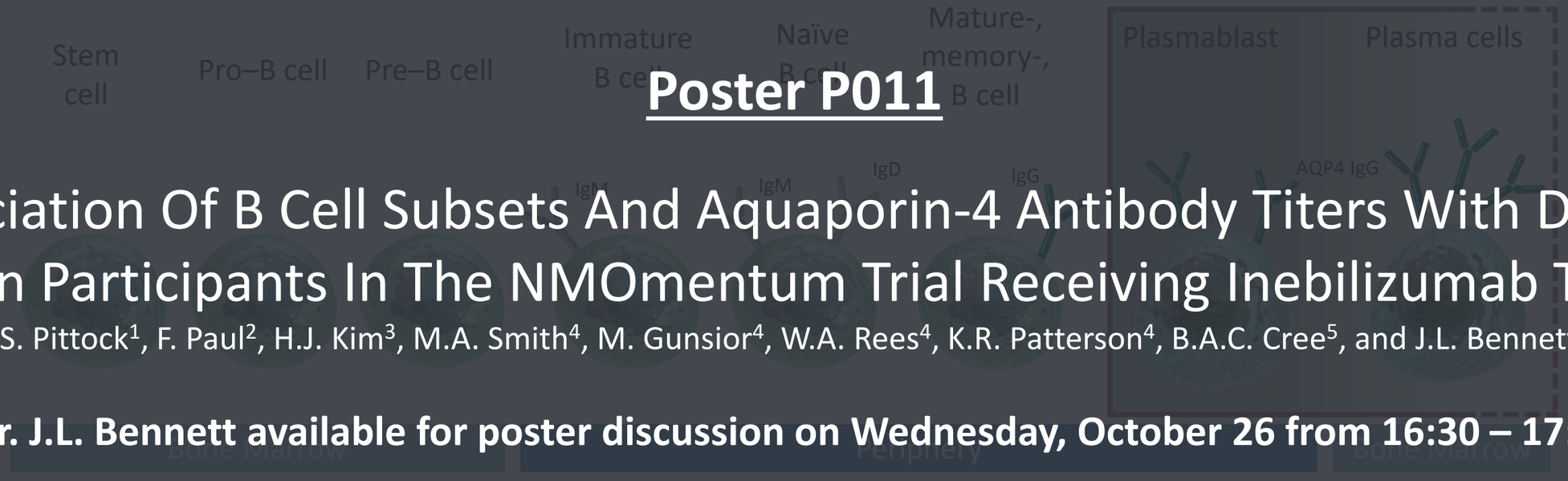
***3-5% of circulating T cell also express CD20[1]**

Ig, immunoglobulin. CD19, cluster of differentiation 19; CD20, cluster of differentiation 20; IgD, immunoglobulin D; IgG, immunoglobulin G; IgM, immunoglobulin M.

1. Schuh et al. J Immunol, 2016; 197(4):1111-7

B cell maturation

CD19 is expressed on the surfaces of B cells as they mature into plasmablasts



*3-5% of circulating T cell also express CD20[1]

Ig, immunoglobulin. CD19, cluster of differentiation 19; CD20, cluster of differentiation 20; IgD, immunoglobulin D; IgG, immunoglobulin G; IgM, immunoglobulin M.

1. Schuh et al. J Immunol, 2016; 197(4):1111-7

Poster P011

Association Of B Cell Subsets And Aquaporin-4 Antibody Titers With Disease Activity In Participants In The NMOmentum Trial Receiving Inebilizumab Treatment

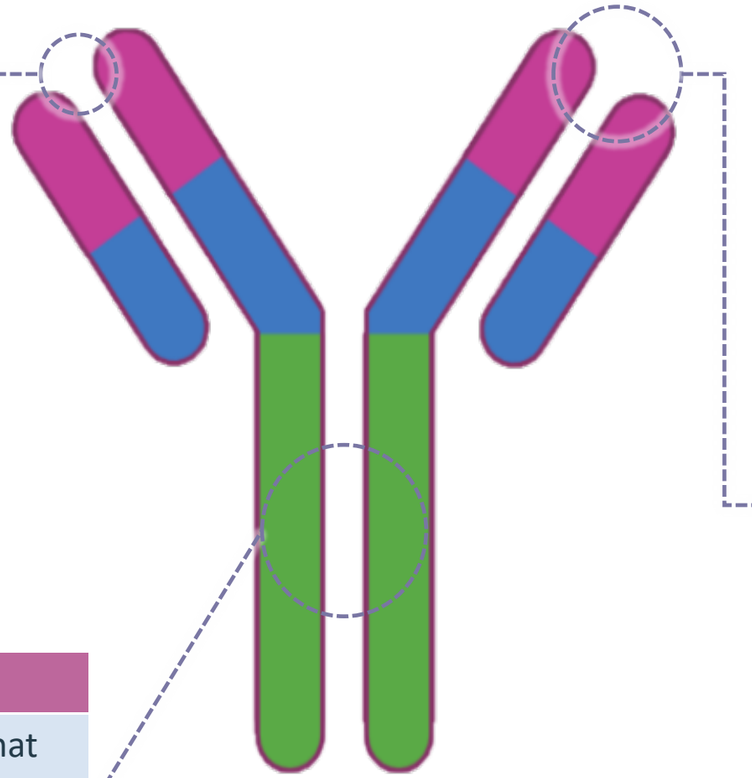
S. Pittock[1], F. Paul[2], H.J. Kim[3], M.A. Smith[4], M. Gunsior[4], W.A. Rees[4], K.R. Patterson[4], B.A.C. Cree[5], and J.L. Bennett[6]

Dr. J.L. Bennett available for poster discussion on Wednesday, October 26 from 16:30 – 17:30

Inebilizumab Has a Unique Mechanism and Clinical Profile

Targeted for CD19 binding

Depletes B cells central to NMOSD pathogenesis, including plasmablasts and some plasma cells[1-4]



Humanized

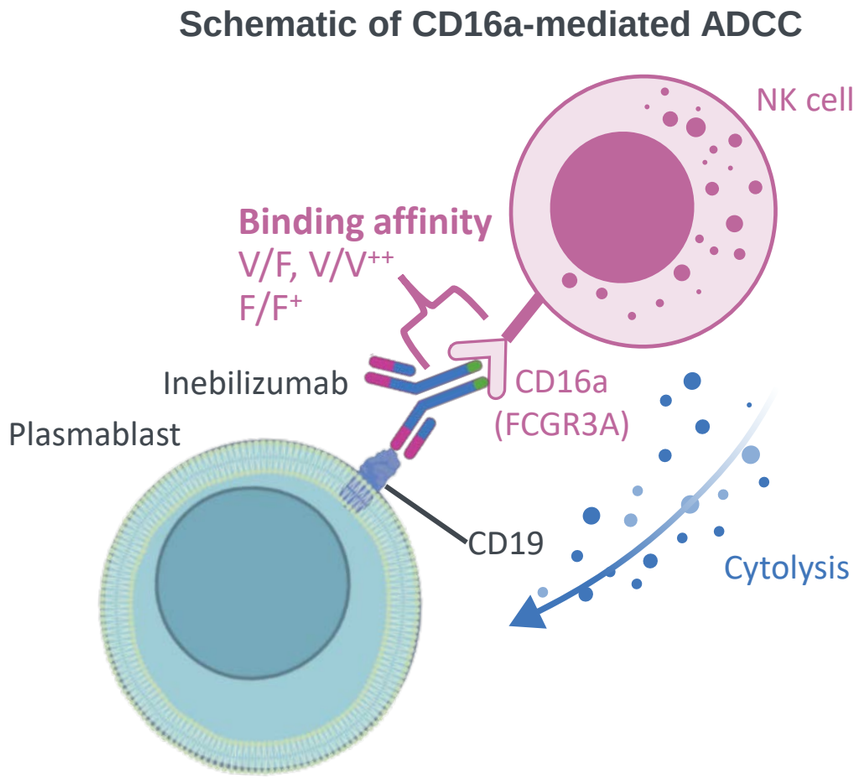
Designed to improve tolerability and decrease infusion reactions[5,6]

Glycoengineered Fc Region

To provide efficacy in those that may have diminished responses to other monoclonal antibody therapies[7]

1. UPLIZNA (inebilizumab-cdon) [Prescribing Information] Horizon. 2. Cree BAC, et al. *Lancet*. 2019;394:1352-1363. 3. Forsthuber TG et al. *Ther Adv Neurol Disord.* 2018;11:1-13. 4. Bennett JL, et al. *Neurol Neuroimmunol Neuroinflamm.* 2015;2(3):e104. 5. Hwang WYK, Foote J. *Methods*. 2005;36(1):3-10. 6. Harding FA, et al. *MAbs*. 2010;2(3):256-265. 7. Herbst R, et al. *J Pharmacol Exp Ther*. 2010;335(1):213-222.

Glycoengineered for Consistent Efficacy



The low-affinity immunoglobulin G (IgG) Fc region receptor III-A gene *(FCGR3A)* encodes a receptor (CD16a) that plays an important role in antibody-dependent cell-mediated cytotoxicity (ADCC)

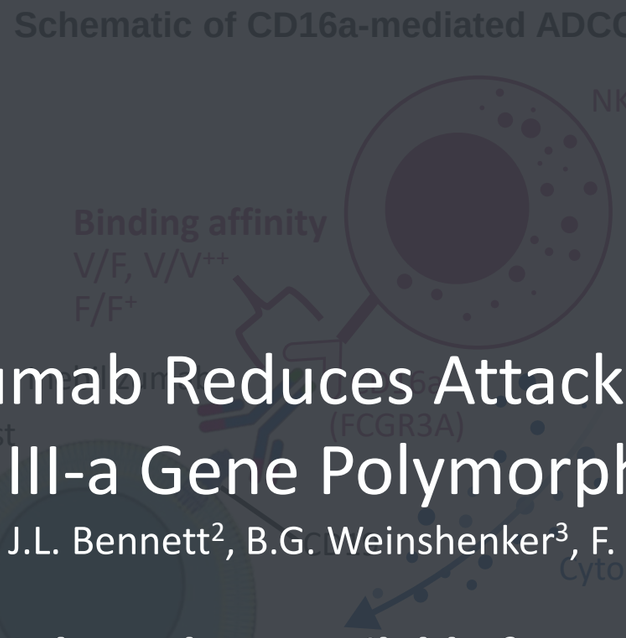
~40% of the population is homozygous for the F allele.[2,3] The F allele is associated with diminished response to certain monoclonal antibody therapies[4,5]

Inebilizumab is glycoengineered to enhance affinity for low-affinity immunoglobulin G (IgG) Fc region receptor III-A gene *(FCGR3A)* and maximize ADCC

ADCC, antibody dependent cellular cytoxicity; *FCGR3A,* Fc region receptor III-A gene; NK, natural killer.

Aktas O, et al. Poster presented at: Consortium of Multiple Sclerosis Centers; June 1-4, 2022; National Harbor, MD.
1. Hayat S et al. Ann Clin Transl Neurol. 2020;7:1040–9. 2. Mahaweni NM et al. Sci Rep. 2018;8:15983. 3. Dong C et al. Arthritis Rheumatol. 2014;66:1291–9 4. Kim SH et al. JAMA Neurol. 2015;72:989–95. 5. Zhong M et al. Neurotherapeutics. 2020;17:1768–84.

Polymorphism of Fc Region Receptor Gene Affects IgG Binding Affinity



- The low-affinity immunoglobulin G (IgG) Fc region receptor III-A gene *(FCGR3A)* encodes a receptor (CD16a) that plays an important role in antibody-dependent cell-mediated cytotoxicity (ADCC)
- **~40% of the population**, including Caucasian and African American individuals, **are homozygous for the F allele**[2,3] The F allele is associated with diminished response to certain monoclonal antibody therapies[4,5]

Inebilizumab is glycoengineered to enhance affinity for low-affinity immunoglobulin G (IgG) Fc region receptor III-A gene (*FCGR3A*) and maximize ADCC

Poster P411

Inebilizumab Reduces Attack Risk Independent Of Low Affinity IgG Fc Region Receptor III-a Gene Polymorphisms In Neuromyelitis Optica Spectrum Disorder

O. Aktas[1], J.L. Bennett[2], B.G. Weinshenker[3], F. Paul,[4] H.J. Kim,[5] H-P. Hartung,[1,6,7] M.A. Smith,[8] W.A. Rees,[8] D. She,[8] B.A.C. Cree[9]

Prof. Orhan Aktas available for poster discussion on Thursday, October 27 from 17:00 – 18:00

[1]Medical Faculty, Heinrich Heine University Dusseldorf, Dusseldorf, Germany; [2]University of Colorado, School of Medicine, Anschutz Medical Campus, Aurora, CO, USA; [3]University of Virginia, Charlottesville, VA, USA; [4]Experimental and Clinical Research Center, Max Delbruck Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, Berlin, Germany; [5]Research Institute and Hospital of National Cancer Center, Goyang, Republic of Korea; [6]Brain and Mind Center, University of Sydney, Sydney, NSW, Australia; [7]Department of Neurology, Medical University of Vienna, Vienna, Austria; [8]Horizon Therapeutics, Gaithersburg, MD, USA; [9]UCSF Weill Institute for Neurosciences, Department of Neurology, University of California San Francisco, San Francisco, CA, USA

Commitment to NMOSD Research

Published 12+ manuscripts in 2021/2022

Pediatric NMOSD trial currently enrolling

Partner with advocacy to support NMOSD registries (e.g., SPHERES)

Support external disease state, epidemiology, biomarker and therapeutic research

Horizon Posters

Poster Session 1: Posters Available in ePoster Area (Hall 12) on Wednesday, October 26

- **P007** Efficacy Comparison Of Time To First Adjudicated Attack With Inebilizumab Vs Satralizumab In NMOSD: A Matching-Adjusted Indirect Comparison Of Monotherapy Registrational Trials
  - Prof. Friedemann Paul available for discussion on Wednesday, October 26 from 16:30-18:30
- **P011** Association Of B Cell Subsets And Aquaporin-4 Antibody Titers With Disease Activity In Participants In The NMOmentum Trial Receiving Inebilizumab Treatment
  - Dr. J.L. Bennett available for discussion on Wednesday, October 26 from 16:30 – 18:30

Poster Session 2: Posters Available in ePoster Area (Hall 12) on Thursday, October 27

- **P411** Inebilizumab Reduces Attack Risk Independent Of Low Affinity IgG Fc Region Receptor Ill-a Gene Polymorphisms In Neuromyelitis Optica Spectrum Disorder
  - Prof. Orhan Aktas available for discussion on Thursday, October 27 from 17:00 – 19:00
- **P419** Safety And Efficacy Of Inebilizumab In AQP4+ NMOSD Participants With History Of Immunosuppression Treatment Prior To N-MOmentum Study
  - Prof. Friedemann Paul available for discussion on Thursday, October 27 from 17:00-19:00

Thank you

Roche's commitment to Neuroscience Rare Diseases

Covering: Satralizumab▼ long-term efficacy and safety in NMOSD, and the ongoing clinical trials

25 October 2022

Ivana Vodopivec

Senior Medical Director, F. Hoffmann-La Roche Ltd.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on the Summary of Product Characteristics (SmPC) for details on how to report adverse reactions.

The SmPC can be found at the following link: www.ema.europa.eu/en/medicines/human/EPAR/enspryng

Satralizumab (ENSPRYNG®) is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive.
Satralizumab is currently not approved for the treatment of Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD), Autoimmune Encephalitis (AIE), or generalised Myasthenia Gravis (gMG).
M-XX-00010932

Disclosures

Ivana Vodopivec (Senior Medical Director) is an employee of F. Hoffmann-La Roche Ltd.

Disclaimer

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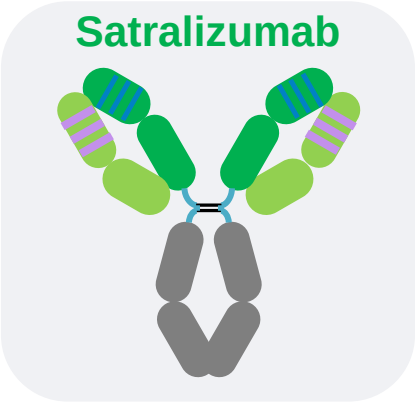
Prescribing information may vary depending on the applicable approval in the respective country. Therefore, before prescribing any product, always refer to applicable local materials such as the prescribing information and/or the Summary of Product Characteristics (SmPC).

Overview of satralizumab

Mechanism of action



Satralizumab is a humanised, IgG2, monoclonal recycling antibody that targets the IL-6 receptor[1–4]

Satralizumab binds to both **membrane-bound** and **soluble forms** of the **IL-6 receptor**, preventing IL-6 from binding and **inhibiting the inflammatory IL-6 signalling pathways**[5,6]

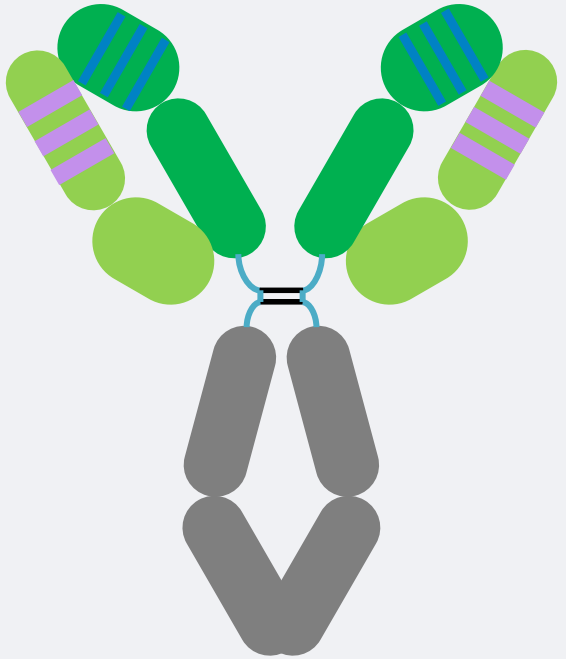
By inhibiting IL-6 activity, satralizumab reduces pro-inflammatory signalling processes associated with many autoimmune disorders[5–7]

Satralizumab was engineered with **Recycling Antibody™** technology to ensure maximal sustained IL-6 suppression[1]

pH

Satralizumab binds to the IL-6 receptor in a pH-dependent manner, which prolongs its plasma persistence and facilitates antibody binding to antigen multiple times[1,2,8]

Satralizumab



Monthly SC home dosing

EMA, European Medicines Agency; FDA, Food and Drug Administration; IgG, immunoglobulin G; IL-6, interleukin-6; SC, subcutaneous.

1. Chugai. Proprietary Innovative Antibody Engineering Technologies in Chugai Pharmaceutical. Available at: https://www.chugai-pharm.co.jp/cont_file_dl.php?f=FILE_1_36.pdf&src=[%0],[%1]&rep=139,36. Accessed September 2022; 2. Reichert JM. *Mabs* 2017;9:167–181; 3. FDA satralizumab Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761149s002lbl.pdf. Accessed September 2022; 4. EMA satralizumab Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/enspryng-epar-product-information_en.pdf. Accessed September 2022; 5. Traboulsee A, et al. *Lancet Neurol* 2020;19:402–412; 6. Yamamura T, et al. *N Engl J Med* 2019;381:2114–2124; 7. Schett G. *Rheumatology* 2018;57:ii43–ii50; 8. Igawa T, et al. *Nat Biotechnol* 2010;28:1203–1207.

Ongoing clinical studies with satralizumab

Satralizumab in:

- **Neuromyelitis Optica Spectrum Disorder (NMOSD)**
- **Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD)**
- **Autoimmune Encephalitis (AIE)**
- **Generalised Myasthenia Gravis (gMG)**

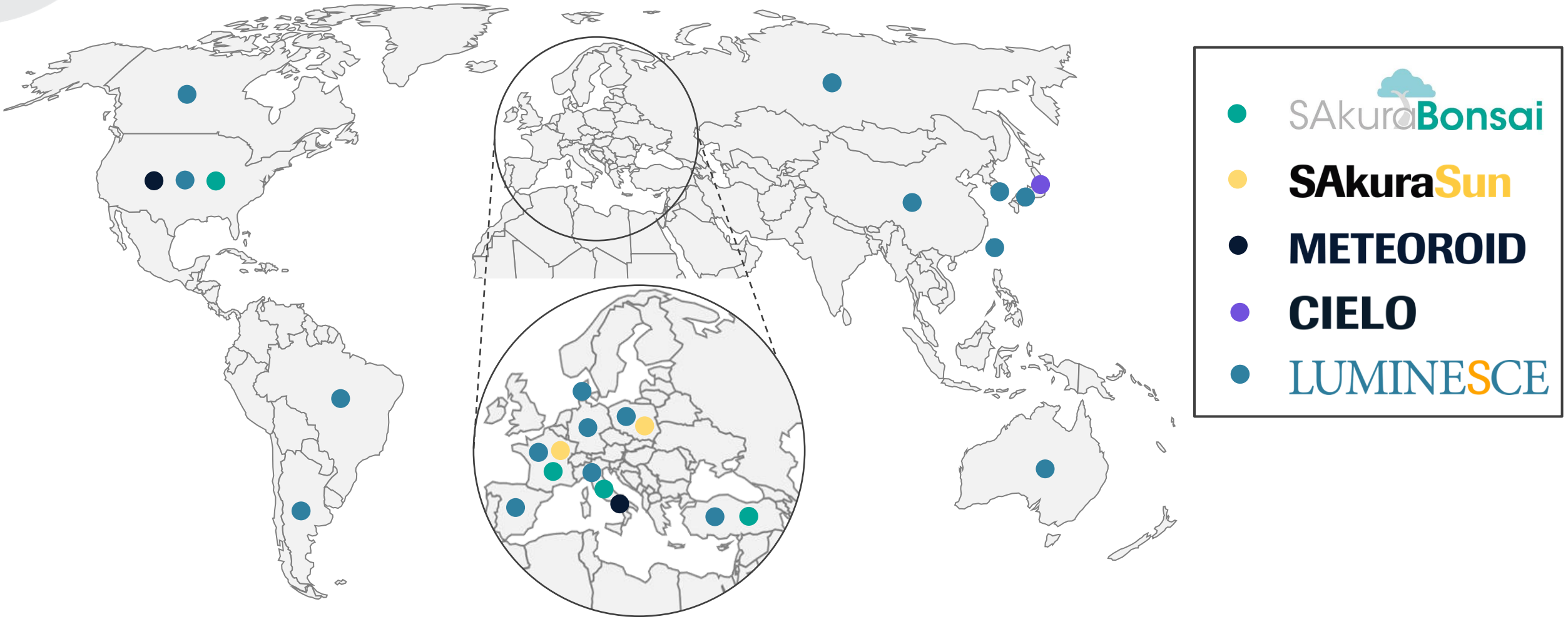
Satralizumab (ENSPRYNG®) is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive. Satralizumab is currently not approved for the treatment of Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD), Autoimmune Encephalitis (AIE), or generalised Myasthenia Gravis (gMG).

Further investigations into the efficacy and safety of satralizumab in neuroscience rare disease are ongoing

SAkuraMoon	**(NCT04660539)** – single-arm study of the long-term efficacy and safety of satralizumab in patients who were enrolled in the open-label extension periods of the SAkuraSky and SAkuraStar studies
SAkuraBonsai	**(NCT05269667)** – study of satralizumab in patients with AQP4-IgG+ NMOSD who are treatment-naïve or had an inadequate response to previous rituximab treatment
SAkuraSun	**(NCT05199688)** – study to evaluate the PK, efficacy, safety, tolerability, and PD of satralizumab in paediatric patients (aged 2–11 years) with AQP4-IgG+ NMOSD
METEOROID	**(NCT05271409)** – The first study to evaluate the efficacy, safety, PK and PD of satralizumab in patients (aged ≥12 years) with MOGAD
CIELO	**(NCT05503264)** – The first study to evaluate the efficacy, safety, PK and PD of satralizumab in patients with NMDAR (aged ≥12 years) and LGI1 AIE (≥18 years)
LUMINESCE	**(NCT04963270)** – The first study to evaluate the efficacy, safety, PK and PD of satralizumab as an add-on therapy in a broad patient population with gMG

AIE, autoimmune encephalitis; AQP4-IgG, aquaporin-4 immunoglobulin G; gMG, generalised myasthenia gravis; LGI1, leucine-rich glioma-inactivated 1; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; NMDAR, N-methyl-D-aspartic acid receptor; NMOSD, neuromyelitis optica spectrum disorder; PD, pharmacodynamics; PK, pharmacokinetics.

Satralizumab portfolio: Actively recruiting study countries



Note: Correct as of 27th September 2022. Each coloured circle represents ≥1 study site activation in the respective country. Circles are not indicative of the number of study sites.

Long-term efficacy and safety of satralizumab

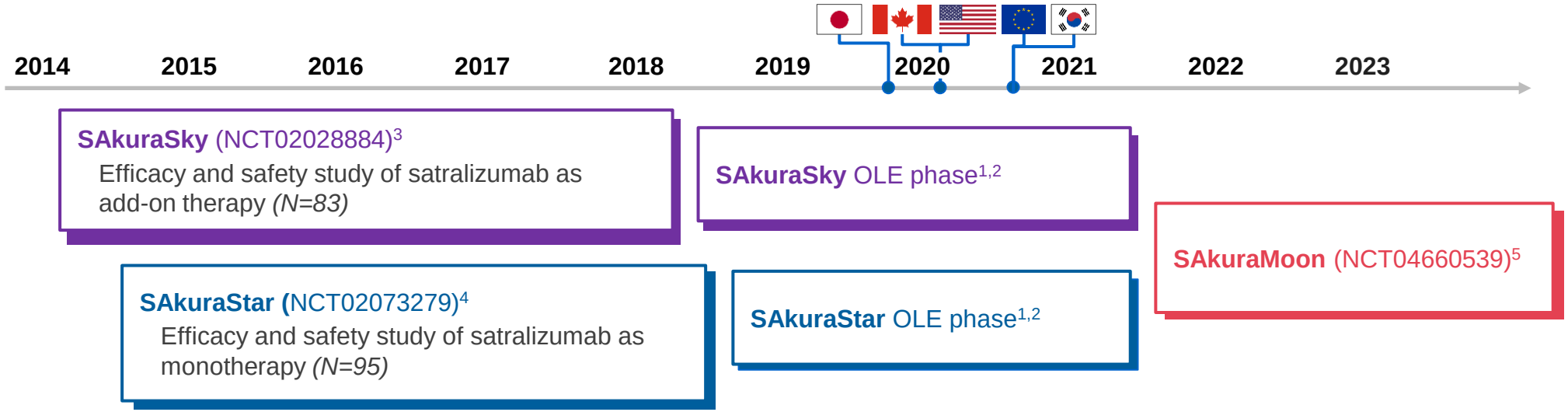
Long-term efficacy and safety of satralizumab in NMOSD: Results from the open-label extension periods of SAkuraSky and SAkuraStar

1. Kleiter I, et al. *Neurol Neuroimmunol Neuroinflamm* 2022 [pending publication]; 2. Yamamura T, et al. *Mult Scler Relat Disord* 2022;66:104025.

Why does this study matter to clinicians?

Because NMOSD is a lifelong disease, a patient's maintenance therapy must remain effective, safe, and tolerable over time

With **up to 7 years of patient exposure** to satralizumab in the SAkuraSky and SAkuraStar studies, we have the opportunity to review long-term outcomes[1,2]



NMOSD, neuromyelitis optica spectrum disorder; OLE, open-label extension; PDR, protocol-defined relapse.

1. Kleiter I, et al. *Neurol Neuroimmunol Neuroinflamm* 2022 [pending publication]; 2. Yamamura T, et al. *Mult Scler Relat Disord* 2022;66:104025; 3. Yamamura T, et al. *N Engl J Med* 2019;381:2114–2124; 4. Traboulsee A, et al. *Lancet Neurol* 2020;19:402–412; 5. ClinicalTrials.gov. SAkuraMoon. Available at: www.clinicaltrials.gov/ct2/show/NCT04660539. Accessed September 2022.

Satralizumab provides sustained long-term relapse prevention with no new safety findings reported from the DB periods in patients with NMOSD[1,2]

Long-term efficacy[1]

Results are for the AQP4-IgG+ population

- At Week 192, **71%** (SAkuraSky) and **73%** (SAkuraStar) of satralizumab-treated patients were **free from relapse***
- At Week 192, **91%** (SAkuraSky) and **90%** (SAkuraStar) of satralizumab-treated patients were **free from severe relapse***†
- At Week 192, **90%** (SAkuraSky) and **86%** (SAkuraStar) had **no sustained worsening of EDSS**

Long-term safety[2]

Results are for the AQP4-IgG+ and AQP4-IgG- populations

- Rates of AEs and serious AEs in the OST were comparable with satralizumab and placebo in the DB periods
- Rates of infections and serious infections in the OST periods were similar to the DB periods, and did not increase over time
- No deaths or anaphylactic reactions related to study treatment were reported
- All injection-related reactions were non-serious, and none led to treatment discontinuation or interruption

*Relapse refers to iPDRs, which are protocol-defined relapses assessed by the investigator (relapse adjudication by an independent CEC was not performed during the OLE periods). †Severe relapse refers to severe iPDRs, which are iPDRs associated with a ≥2 point increase in EDSS score‡ (threshold selected post hoc based on published data)[3]. ‡Difference in EDSS score between visit at relapse and prior EDSS assessment visit. AE, adverse event; AQP4-IgG+/-; aquaporin-4 immunoglobulin G seropositive/seronegative; CEC, clinical endpoint committee; DB, double-blind; EDSS, expanded disability status scale; iPDR, investigator-reported protocol-defined relapse; OLE, open label extension; OST, overall satralizumab treatment.

1. Kleiter I, et al. *Neurol Neuroimmunol Neuroinflamm* 2022 [pending publication]; 2. Yamamura T, et al. *Mult Scler Relat Disord* 2022;66:104025; 3. Levy M, et al. *ECTRIMS Online Library* 2017;200411:P756.

SAkuraBONSAI

A prospective, open-label study of satralizumab investigating novel imaging, biomarker, and clinical outcomes in patients with AQP4-IgG-seropositive NMOSD

SAkuraBonsai

NCT05269667

1.Traboulsee A, et al. *Neurology* 2022;98(18 Supp):P15-1.002. Presented at AAN 2022; 2. ClinicalTrials.gov. SAkuraBONSAI. Available at: https://clinicaltrials.gov/ct2/show/NCT05269667. Accessed October 2022.

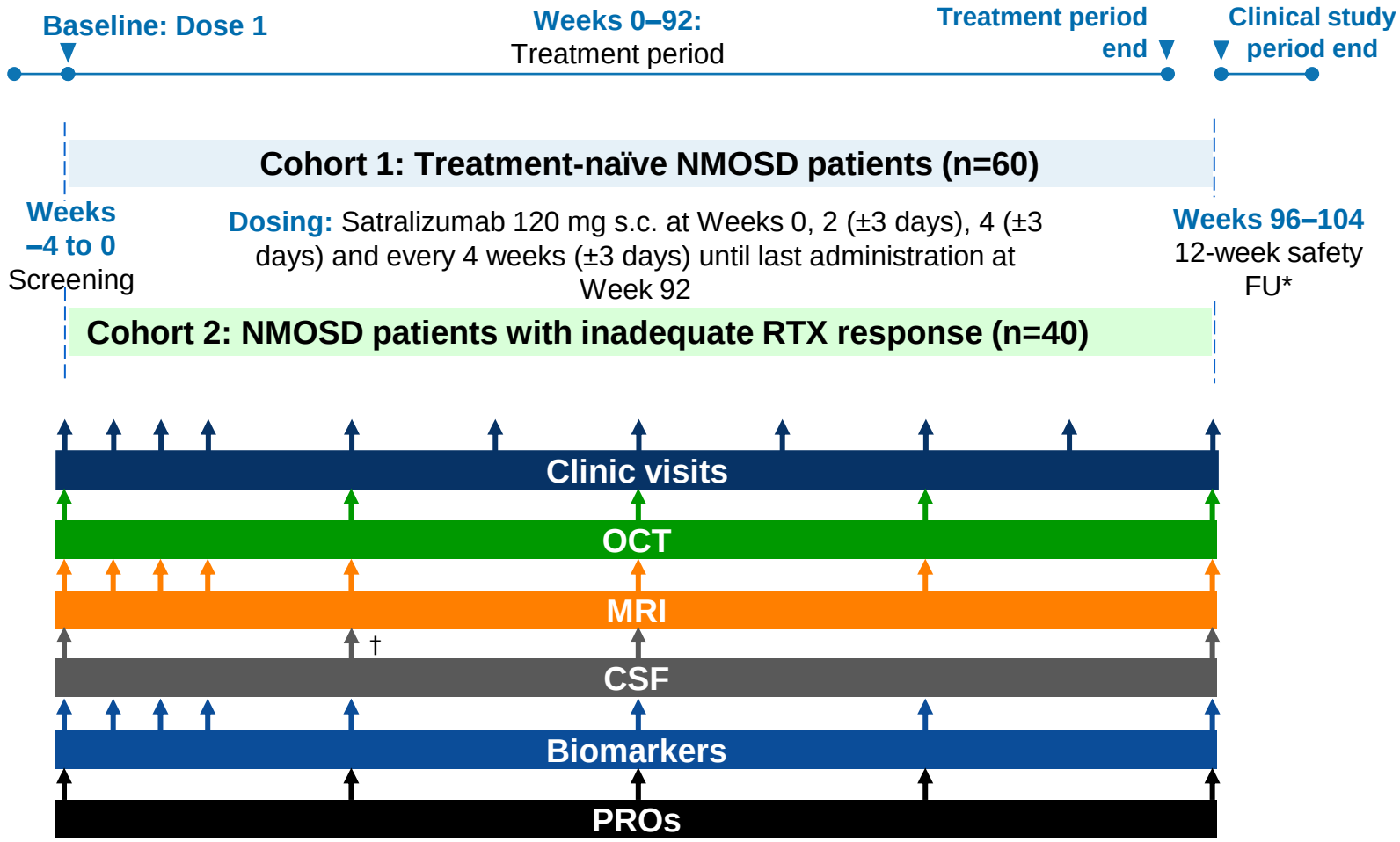
SAkuraBONSAI: A prospective, multicentre, open-label study

- A prospective, multicentre, open-label study:
  - ***Cohort 1*: Treatment-naïve** NMOSD patients (n=60)
  - ***Cohort 2*:** NMOSD patients with an **inadequate response to prior RTX treatment** (n=40)
- Patients will be 18–74 years with a confirmed diagnosis of AQP4-IgG+ NMOSD

Scan the QR code for further information about **SAkuraBONSAI** on ClinicalTrials.gov

⚠ *Off-label use*

Rituximab[§] is not approved globally for the treatment of NMOSD.



*For patients withdrawing from satralizumab treatment, i.e. those discontinuing early or not continuing with treatment outside of the study. †Optional CSF at Week 24. §Rituximab received approval in Japan on June 20, 2022 for use in patients with NMOSD.

AQP4-IgG+, aquaporin-4-immunoglobulin-G-seropositive; CSF, cerebrospinal fluid; FU, follow-up; MRI, magnetic resonance imaging; NMOSD, neuromyelitis optica spectrum disorder; OCT, optical coherence tomography; PRO, patient-reported outcome; RTX, rituximab; s.c., subcutaneous.

Traboulsee A, et al. *Neurology* 2022;98(18 Supp):P15-1.002. Presented at AAN 2022; ClinicalTrials.gov. SAkuraBONSAI. Available at: https://clinicaltrials.gov/ct2/show/NCT05269667. Accessed October 2022.

SAkuraSun

A Phase 3, open-label, multicentre, uncontrolled study of satralizumab in paediatric patients with AQP4-IgG seropositive NMOSD

SAkuraSun

NCT05199688

ClinicalTrials.gov. SAkuraSun. Available at: https://clinicaltrials.gov/ct2/show/NCT05199688. Accessed October 2022.

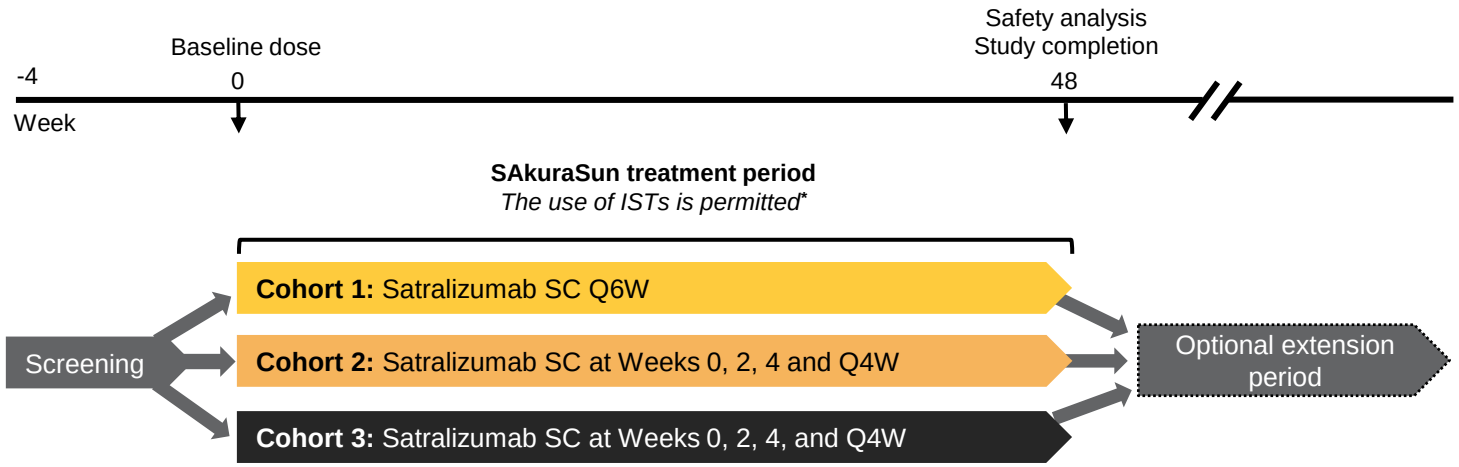
SAkuraSun: A Phase 3, open-label, multicentre, uncontrolled study of satralizumab in paediatric patients with AQP4-IgG seropositive NMOSD

SAkuraSun

Clinical value

Currently, there are no approved therapies for treating pediatric patients (<12 years of age) with NMOSD. SAkuraSun (NCT05199688) is the **first study** to investigate the PK, PD, safety, tolerability, and efficacy of satralizumab in paediatric patients with AQP4-IgG seropositive NMOSD

Study design



Inclusion criteria

The study will enrol at least **8 patients** that are **2–11 years old** with **AQP4-IgG seropositive** NMOSD

Patients are assigned to Cohorts 1, 2, or 3 based on their body weight:

- **Cohort 1: ≥10 kg to <20 kg**
- **Cohort 2: ≥20 kg to <40 kg**
- **Cohort 3: ≥40 kg**

*For patients receiving a baseline IST and planning to continue on these therapies, treatment must be at stable dose for 4 weeks prior to baseline.
AQP4-IgG, aquaporin-4 immunoglobulin G; NMOSD, neuromyelitis optica spectrum disorder; PD, pharmacodynamic; PK, pharmacokinetics; Q4W, every 4 weeks; Q6W, every 6 weeks; SC, subcutaneous injection.
ClinicalTrials.gov. SAkuraSun. Available at: https://clinicaltrials.gov/ct2/show/NCT05199688. Accessed October 2022.

SAkuraSun: Study endpoints

SAkuraSun

Pharmacokinetics:
Observed serum satralizumab concentration (C_{trough}), apparent CL/F and V/F of satralizumab, and AUC of satralizumab

Safety:
Incidence and severity of adverse events evaluated over 48 weeks

Efficacy:
Proportion of relapse-free patients, TFR, ARR, requirement of rescue therapy, disability progression (EDSS), visual acuity, pain (FACES®) and health utility (EQ-5D-Y) evaluated over 48 weeks

Scan the QR code for further information about **SAkuraSun** on ClinicalTrials.gov

ARR, annualised relapse rate; AUC, area under the concentration–time curve; CL/F, apparent clearance; C_{trough}, trough concentration; EDSS, Expanded Disability Status Scale; EQ-5D-Y, EuroQol 5-Dimensional Questionnaire, Youth Version; TFR, time to first relapse; V/F, apparent volume of distribution.

ClinicalTrials.gov. SAkuraSun. Available at: https://clinicaltrials.gov/ct2/show/NCT05199688. Accessed October 2022.

SPHERES Registry for NMOSD

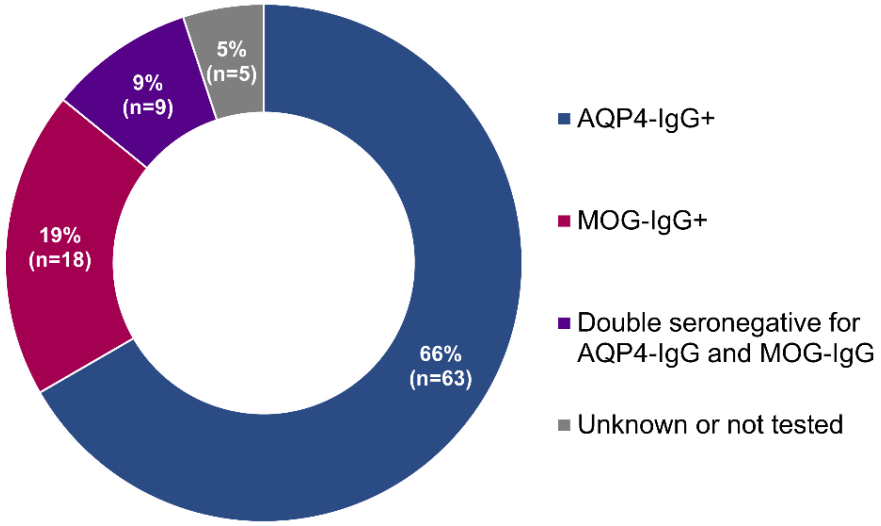
Baseline characteristics of initial patients in the CorEvitas SPHERES Registry as of August 2022

Exuzides A, et al. ECTRIMS 2022. P408.

SPHERES is actively following patients with NMOSD who exhibit distinct serotypes, clinical courses, and treatment regimens

SPHERES is a collaborative observational registry designed to collect real-world data on NMOSD patients to characterise the natural history of the disease, understand patterns of care, and explore clinical outcomes including effectiveness, patient experience, biomarkers and safety events[1,2]

Proportion of patients by serology status at enrolment (N=95)[3]



CorEvitas launched the SPHERES registry in June 2021, with the goal of enrolling 800 patients through 35 academic institutions and private practices across North America[2]

Scan the QR code for further information about the SPHERES Registry and enrolment on CorEvitas.com

AQP4-IgG(+), aquaporin-4 immunoglobulin G (seropositive); MOG-IgG(+), myelin oligodendrocyte glycoprotein immunoglobulin G (seropositive); NMOSD, neuromyelitis optica spectrum disorder; SPHERES, Synergy of Prospective Health & Experimental Research for Emerging Solutions.

1. CorEvitas. SPHERES: Neuromyelitis Optica Spectrum Disorder (NMOSD) Registry. Available at: www.corevitas.com/registry/nmosd. Accessed September 2022; 2. Harrold LR, et al. ACTRIMS 2022. P287; 3. Exuzides A, et al. ECTRIMS 2022. P408.

METEOROID

A Phase 3, randomised, double-blind, placebo-controlled study of satralizumab in adults and adolescents with MOGAD

METEOROID

NCT05271409

1. Paul F, et al. ECTRIMS 2022. EP1040; 2. ClinicalTrials.gov. METEOROID. Available at: https://clinicaltrials.gov/ct2/show/NCT05271409. Accessed October 2022.

Investigating IL-6 inhibition for the unmet need for approved therapies in MOGAD

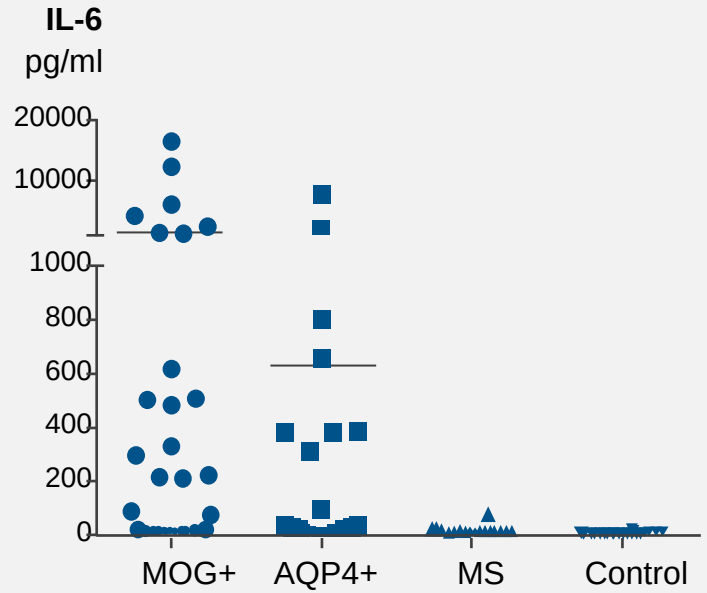
Pre-clinical evidence

- 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 phase[5]

Clinical evidence

- The IL-6 receptor inhibitor tocilizumab, used off-label, was shown to be effective in >20 patients with MOGAD[6–12]
- Satralizumab significantly reduced relapse risk in AQP4-IgG+ NMOSD, an antibody-driven disease that is clinically similar to MOGAD[13,14]

Figure 1. CSF IL-6 levels in patients with demyelinating diseases[2]



Adapted with permission from Kaneko et al. J Neurol Neurosurg Psychiatry 2018[2]

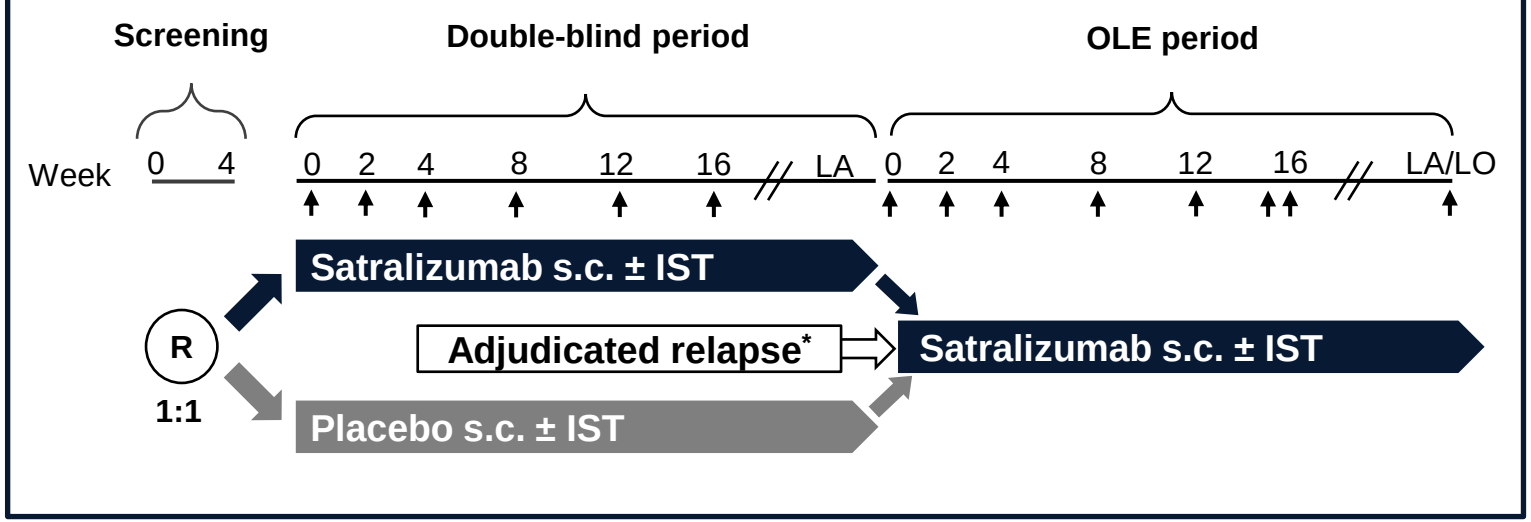
AQP4-IgG+, aquaporin-4 immunoglobulin G seropositive; CSF, cerebrospinal fluid; IL-6, interleukin 6; MOG, myelin oligodendrocyte glycoprotein; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder; PD, pharmacodynamics; PK, pharmacokinetics.

1. Kothur K, et al. *PLoS One* 2016;11:e0149411; 2. Kaneko K, et al. *J Neurol Neurosurg Psychiatry* 2018;89:927–936; 3. Serguera C, et al. *J Neuroinflammation* 2019;16:244; 4. Hofer 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 I, et al. *J Neuroophthalmol* 2019;39:3–7; 10. Rigal J, et al. *Mult Scler Relat Disord* 2020;46:102483; 11. Elsbernd PM, et al. *Mult Scler Relat Disord* 2021;48:102696; 12. Ringelstein M, et al. *Neurol Neuroimmunol Neuroinflamm* 2022;9:e1100; 13. Yamamura T et al. *N Engl J Med* 2019;381:2114–2124; 14. Traboulsee A, et al. *Lancet Neurol* 2020;19:402–12.

METEOROID: A phase 3, randomised, double-blind, placebo-controlled study of satralizumab in adults and adolescents with MOGAD

METEOROID

Study design



Inclusion criteria

This study will **enrol 152 patients aged ≥12 years with relapsing MOGAD**

- Confirmed MOGAD diagnosis **with ≥2 MOGAD attacks ≤24 months prior to screening,** accompanied by other clinical symptoms of MOGAD and exclusion of alternative diagnoses
- Individuals are eligible if they are either receiving or not receiving chronic IST for MOGAD

Administration of study drug. *Adjudicated relapse refers to a MOGAD relapse confirmed by an independent Clinical Endpoint Committee.
DB, double blind; IST, immunosuppressive therapy; LA, last administration; LO, last observation; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; OLE, open-label extension; R, randomisation; s.c., subcutaneous.

ClinicalTrials.gov. METEOROID. Available at: https://clinicaltrials.gov/ct2/show/NCT05271409. Accessed October 2022.

METEOROID: Study endpoints

Primary efficacy endpoint:

- Time to first MOGAD relapse in the DB period, as determined by an independent adjudication committee

Secondary efficacy endpoints:

- Annualised rates of adjudicated MOGAD relapses
- Active lesions on MRI of the neuroaxis,
- Inpatient hospitalisations
- Proportion of patients receiving rescue therapy

Scan the QR code for further information about **METEOROID** on ClinicalTrials.gov

DB, double blind; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, magnetic resonance imaging.

ClinicalTrials.gov. METEOROID. Available at: https://clinicaltrials.gov/ct2/show/NCT05271409. Accessed October 2022.


Roche

Therapeutic Decision Making

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Therapeutic Decision Making

Case Vignette 1

Course: 30 y/o female; *bona fide* relapse after 2 yr relapse free on RTX
Anti-AQP4+; CD19+ B cell count = 0 (undetectable)
Rescue therapy included IVMP and PLEX (X5) followed by IVIG

Issues: A) relapse on maintenance therapy
B) significant immune suppression

Views:

1) Should there be a change in maintenance therapy regimen due to relapse ?

2) Is there a clear first choice for selection of maintenance therapy in this case ?

3) Does rescue therapy influence selection or timing of maintenance therapy ?

4) Case by case or more systematic themes for therapeutic decision making ?

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Therapeutic Decision Making

Case Vignette 2

Course: 42 y/o male; relapse free last 5yr on RTX maintenance therapy
Anti-MOG+; serum IgG = 500 mg/dL
Has recurring RTIs (3-4 per year); some require hospitalization

Issues:
A) efficacy vs. AE and SAE profiles
B) minimizing risks of recurrent ID

Views:

1) Should there be a change in maintenance therapy regimen due to infection ?

2) Is there a clear first choice for selection of maintenance therapy in this case ?

3) Beyond appropriate vaccines, should antibiotic prophylaxis be considered ?

4) Case by case or more systematic themes for therapeutic decision making ?

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Therapeutic Decision Making

Case Vignette 3

Course: 12 y/o female; severe first TM following 3 wks N/V
No known co-morbidities
Anti-AQP4+; rescue IVMP and PLEX (5X); MRI = BS+

Issues: A) no therapy approved as yet for pediatric AQP4+
B) special considerations regarding disease localization

Views:

1) What are the chief factors influencing selection of a maintenance therapy ?

2) Is there a clear first choice for selection of maintenance therapy in this case ?

3) Are there special safety considerations or laboratory monitoring practices ?

4) Case by case or more systematic themes for therapeutic decision making ?

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Therapeutic Decision Making

Case Vignette 4

Course: 25 y/o female; stable on regulatory-approved therapy
Anti-AQP4+ titers invariably high
Planning to have children; considering egg storage

Issues: A) limited safety data (fetus, pregnancy, post-partum)
B) considerations in long-term use of AZA or MMF

Views:

1) Should current regimen be modified for conception, gestation, parturition ?

2) What safety and/or fertility practices to preserve options in family planning ?

3) What is contingency plan in event of relapse during or following pregnancy ?

4) Case by case or more systematic themes for therapeutic decision making ?

IPNMD 2025: Updating Diagnostic Criteria

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2024

IPNMD: THE FUTURE 2025

NMOSD, MOGAD, AND BEYOND 2026

DEAN WINGERCHUK

BRIAN WEINSHENKER

MICHAEL YEAMAN

WITH THE GJCF INTERNATIONAL CLINICAL CONSORTIUM

OBJECTIVE

- To discuss:
  - the need for update and reappraisal of the IPND 2015 NMOSD diagnostic criteria
  - reappraisal process

RATIONALE FOR REAPPRAISAL

1. Advances in the field

- Experience with 2015 criteria
- Validation studies
- Advances in serology
- Advances in neuroimaging

2. MOGAD

- Validation of MOGAD as a distinct disorder
- Pending MOGAD definition
- Confusion re: MOGAD position under NMOSD umbrella

RATIONALE FOR REAPPRAISAL

3. Reassessment of nomenclature

- NMO or NMOSD (or neither?)
- Antibody-anchored diagnosis
- Terminology (e.g., ”astrocytopathy”)
- “Seronegative” patients

4. Reassessment of clinical definitions

- AQP4+
- Current AQP4-/MOG- [”Double-seronegative”]
- “Seronegative” – e.g., non-MS, pan-seronegative
- Reassess isolated relapsing seronegative non-MS syndromes (rON, rLETM)

PROPOSED REAPPRAISAL PROCESS

- Consensus-based process
- Steering committee
  - Define scope of reappraisal and detailed process
  - Representation
    - diversity, areas of expertise (clinical/MRI/serology/peds/etc)
    - equity & inclusivity (demography; international; career stage)
- Contributors
  - Derived from ICC
  - Additional feedback/expertise on select topics
- ICC
  - Endorsement of final product
- Support
  - Guthy Jackson Charitable Foundation
  - Potential neutral support from industry

TIMELINE

- **2022**
  - **Q4** Establish steering committee, process, and responsibilities
    Develop scope and methods of reappraisal
- **2023**
  - **Q2** Advance preliminary reappraisal
    *In-person meeting/update at AAN (April; Boston)
  - **Q3** Distribute to Contributors for select feedback
    Complete revised reappraisal
  - **Q4** *In-person meeting/update at ECTRIMS (October; Milan)
    Finalize reappraisal
    ICC endorsement
- **2024**
  - **Q1** Submit manuscript
  - **Q2-3** Revision/acceptance

- **2025** Publication

WE INVITE YOU TO:

- PROVIDE FEEDBACK
- DECLARE INTEREST
- ACTIVELY PARTICIPATE
- REVIEW PRODUCT

Addressing Unmet Needs

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Global Access to Serology & Therapeutics

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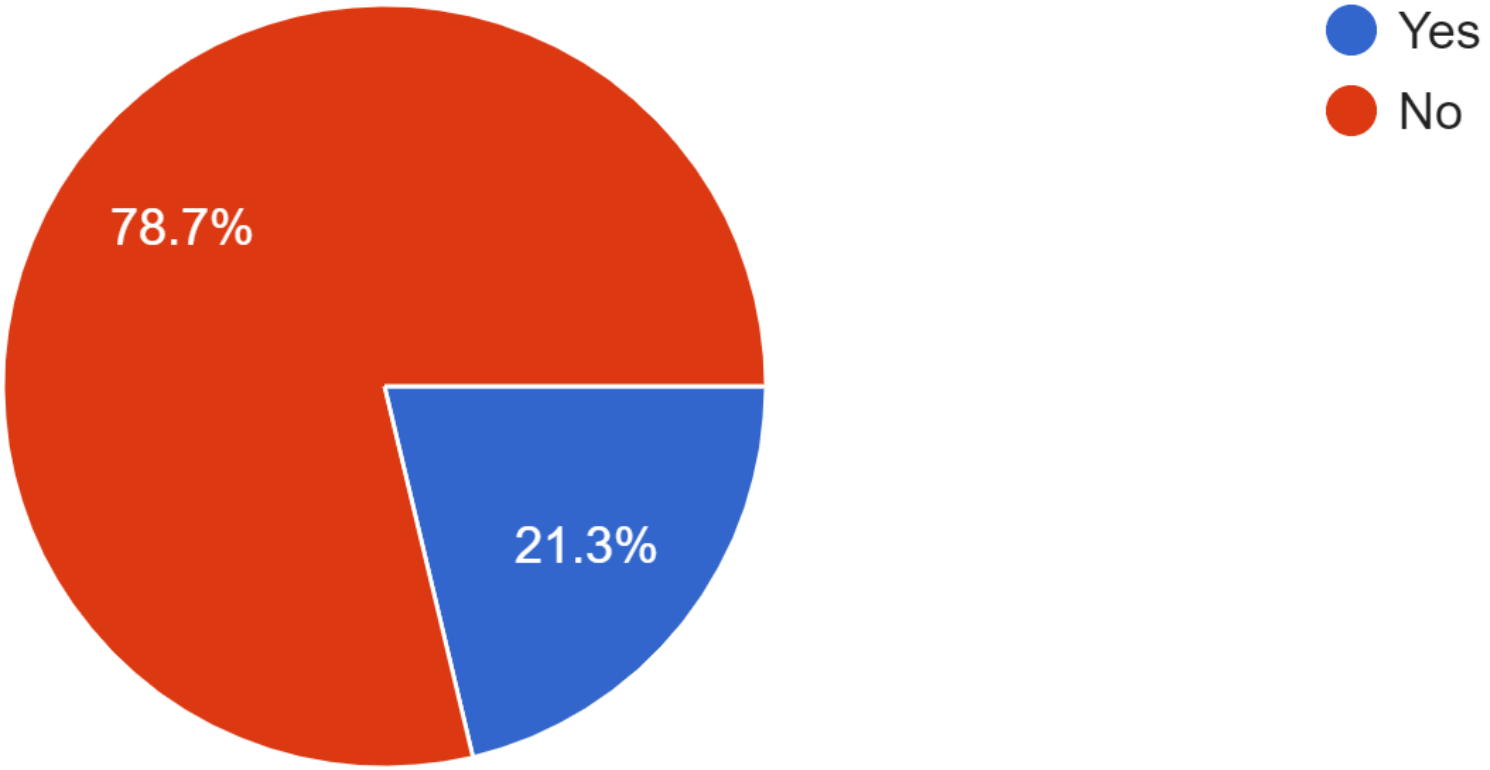
Do you have access to rapid (within 72 hrs) ELISA serotesting for anti-AQP4 ?



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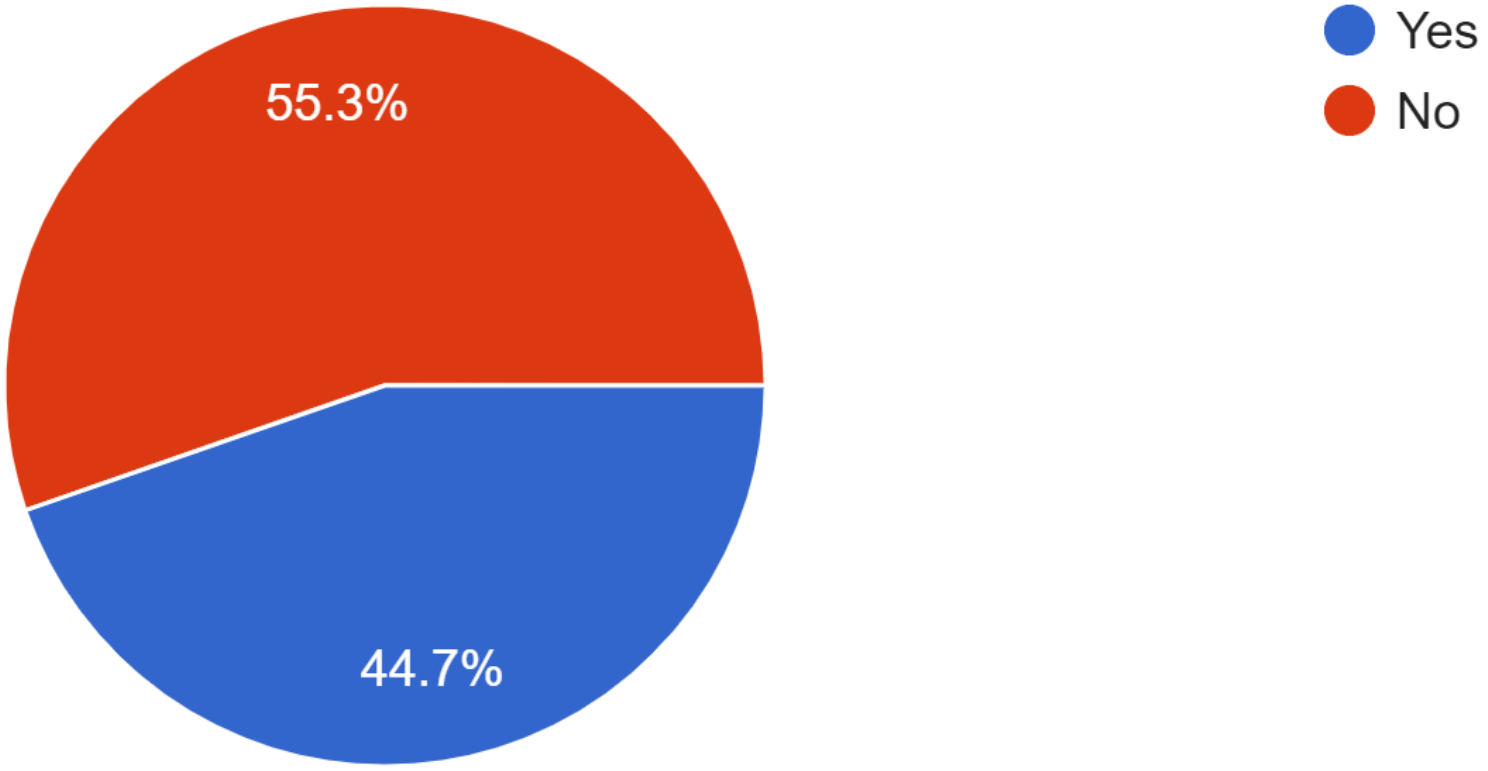
Do you have access to rapid (within 72 hrs) cell-based serotesting for anti-AQP4 ?



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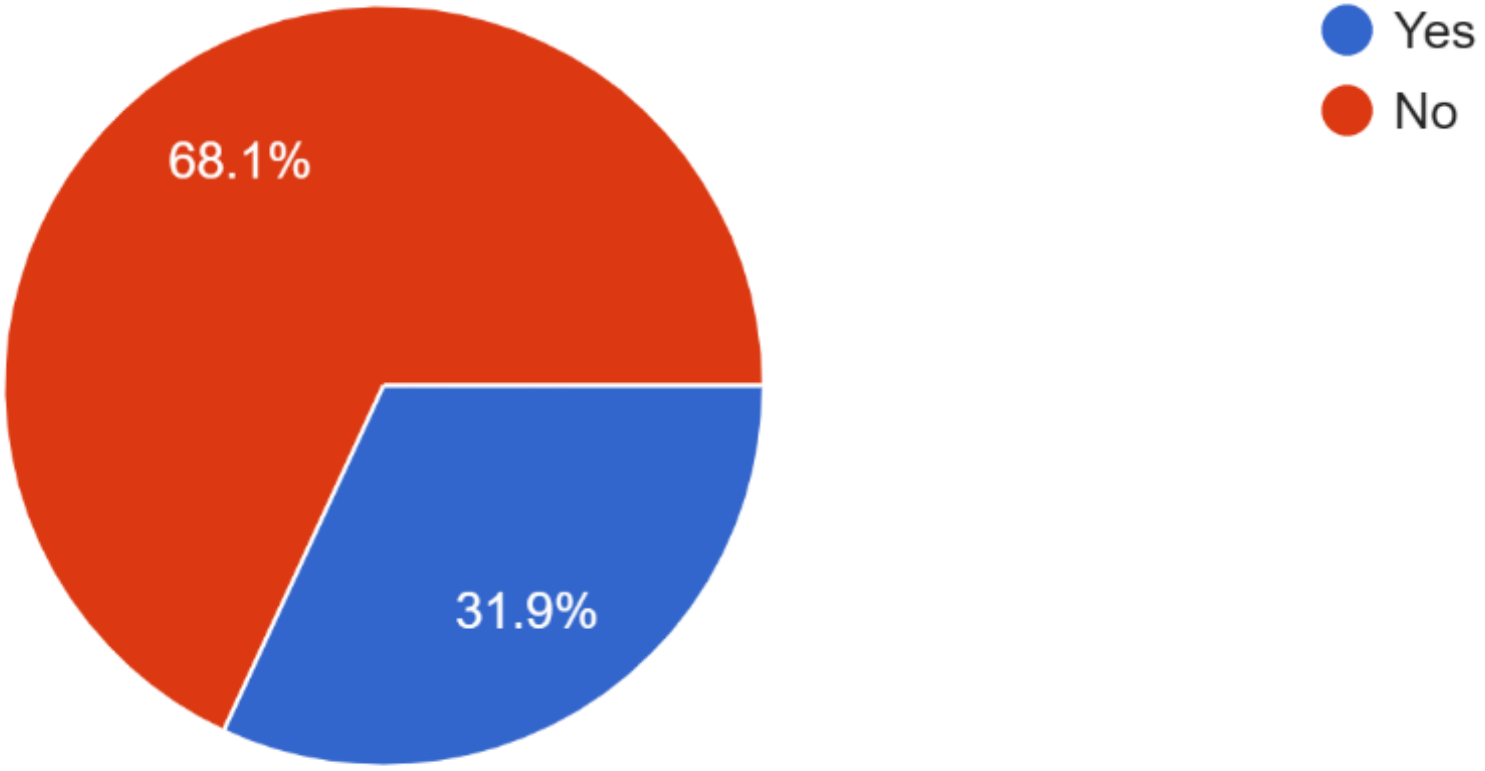
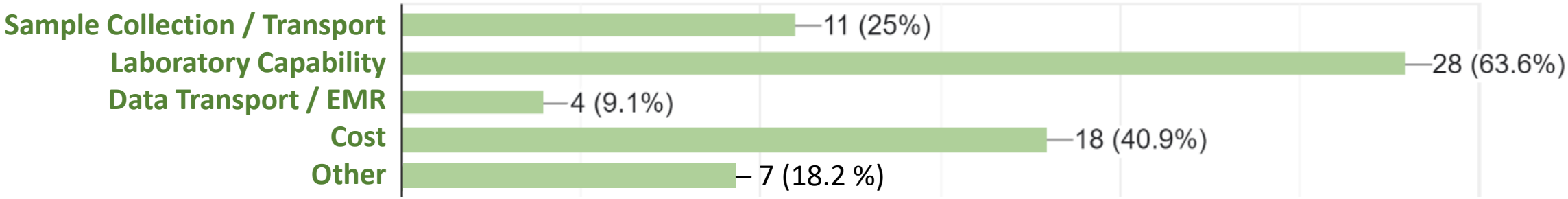
Do you have access to rapid (within 72 hrs) cell-based serotesting for anti-MOG ?



What are the main barriers to serodiagnostic imperatives in NMOSD & MOGAD ?



Comments:

- Access to CBA but rarely within 72 hours
- 5-7 days to get results
- Laboratory takes 3 to 4 weeks for results
- We send to Mayo; typically 2 weeks for results
- Insurance coverage
- Perceptions of CBA vs. commercial assays / kits
- Pooled batch analysis influences result time

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Session III / Panel 1

Global Access to Serology & Therapeutics

Discussion Points:

1) What is an acceptable time-to-results for anti-AQP4 and anti-MOG serotesting ?

2) Would next-gen platforms that do not require CBA capabilities improve access ?

3) Would a remote testing method and centralized laboratory network be realistic ?

4) What other opportunities exist to improve serodiagnostic speed and accuracy ?

Relapse-Independent Disease Activity & Symptoms

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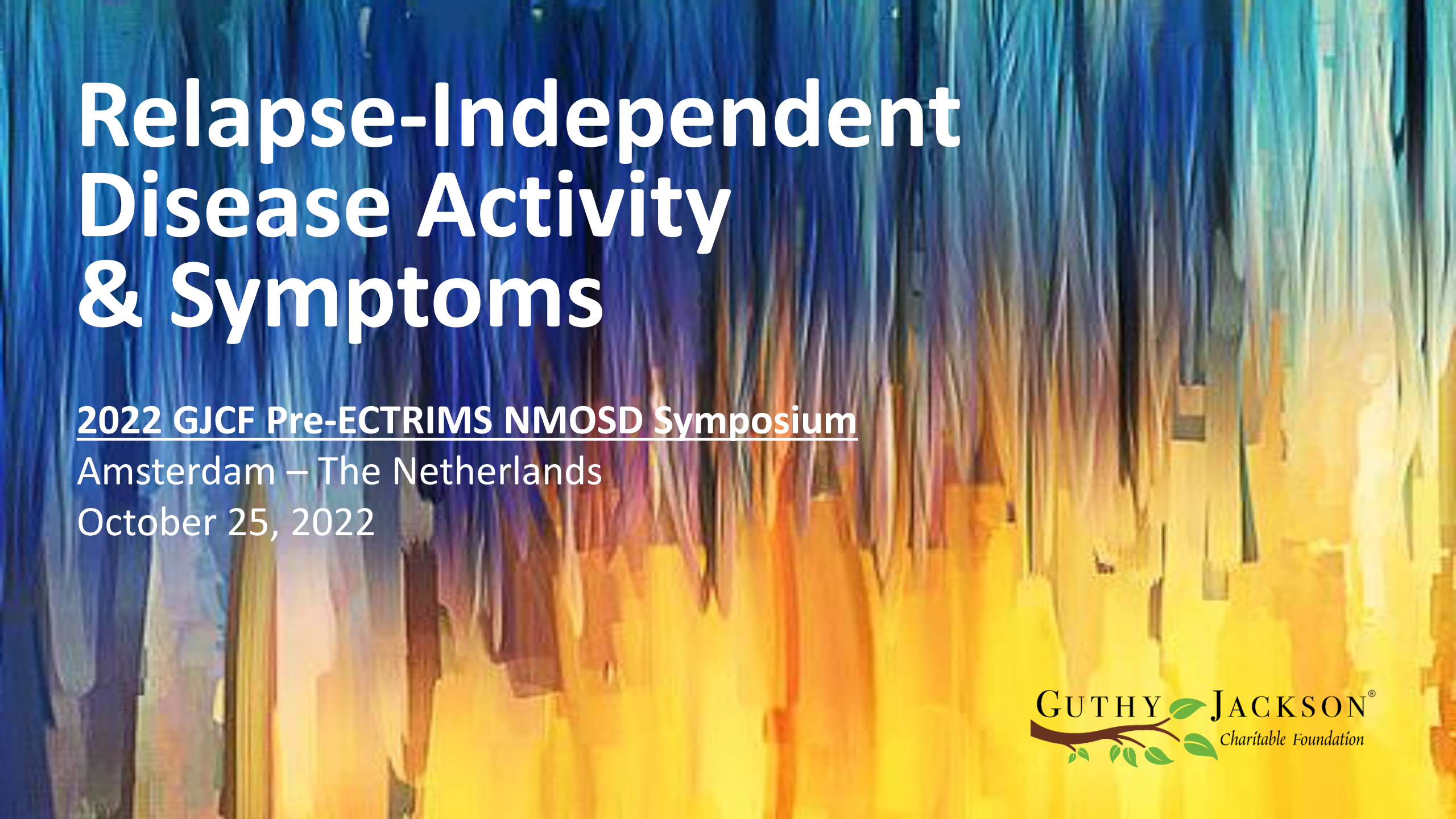

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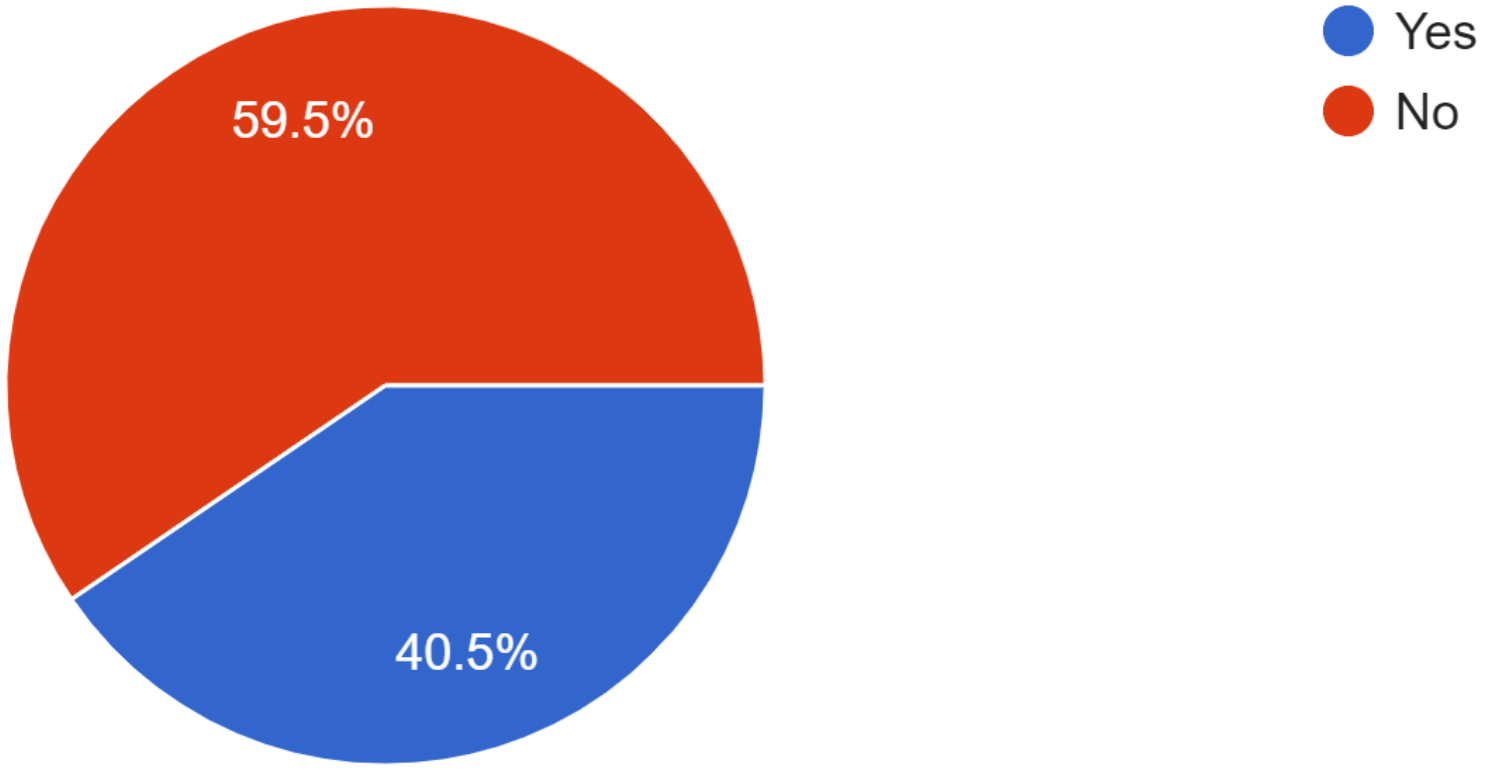
Does relapse-independent disease activity / progression occur in anti-AQP4+ NMOSD ?



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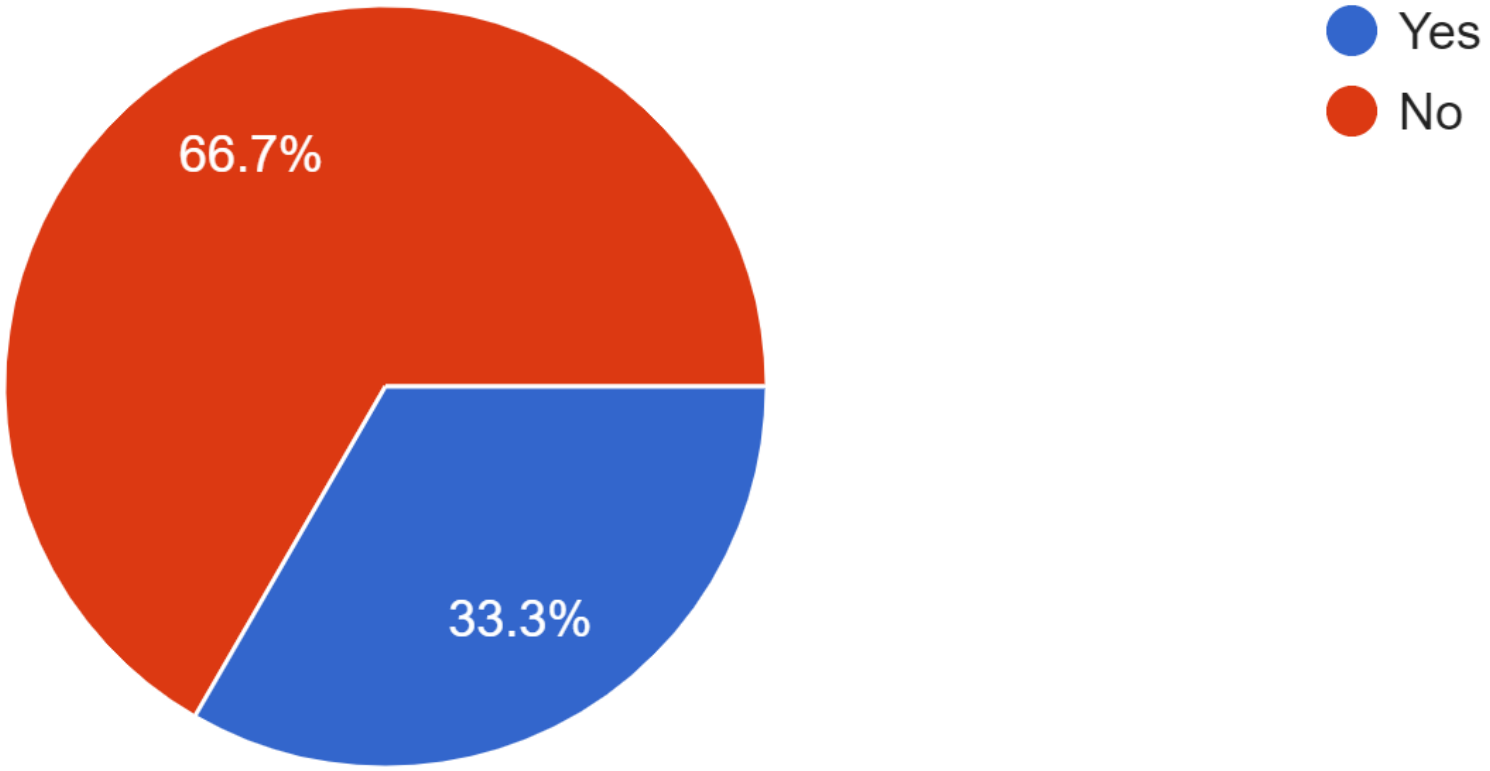
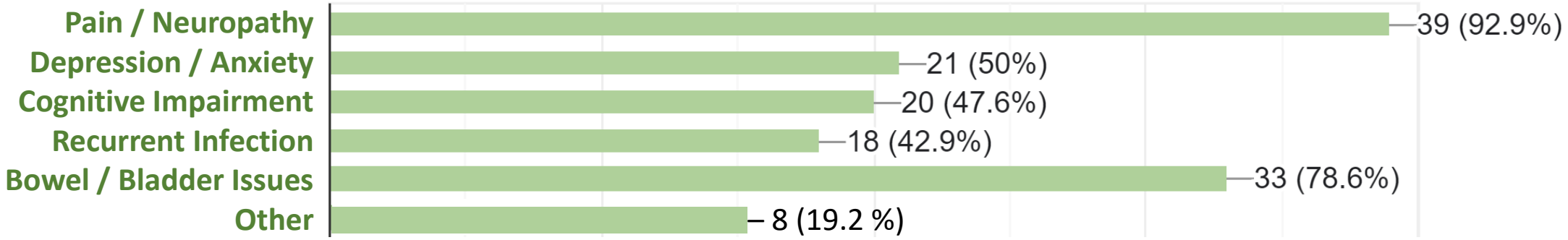
Does relapse-independent disease activity / progression occur in anti-MOG+ MOGAD ?



What chronic symptoms warrant greater detection / management in NMOSD or MOGAD ?



Comments:

- Visual impairment / reduced acuity
- Mobility and fine motor skills (real world)
- Spasticity / tonic spasms
- Sleep disorders
- Sexual dysfunction
- Fatigue

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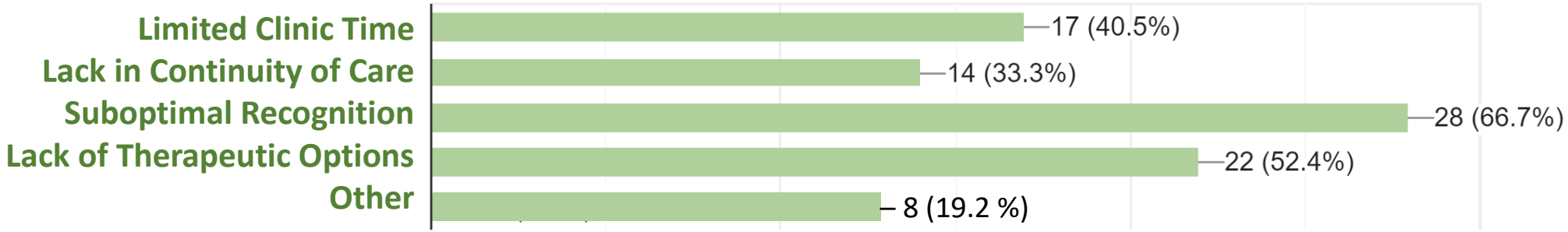
What are the main barriers to better detect and manage these chronic symptoms ?



Comments:

- Lack of proper disability scales
- Poor recognition / under-diagnosis
- Access to good rehabilitation services
- Lack of effective multidisciplinary teams

Session III / Panel 2

Relapse-Independent Disease Activity

Discussion Points:

1) Are there more feasible methods to better recognize / assess subclinical disease ?

2) Could active or passive remote monitoring help to detect worsening conditions ?

3) Which multidisciplinary team strategies exist that may serve as effective models ?

4) What other opportunities exist to improve non-relapse symptoms management ?

Healthcare Provider Awareness & Education

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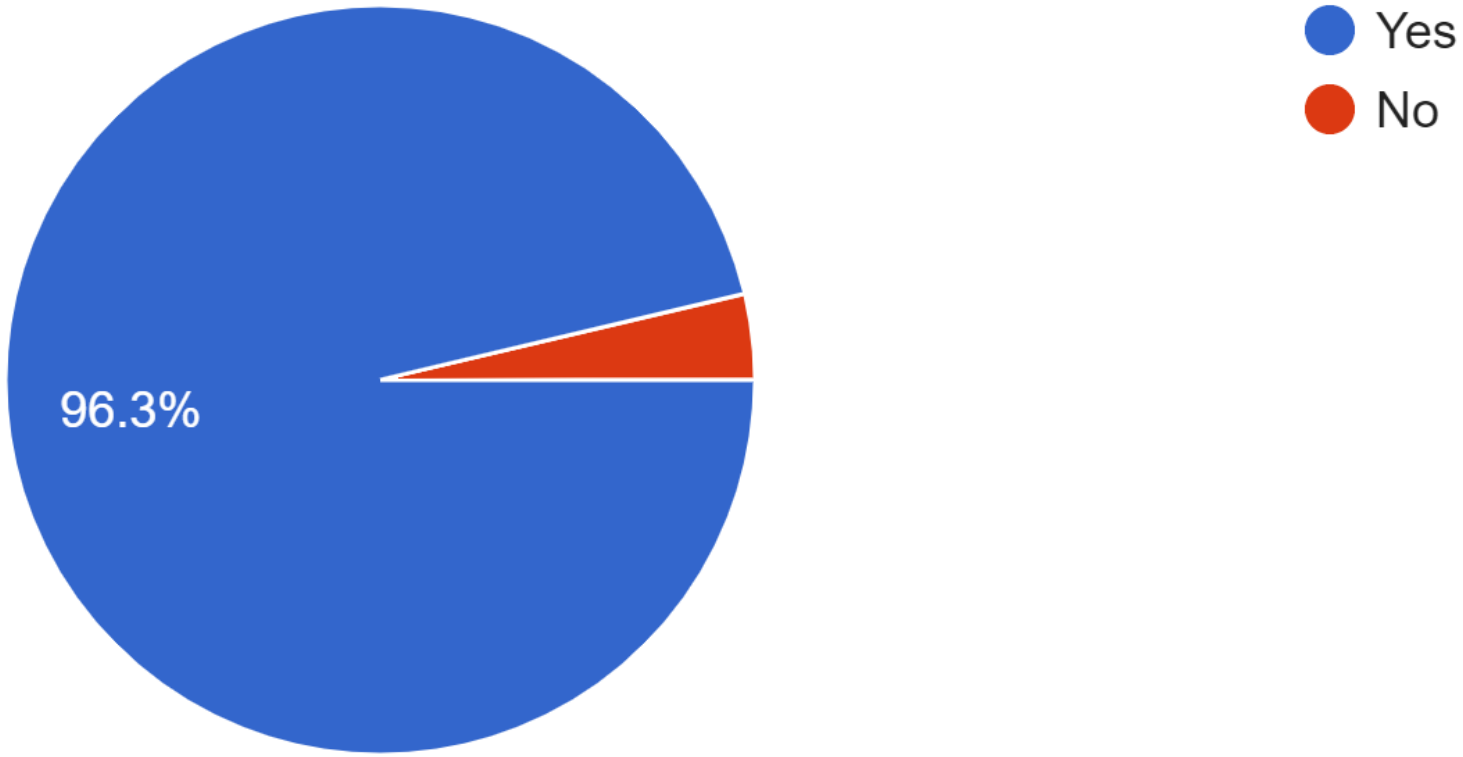
Do you consider yourself facile with current NMOSD & MOGAD diagnostic criteria ?



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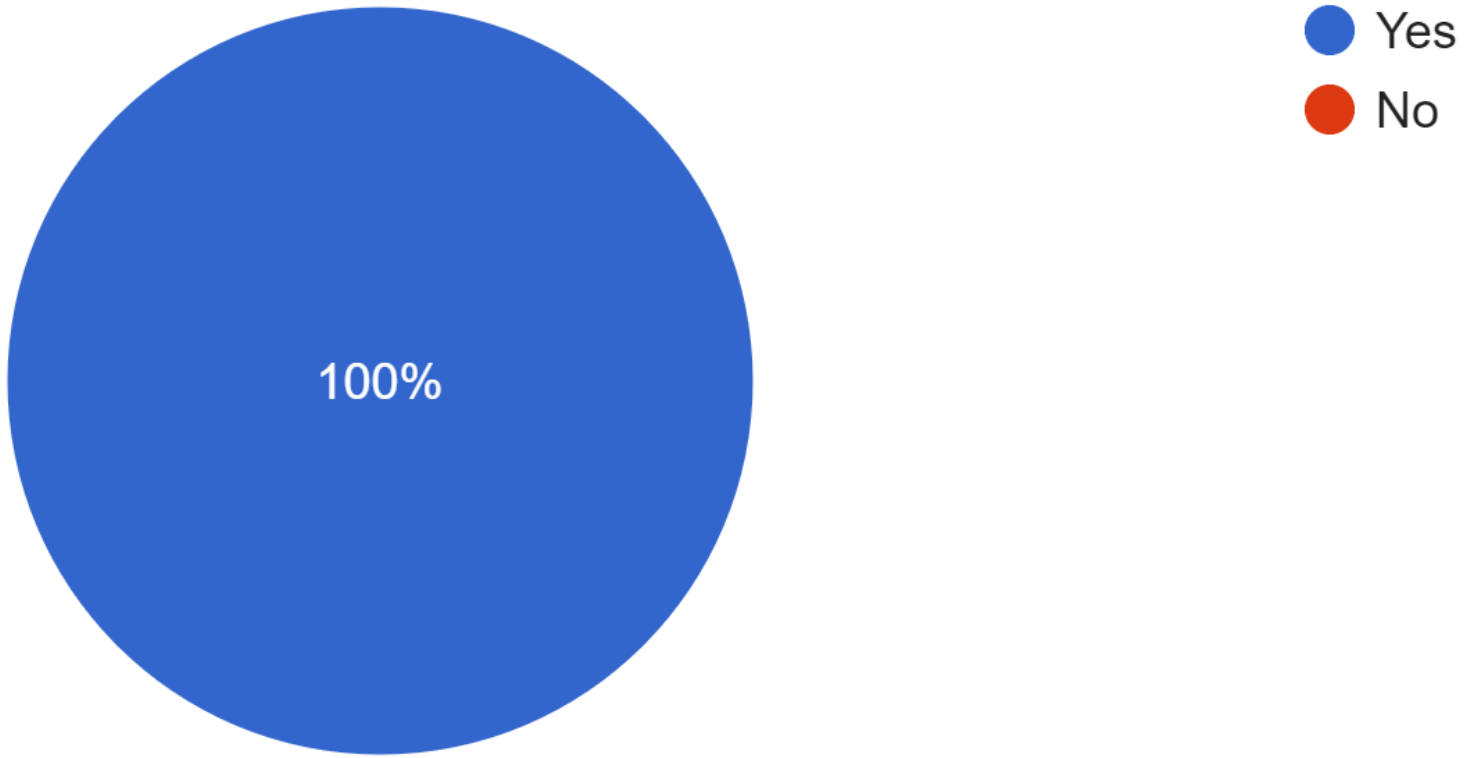
Do you fully understand the mechanisms and use of approved therapeutics ?



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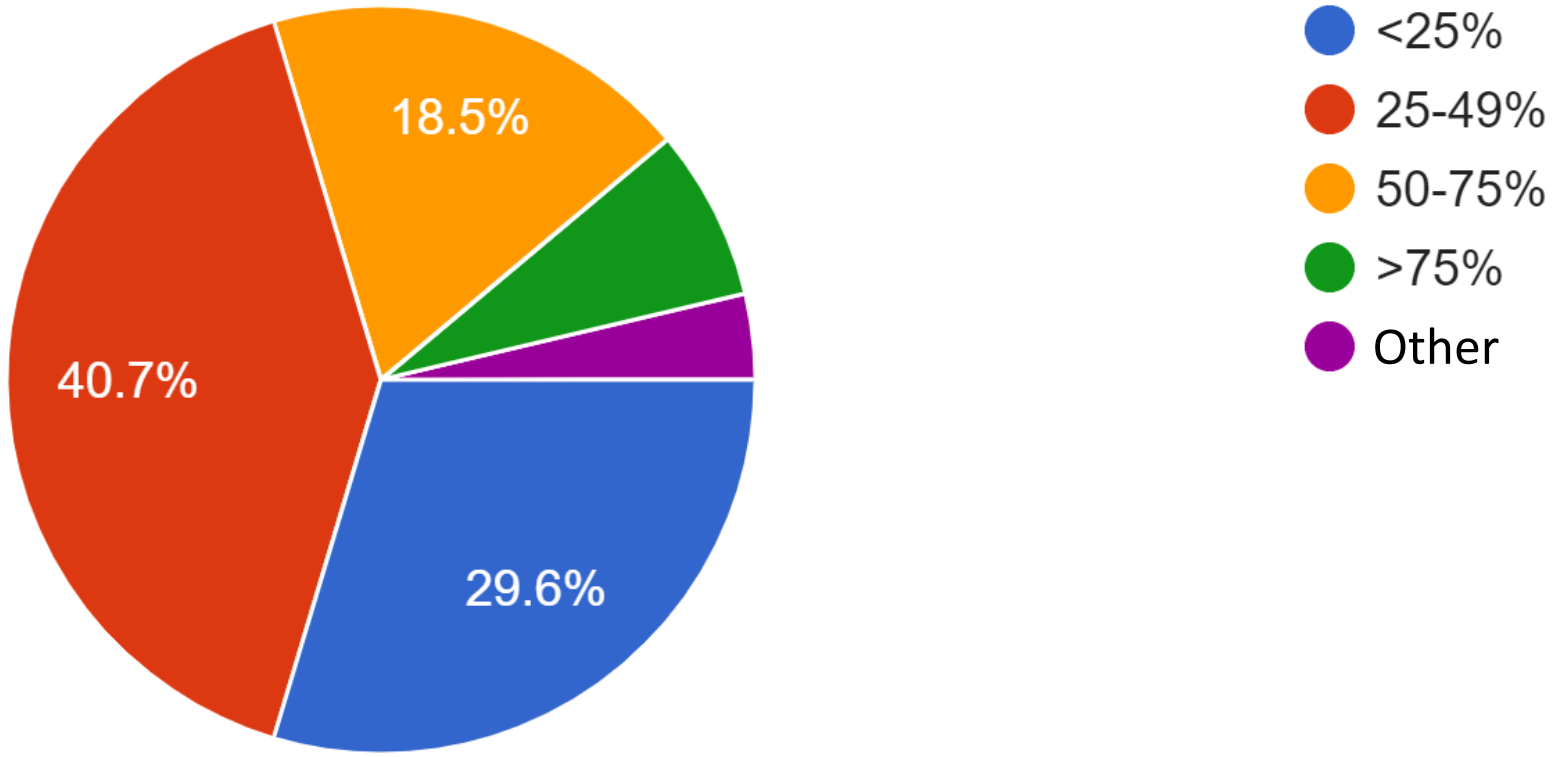
What percentage of neurologists could accurately diagnose NMOSD & MOGAD ?



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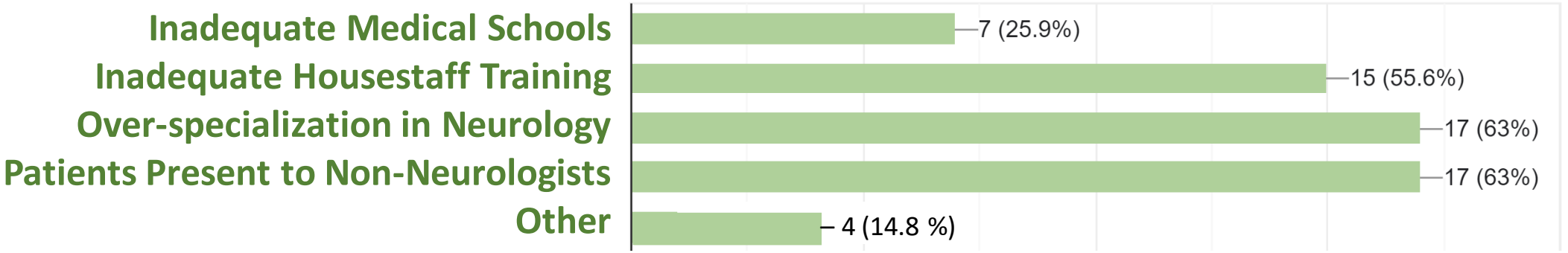
What are the main barriers to more accurate diagnosis of NMOSD & MOGAD ?



Comments:

- Disease rareness imposes lack of recognition
- Lack of specialized programmatic education
- Inadequate training of general neurologists
- Limited access to high-quality information

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Session III / Panel 3

Healthcare Provider Awareness & Education

Discussion Points:

1) What realistic strategies would improve neurology specialty training programs ?

2) What realistic strategies would improve awareness among general neurologists ?

3) Is there an opportunity to build a network for rural NMOSD / MOGAD diagnosis ?

4) What other opportunities may exist to improve healthcare provider education ?

Recognizing & Overcoming Disparities

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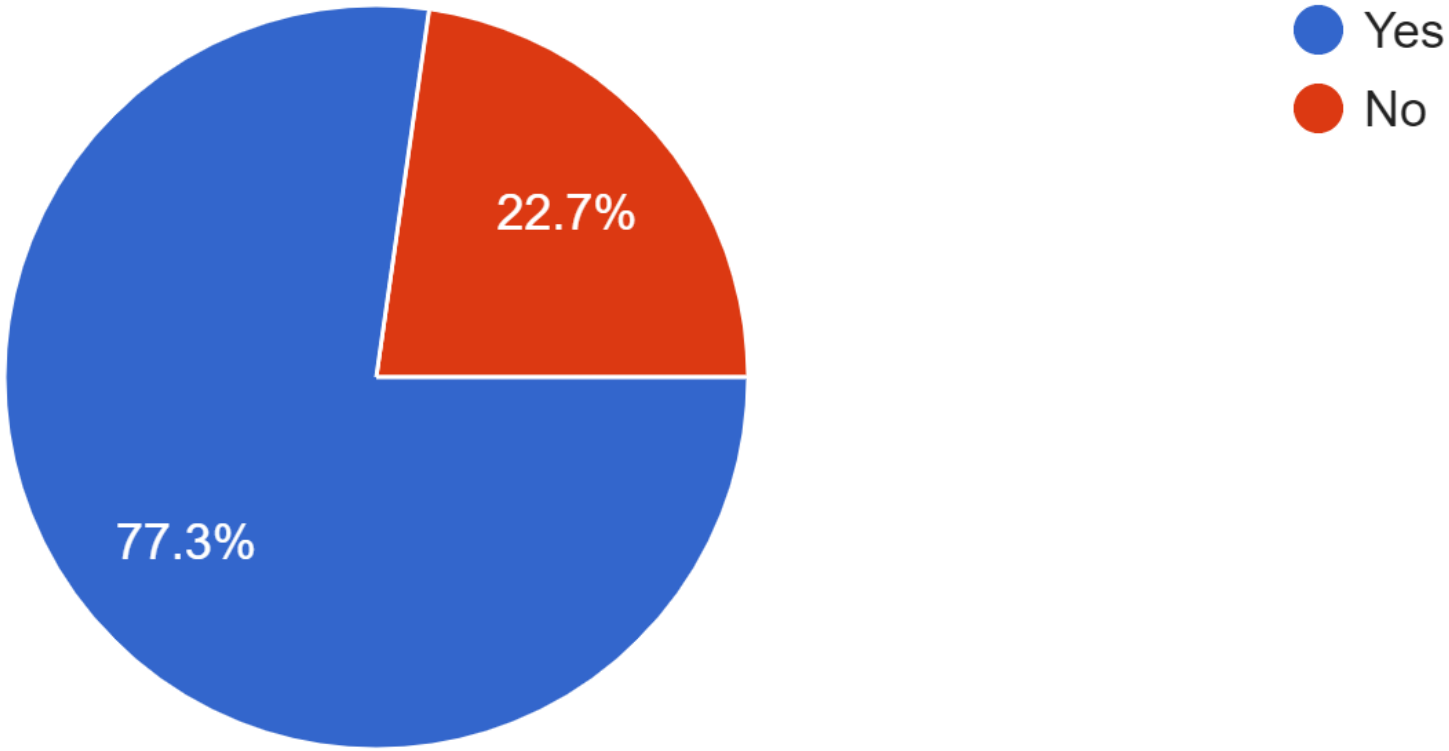
Are there significant healthcare disparities that affect outcomes in NMOSD & MOGAD ?



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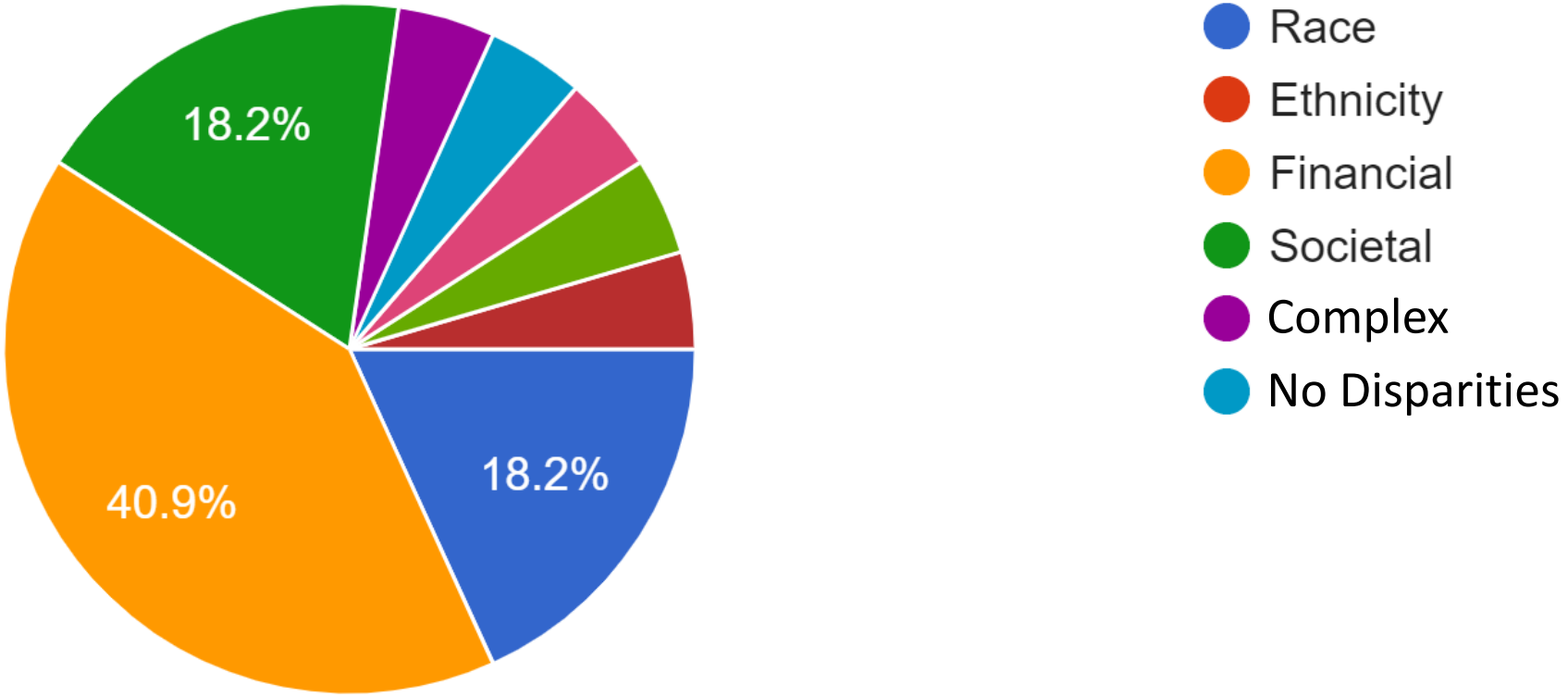
What is the most significant determinant of NMOSD & MOGAD healthcare disparity ?



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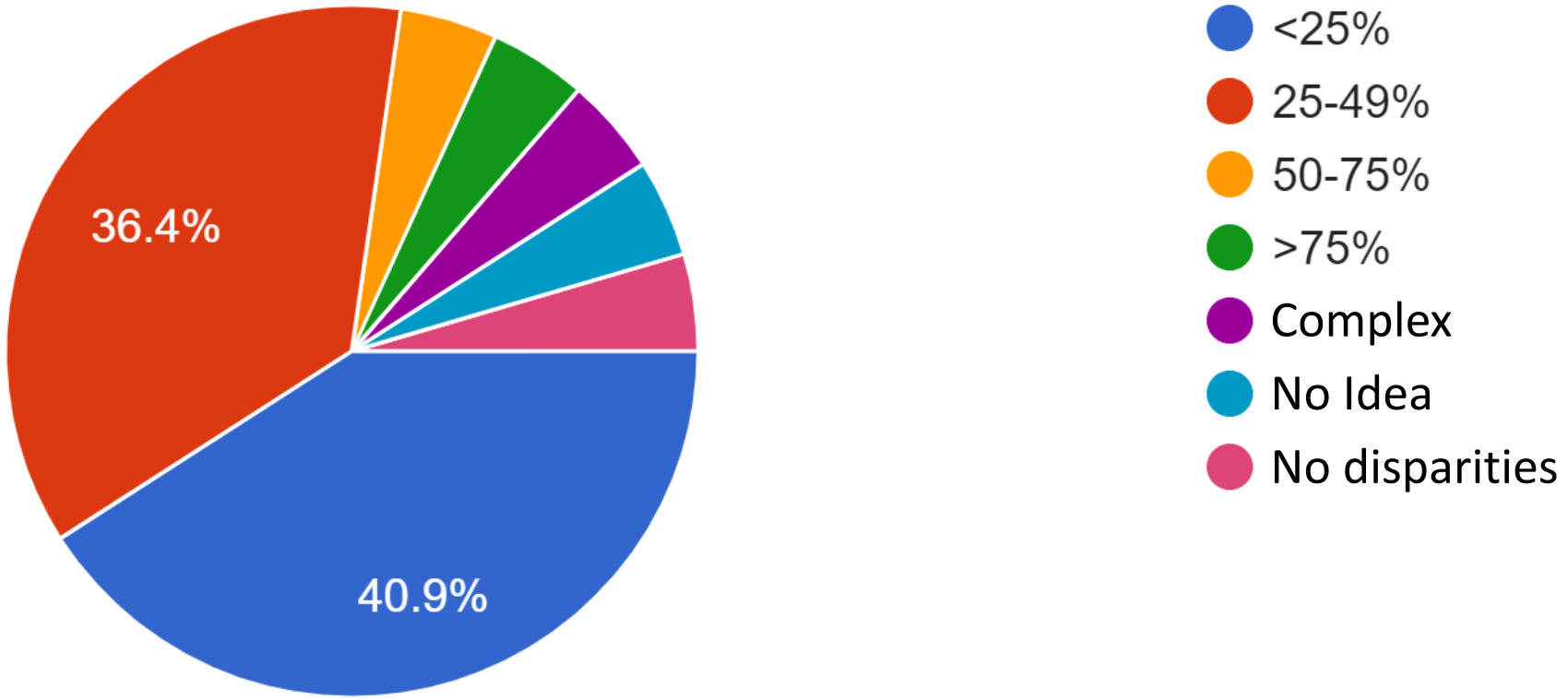
What percentage of patient outcomes are determined by healthcare disparities ?



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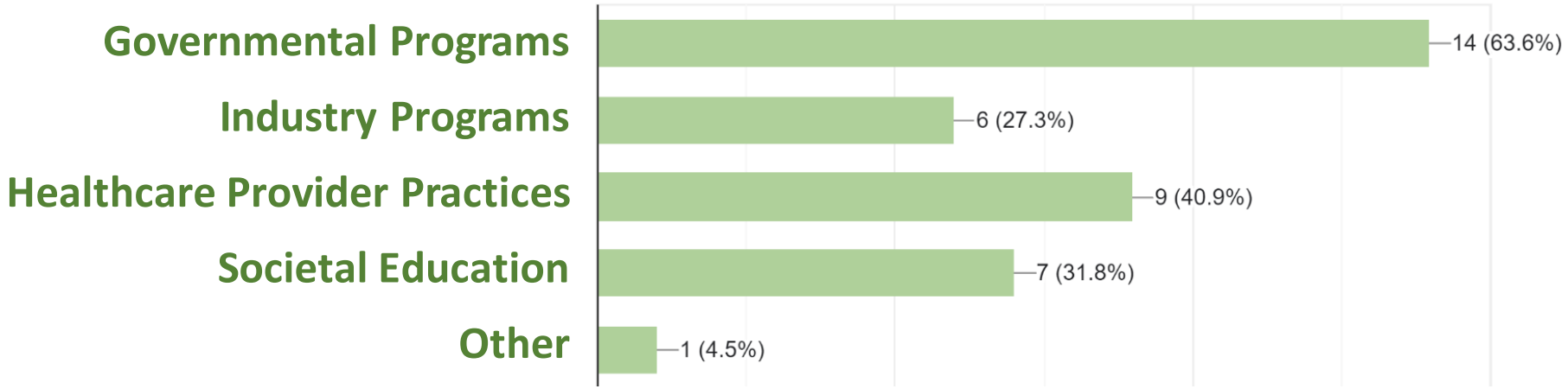
What is the most actionable solution to overcoming these healthcare disparities ?



Comments:

- None

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Session III / Panel 4

Recognizing & Overcoming Disparities in Healthcare

Discussion Points:

1) What are specific and realistic strategies to improve recognition of disparities ?

2) Are there models that illustrate successful promotion of healthcare equitability ?

3) How can patients participate in better recognition and reduction of disparities ?

4) What other opportunities may exist to help reduce disparities in healthcare ?

With Thanks…

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