

PLEX & IVIG in Acute Relapse Settings

No treatments have been licensed for acute treatment in NMOSD nor MOGAD

Jacqueline Palace

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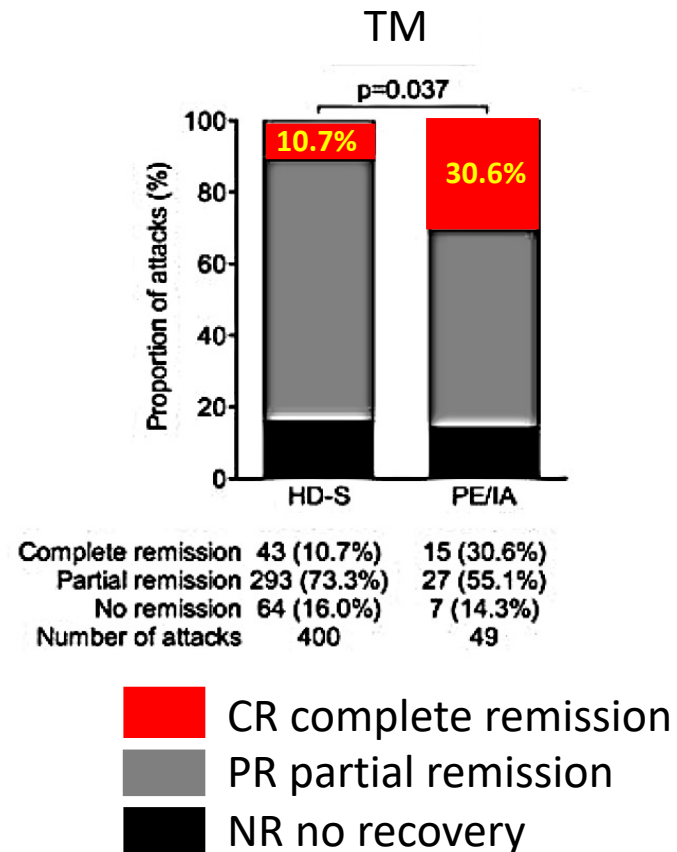
NMOSD PLEX

NMOSD PLEX

Kleiter et al, Ann Neurol 2016;79:2016

No difference in high dose MPred vs PLEX/IA 1st line except

TM: ↑ complete remission w PLEX/IA



871 attacks in 185 patients

84% AQP4-Ab +ve

analysed: all, TM, ON, ON+TM attacks,

TABLE 3. Factors Associated with Complete Remission from NMO Attacks

Factor	Multivariate Analysis	
	<i>p</i>	Odds Ratio (95% CI)
Female gender vs male	0.125	0.509 (0.21–1.21)
Age at attack per 1 year	0.011	0.973 (0.95–0.99)
Time from onset of disease to attack per 1 year	0.796	0.993 (0.94–1.05)
AQP4 positive vs negative	0.536	1.417 (0.47–4.27)
NMO vs NMOSD	0.756	1.148 (0.48–2.74)
MY present vs absent	0.002	0.382 (0.21–0.70)
MY+ON present vs absent	0.633	1.315 (0.43–4.06)
Time since previous attack per 1 month	0.289	1.008 (0.99–1.02)
CR of previous attack vs NR+PR	<0.001	6.847 (3.65–12.84)
Time from onset of attack to start of therapy per 1 day	0.083	0.952 (0.90–1.01)
PE/IA as 1st course vs HD-S	0.006	4.383 (1.54–12.50)
Other therapy as 1st course vs HD-S	0.205	3.176 (0.53–18.99)
Center number	0.396	0.983 (0.94–1.02)

NMOSD aphoresis

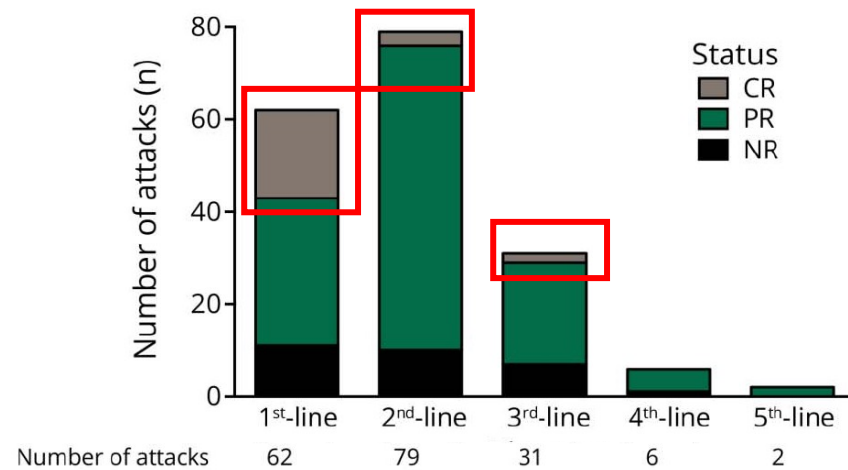
Kleiter et al, *Neurol Neuroimmunol Neuroinflamm* 2018;5:e504.

230 attacks in 105 patients, w descriptive data 192 PLEX, 38 IA

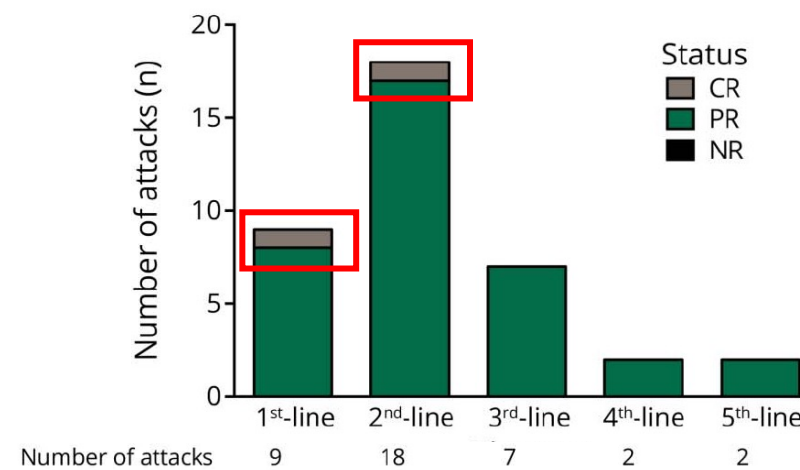
Analysis 139 attacks in 79 patients

87% AQP4-Ab +ve

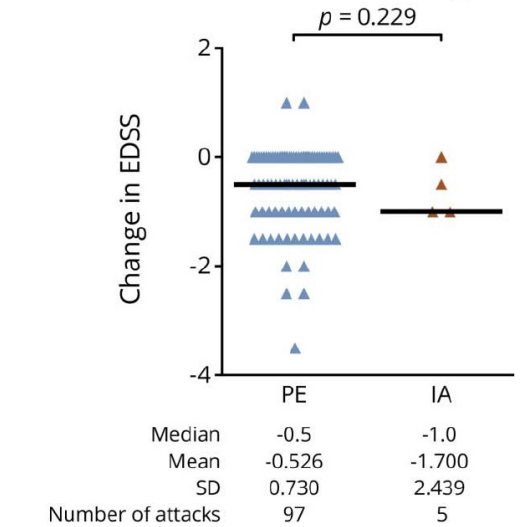
A. Remission status PE



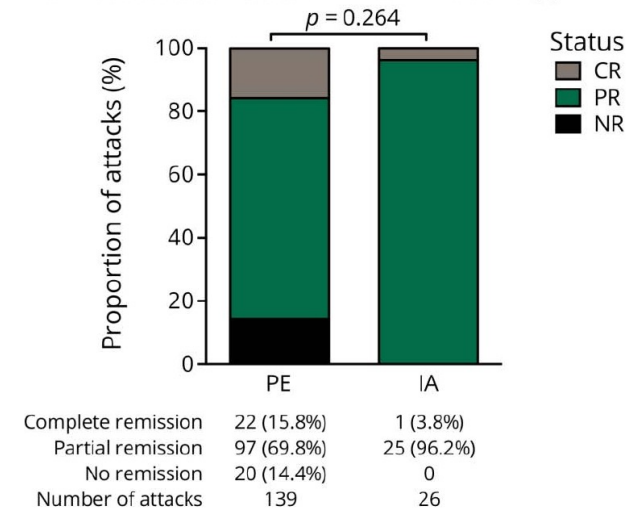
B. Remission status IA



D. EDSS after 1st- or 2nd-line therapy



Remission status after 1st- or 2nd-line therapy



NMOSD aphoresis

Kleiter et al, *Neurol Neuroimmunol Neuroinflamm* 2018;5:e504.

230 attacks in 105 patients, w descriptive data 192 PLEX, 38 IA
Analysis 139 attacks in 79 patients

87% AQP4-Ab +ve

E. Remission status according to delay of PE or IA

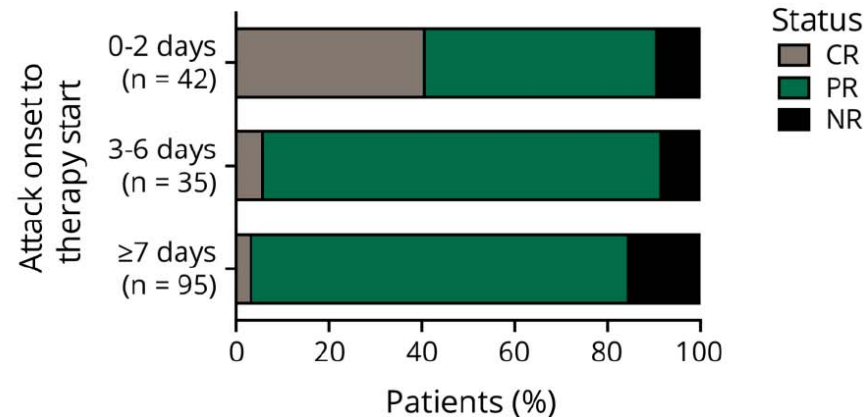


Table 3 Factors associated with complete remission from NMOSD attacks after apheresis therapy

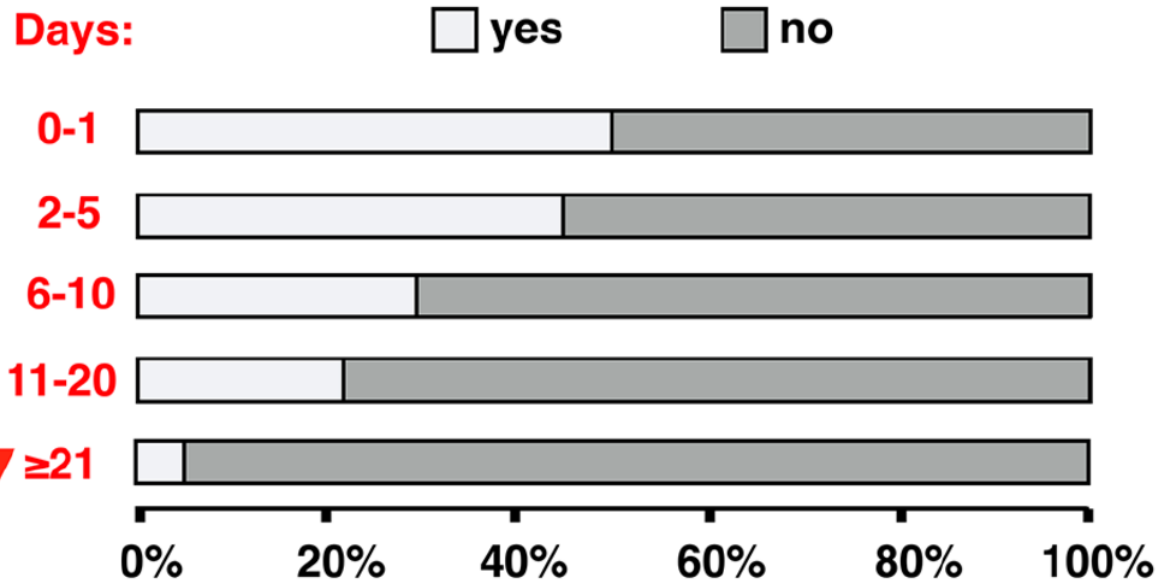
	Multivariate analysis	
	p Value	OR (95% CI)
Female sex (vs. male)	0.456	3.447 (0.13–89.40)
Age at attack (per 1 y)	0.081	0.925 (0.85–1.01)
Time from onset of disease to attack (per 1 y)	0.247	0.926 (0.81–1.06)
AQP4-ab positive (vs negative)	0.019	33.338 (1.76–631.17)
NMO (vs NMOSD)	0.316	2.951 (0.36–24.41)
MY present (vs absent)	0.726	1.350 (0.25–7.2)
Isolated ON or MY (vs simultaneous ON + MY)	0.046	4.709 (1.03–21.62)
Prophylactic immunotherapy present (vs absent)	0.532	1.683 (0.33–8.63)
Time from onset of attack to start of therapy (per 1 d)	0.014	0.937 (0.89–0.99)
First-line apheresis therapy (vs second-line)	0.047	12.271 (1.04–144.91)
PE (vs IA)	0.107	4.946 (0.71–34.59)

0.63 7 days
0.16 30 days

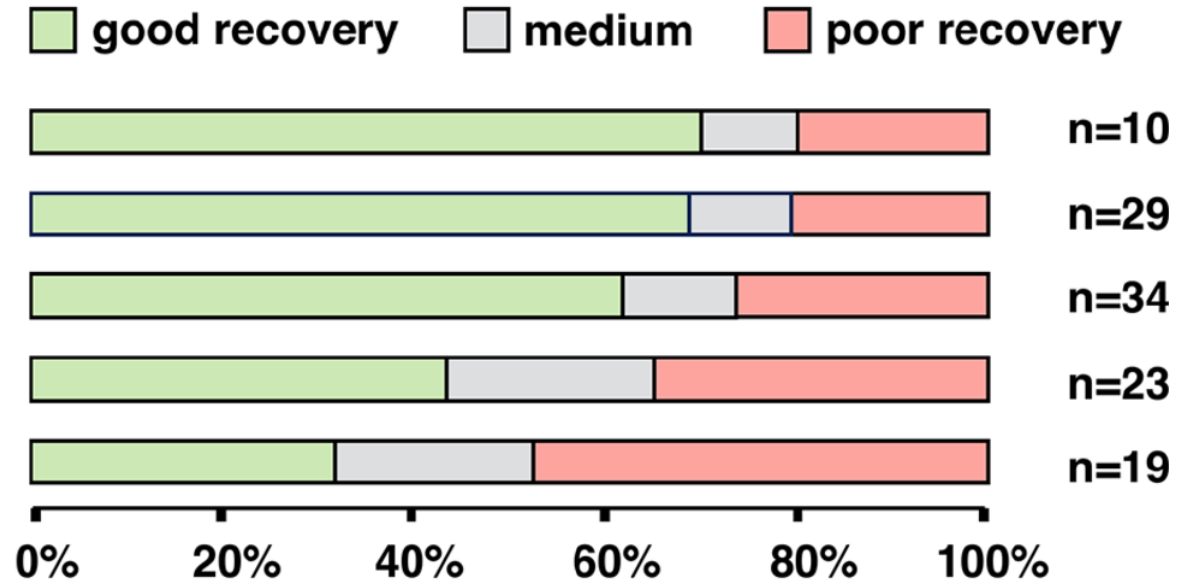
NMOSD time to PLEX

N=60 treated with PLEX,
66% AQP4+ve,

Late score equal to pre-treatment:



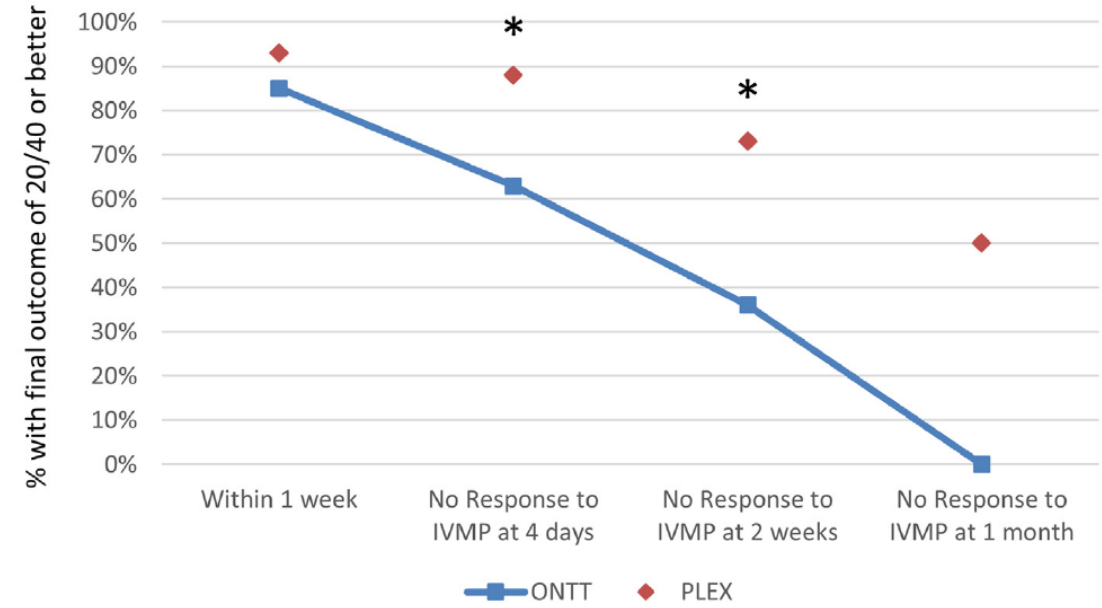
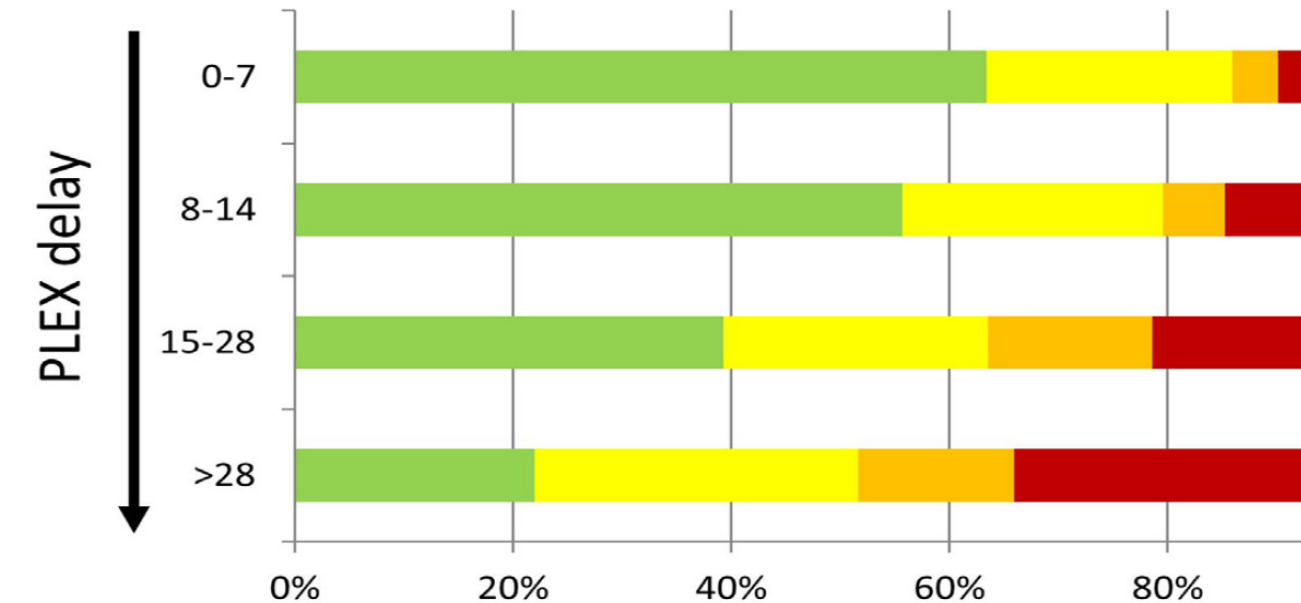
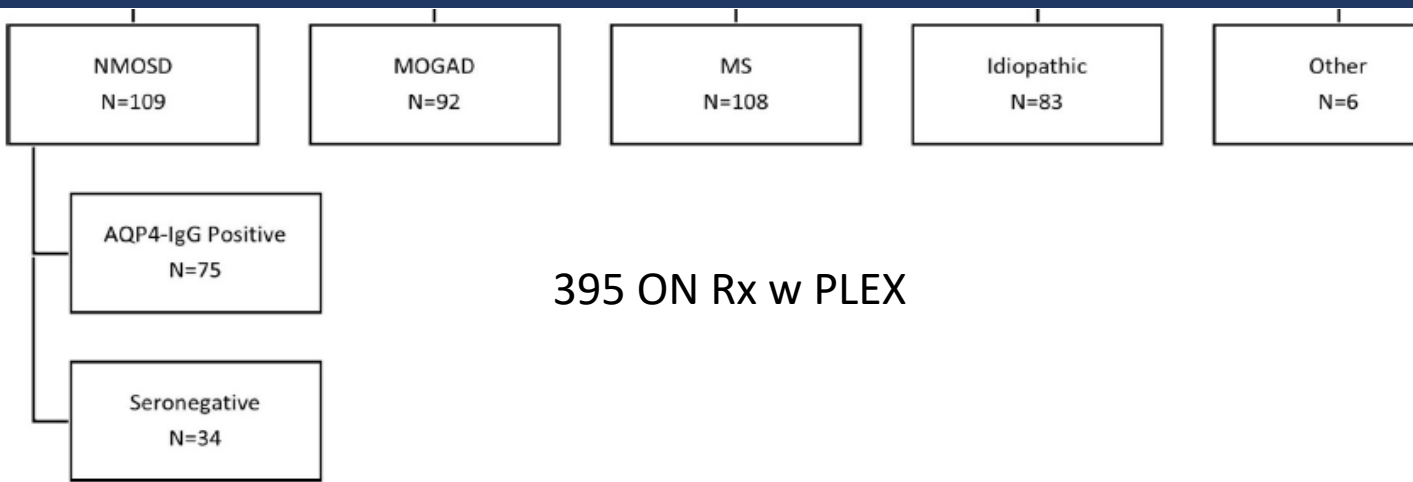
Strates of improvement:



OR 5.3 CI given within 5 days vs ≥ 11 days

ALL PLEX

ON and PLEX



Vision 20/200 or worse

There is currently no treatment approved for the management of MOGAD.

NMOSD IVIG

NMOSD: IVMP vs IVMP then IVIG

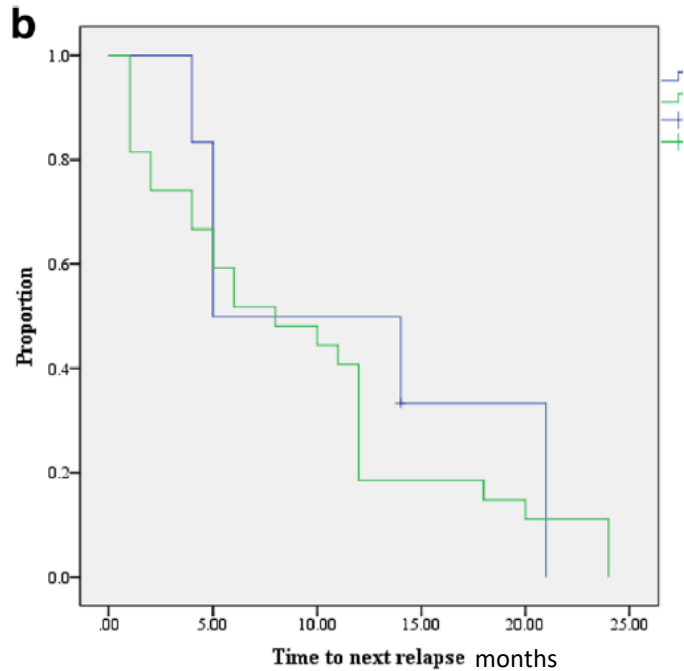
	IVMT + IVIG	IVMT
Patients, No.	20	39
Events, No.	31	72
AQP4-ab serostatus per event		
Positive	27 90% (27/20)	41 95% (41/43)
Negative	3	2
Unknown	1	29

	IVMT + IVIG	IVMT	<i>p</i> value
EDSS			
Acute attack	6.24±1.64	3.97±1.26	<0.001
Discharged	4.55±1.63	2.95±1.29	<0.001
ΔEDSS	1.63±0.77	0.94±0.65	<0.001
Onset attack	2.33±1.17 (<i>n</i> =6)	1.37±1.10 (<i>n</i> =27)	>0.05
Relapsed	1.54±0.75 (<i>n</i> =25)	0.81±0.39 (<i>n</i> =45)	<0.001
AQP4-Ab seropositive	1.70±0.91 (<i>n</i> =27)	1.02±0.81 (<i>n</i> =41)	0.003

NMOSD: IVMP vs IVMP then IVIG

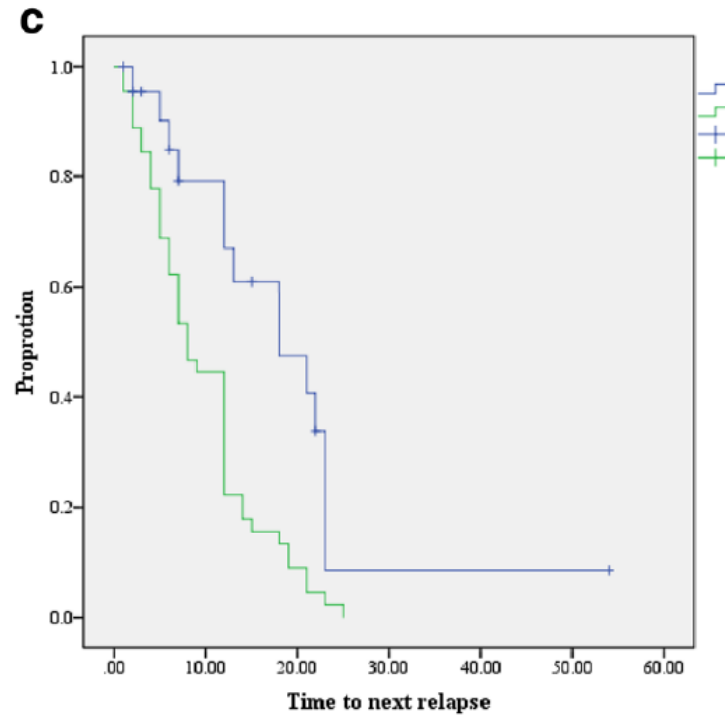
Time to relapse

Onset attack



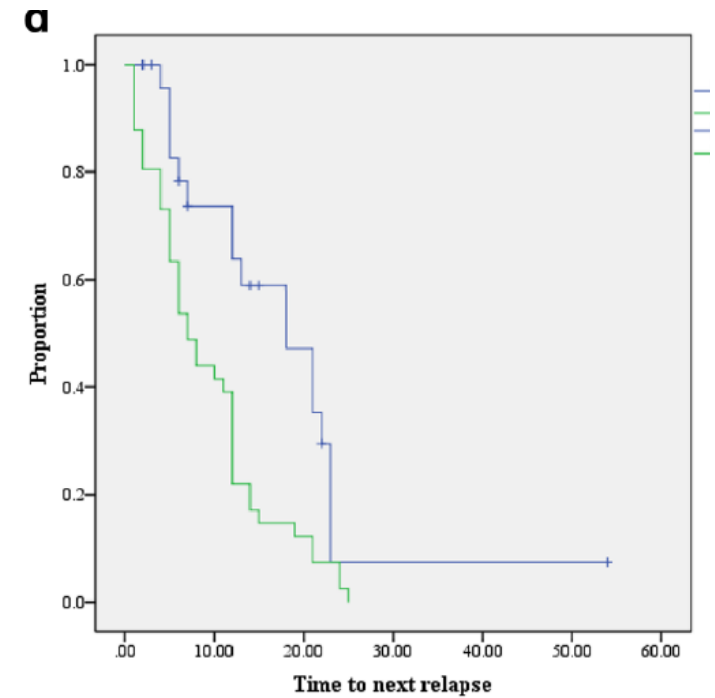
ns

relapse



$p=0.001$

AQP4



$p=0.003$

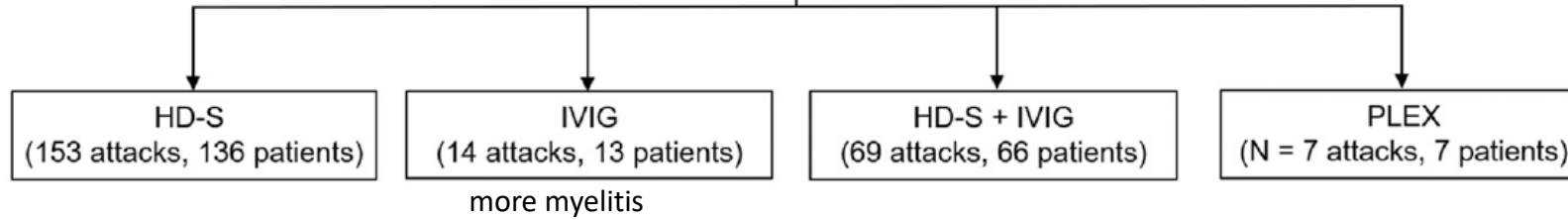
— IVMP + IVIG
— IVMP

NMOSD: IVMP vs IVIGH

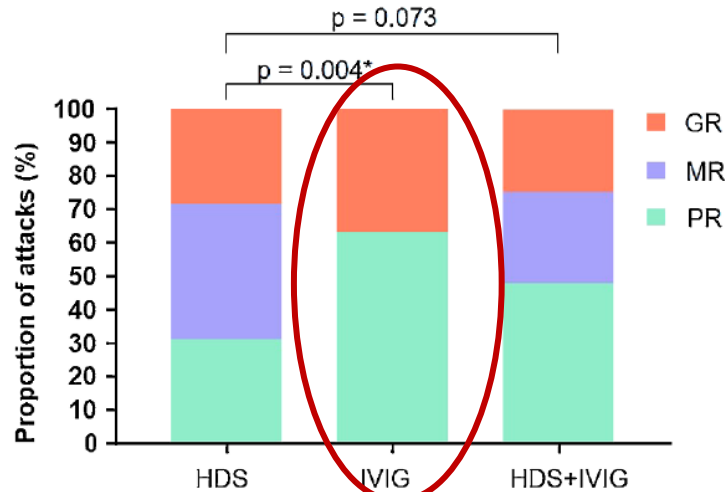
243 attacks from 198 patients
70% AQP4 IgG+ve

243 NMOSD attacks (198 patients)
were assigned

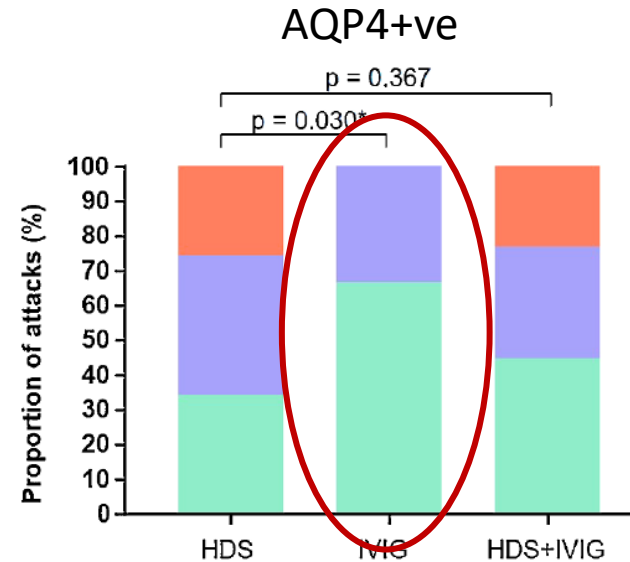
Li *et al* <https://doi.org/10.1016/j.msard.2020.102325>



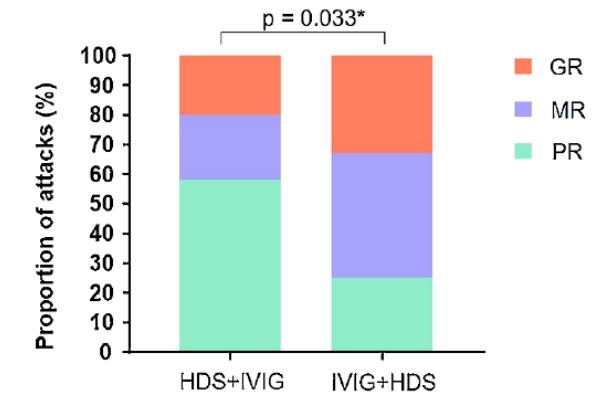
B



C



D



Good remission	44 (28.7%)	0 (0.0%)	17 (24.6%)
Moderate remission	62 (40.5%)	5 (36.7%)	19 (27.5%)
Poor remission	47 (30.8%)	9 (63.3%)	33 (47.8%)
Number of attacks	153	14	69

Good remission	26 (25.5%)	0 (0.0%)	11 (23.4%)
Moderate remission	41 (40.2%)	3 (33.3%)	15 (31.9%)
Poor remission	35 (34.3%)	6 (66.7%)	21 (44.7%)
Number of attacks	102	9	47

Good remission	9 (25.0%)	8 (33.0%)
Moderate remission	10 (22.0%)	10 (42.0%)
Poor remission	26 (58.0%)	6 (25.0%)
Number of attacks	45	24

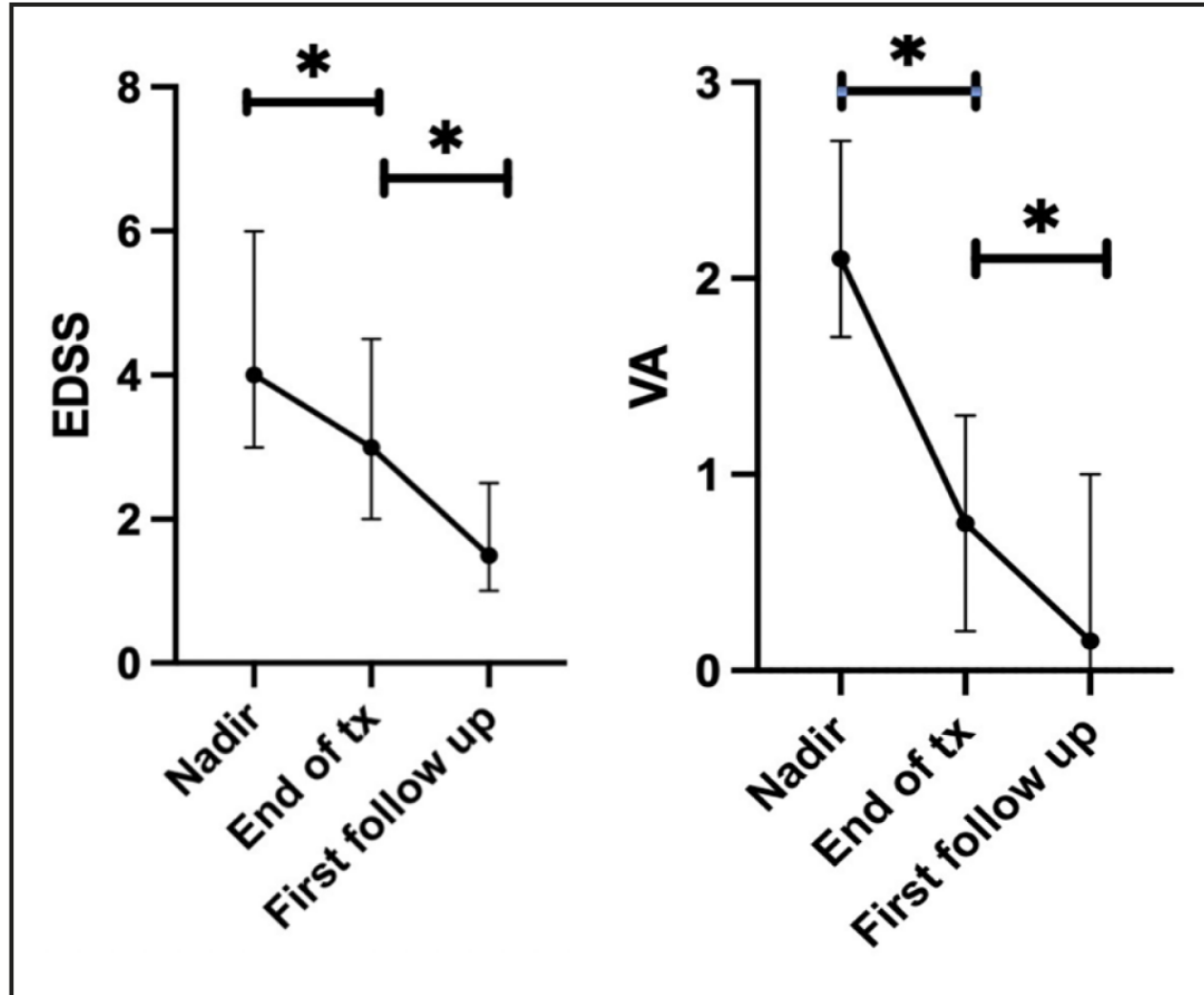
severe attacks HDS+ IVIG better than HDS

MOGAD IVIG

MOGAD: IVIG

39 attacks in 39 patients

5 countries
Follow up ≥ 3 months
high dose ($\geq 2\text{g/kg}$) vs low
dose no real diff

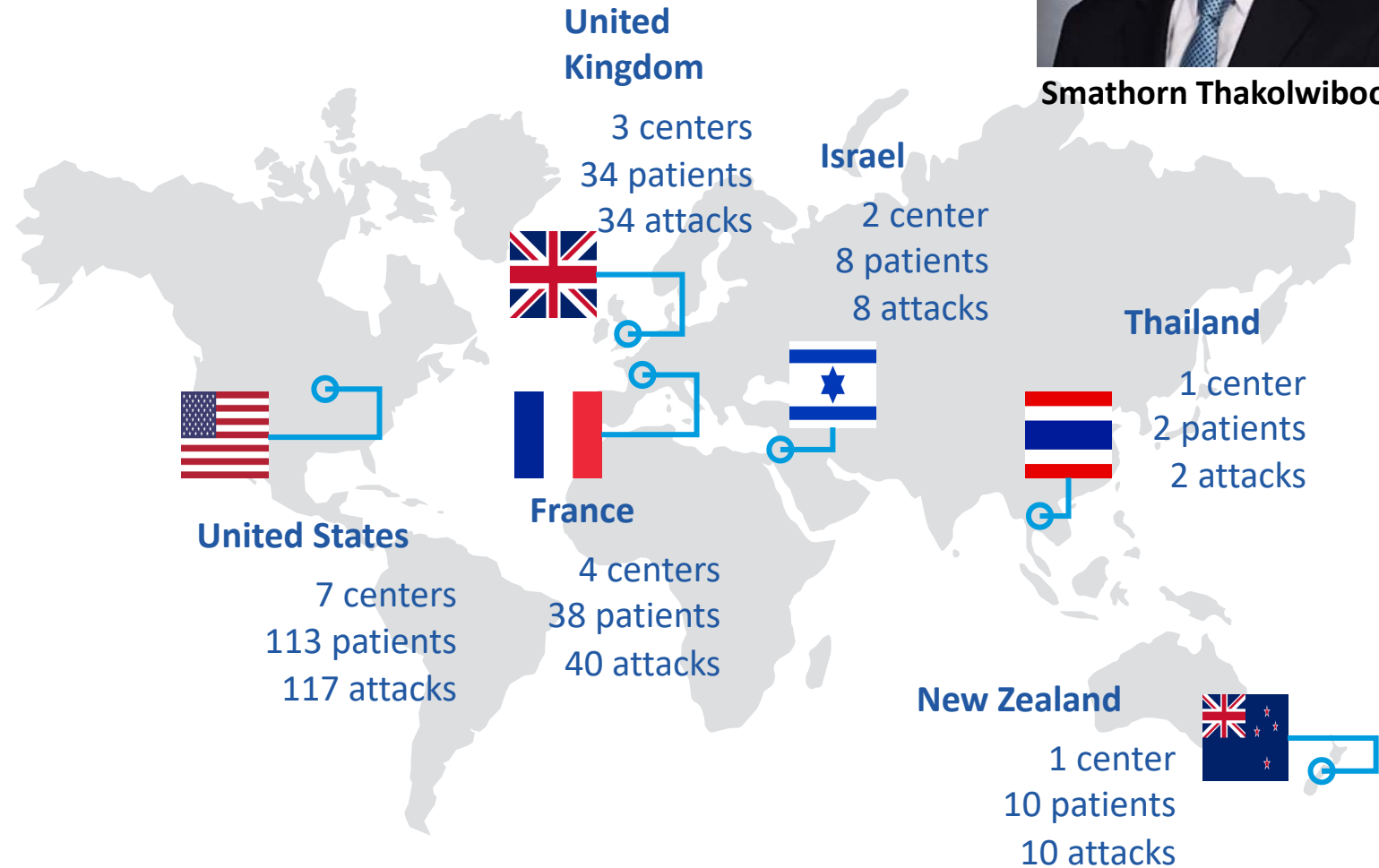


MOGAD PLEX

Method

Study design

- International multicenter
- Retrospective cohort
 - 18 centers
 - 205 patients
 - 211 attacks
- Outcome evaluation at least 3 months after PLEX



Smathorn Thakolwiboon

Method

Outcomes



Early relapse (30d post attack, $<3/12$ after PLEX)



Complete recovery



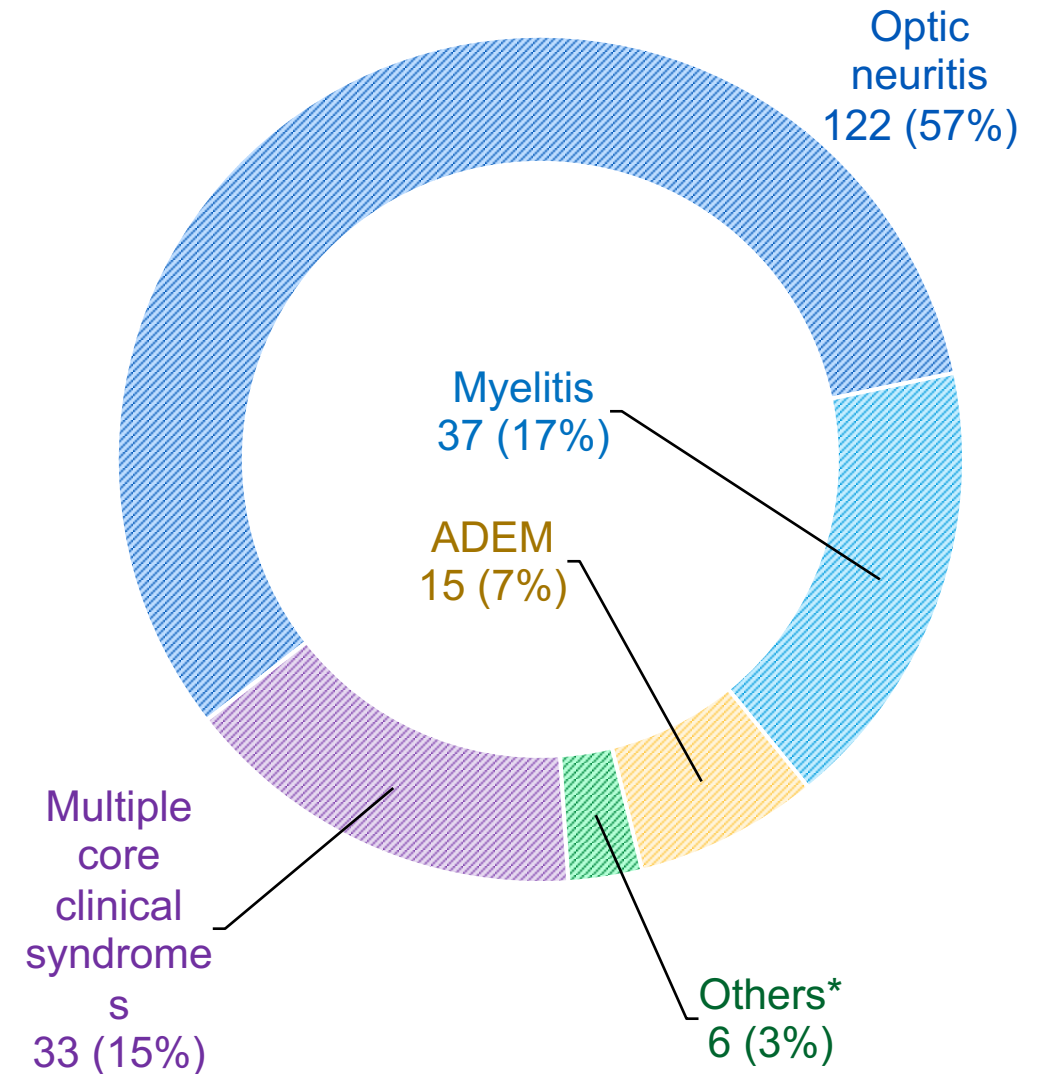
Clinically significant improvement

≥ 1.0 if EDSS ≤ 5.0 , ≥ 0.5 if EDSS > 5.0 or VA 3 lines better

Results

205 patients, 146 1st attacks, 19% <18yrs

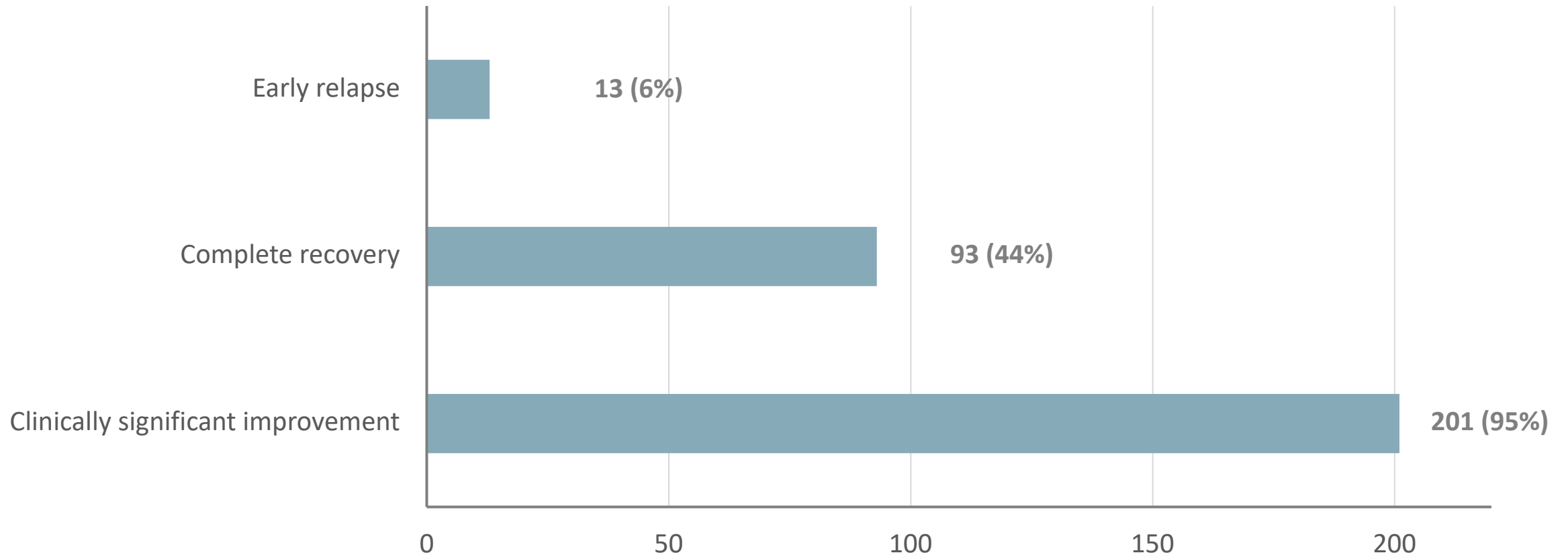
- PLEX as the first line therapy 33 (16%)
- Additional acute therapy
 - High-dose steroid 209 (99%)
 - IVIG 25 (12%)



* Cerebral polyfocal deficit 1, brainstem or cerebellar deficit 1, and cerebral-cortical encephalitis 1

Result

Treatment outcomes



Results

Outcome predictors

Early relapse

- Logistic regression did not identify any outcome predictor for early relapse

Complete recovery

First attack	0.33 (0.14-0.78)
EDSS at nadir	0.71 (0.57-0.88)
Time to PLEX	0.98 (0.96-0.99)

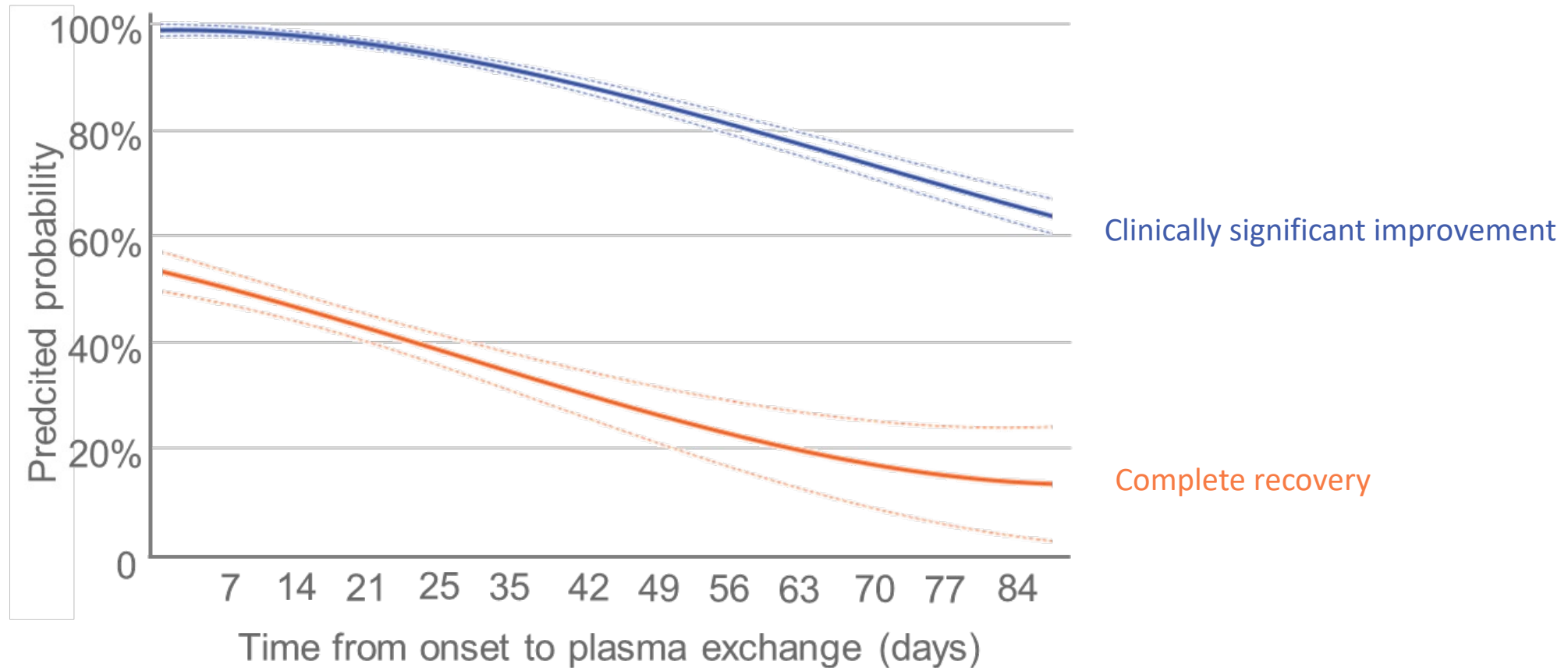
Clinically significant improvement

OR (95%CI)	
EDSS at nadir	0.93 (0.71-1.24)
Time to PLEX	0.92 (0.87-0.97)

Results

Effect of timing of PLEX

New data



Discussion

PLEX in MOGAD

- Delayed plasma exchange decreases the likelihood of recovery
- Similar to prior studies of PLEX in NMOSD^{1,2}
- Early MOG IgG washout potentially reduce damage resulting from complement activation and antibody-dependent cellular toxicity

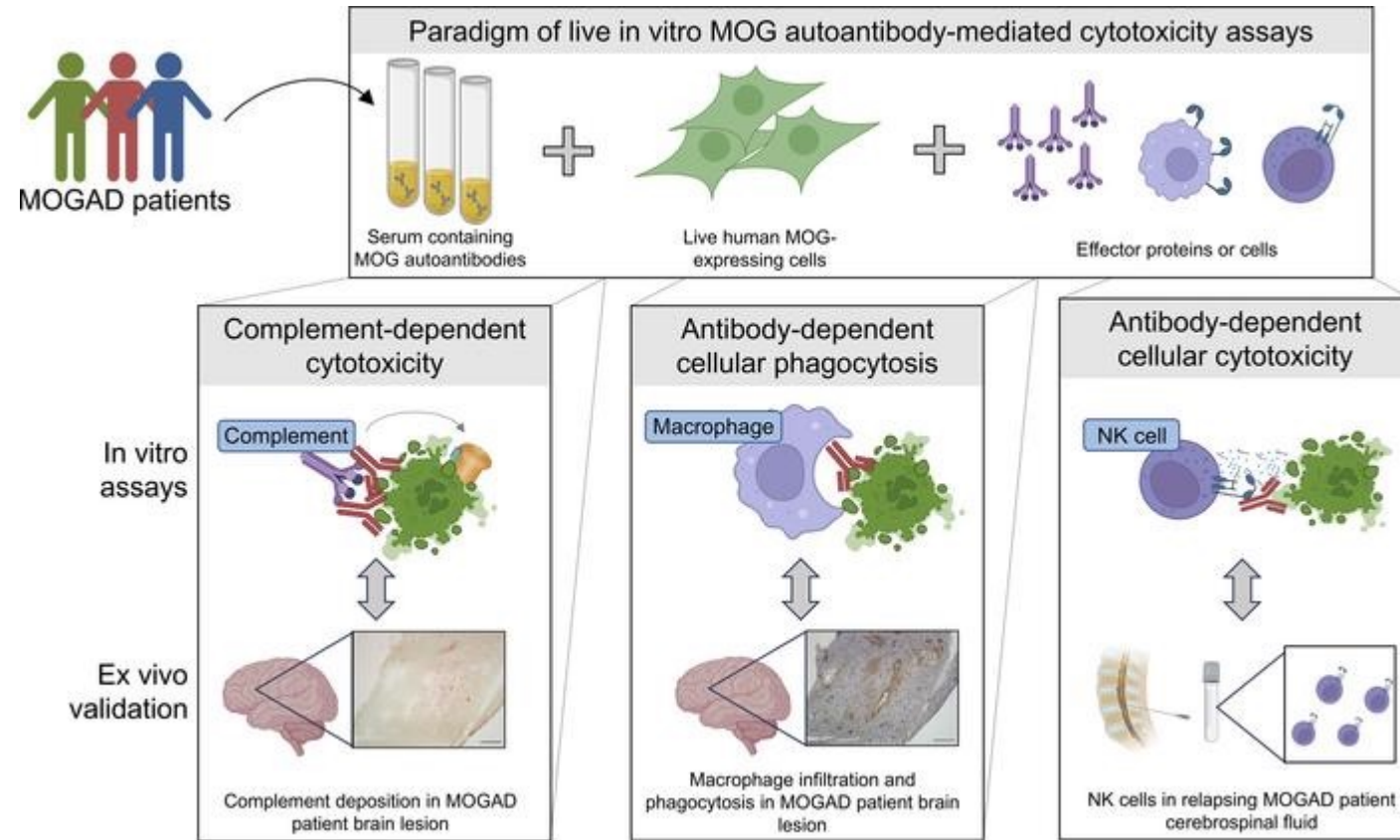


Figure from Yandamuri SS, et al. *JCI Insight* 2023;8(11):e165373

¹ Kleiter I, et al. *Neurol Neuroimmunol Neuroinflamm* 2018;26(5):e504

² Bonan M, et al. *J Neurol Neurosurg Psychiatry* 2018;89(4):346-351

Conclusions

- Convincing data that PLEX works in AQP4-NMOSD and MOGAD and earlier the better
- Practical issues to giving to all patients first line, and very early (late still worthwhile)
vs selecting those less likely to do well (AQP4: older, TM, prev poor recovery,
MOGAD: 1st attack, severe nadir)
- IVIG data less clear, ? Less effective than MP in NMOSD
studies limited and numbers low
- Add on better outcomes in NMOSD, ? Order important
- AQP4 neg NMOSD (not DSN-NMOSD) may respond differently:
 - 1 PLEX study AQP4 pos better response than neg (large ↑ OR CR)
 - 1 IVIG study AQP4 pos vs all worse outcome (↓ % CR)maybe just chance observations, or MOGAD within the group

