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GENERAL HOSPITAL

NEUROLOGY



HARVARD
MEDICAL SCHOOL

Novel Rescue Strategies for Relapse

Michael Levy, MD, PhD

Associate Professor

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

Acute vs. Preventive



Acute

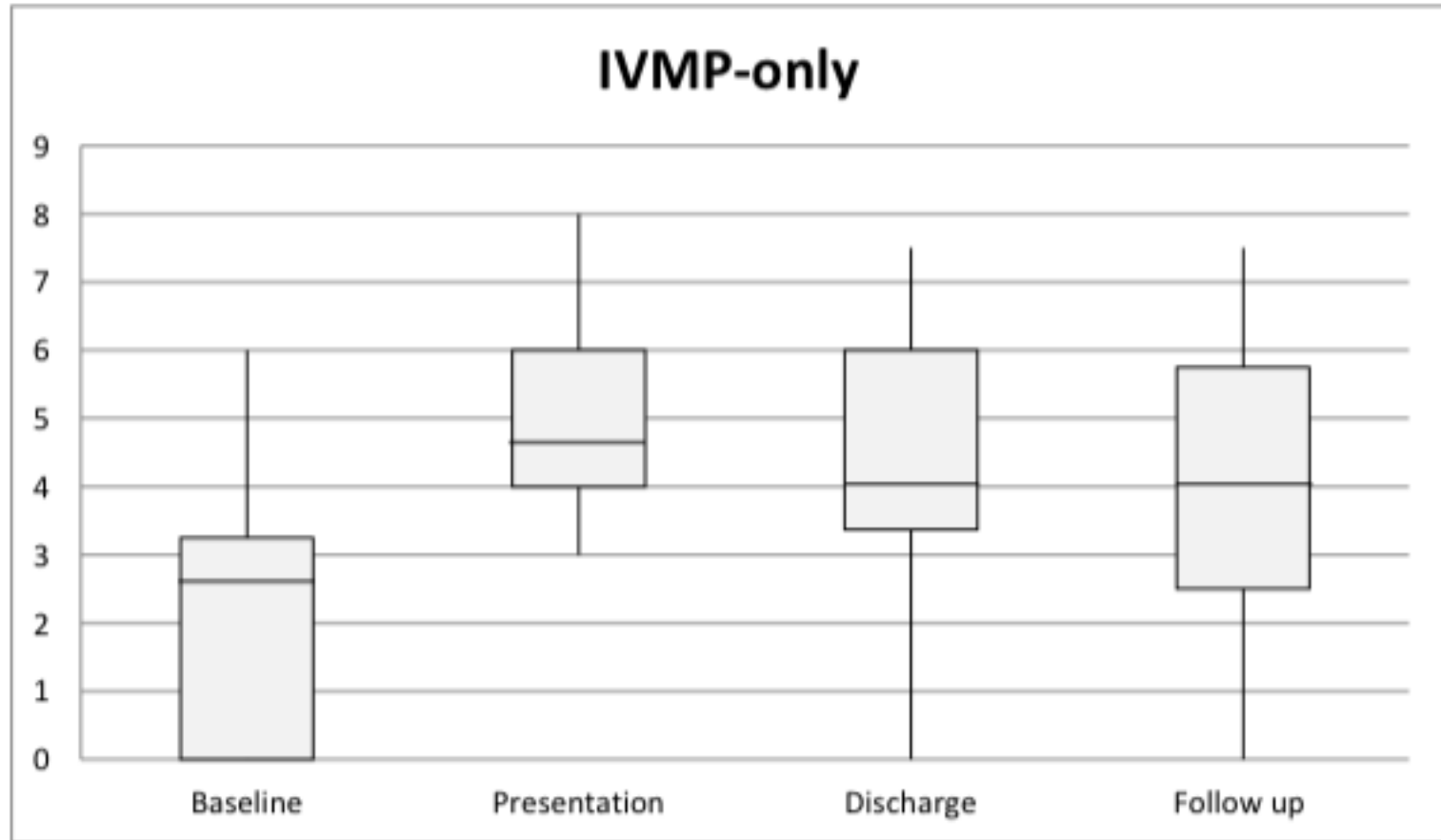


Preventive

Acute: Standard of Care

- Methylprednisolone IV 1000 mg daily x5 days
- In parallel: PLEX 1-1.5 volumes x5 cycles

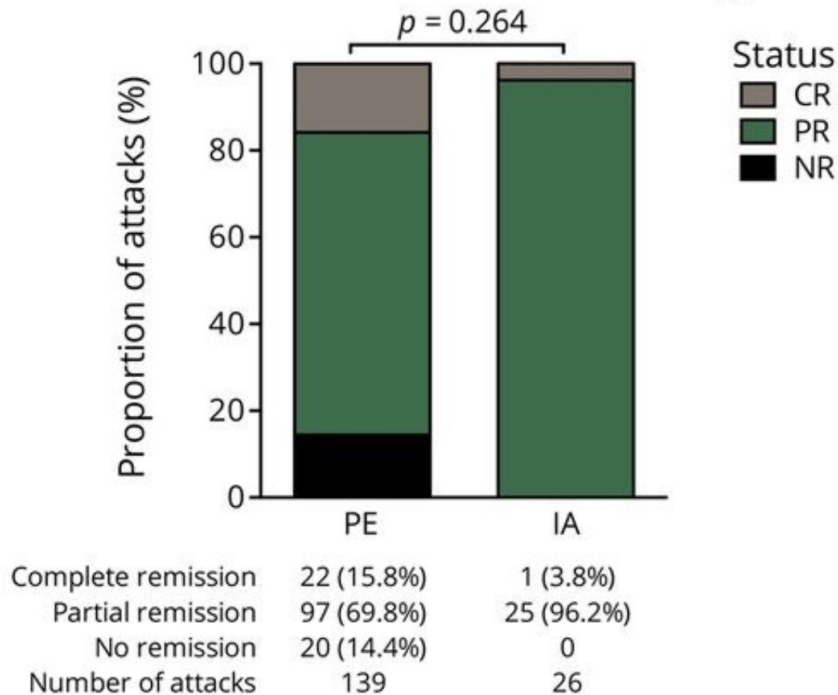
Steroids Only for Acute NMO



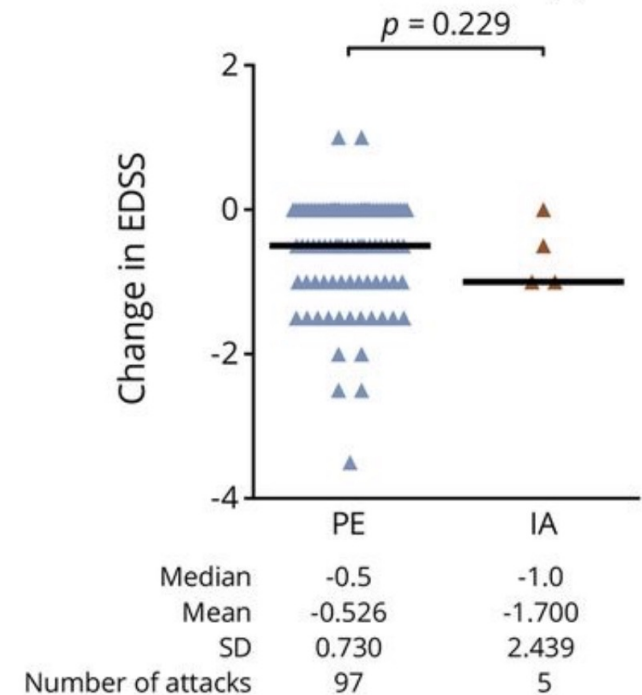
Abboud H. *Multiple Sclerosis Journal*. Mult Scler. 2015 Apr 28.

Therapeutic Plasma Exchange

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

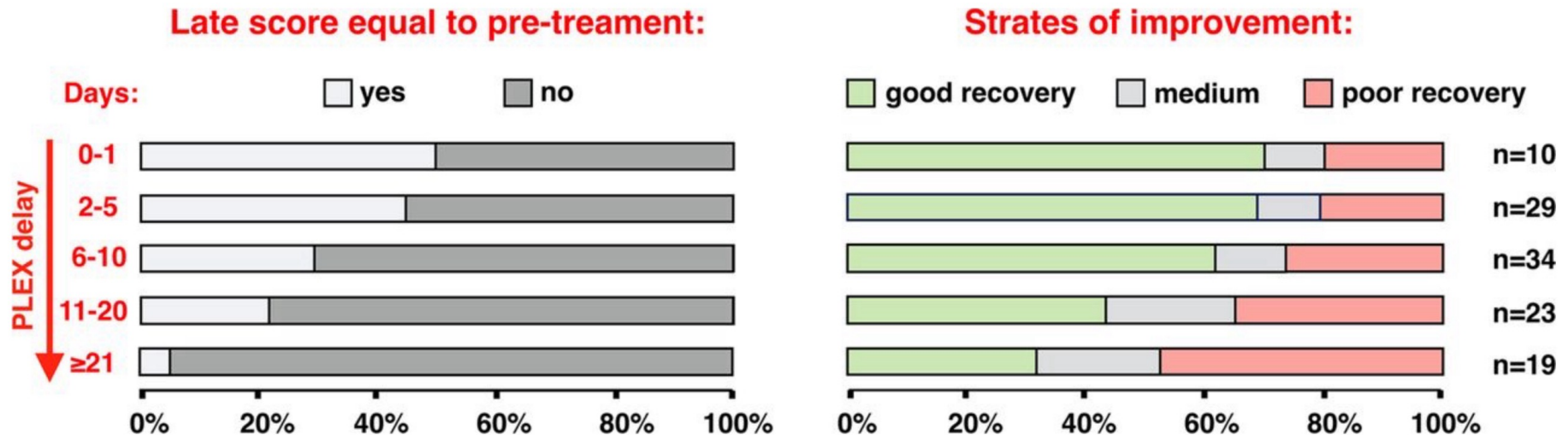


D. EDSS after 1st- or 2nd-line therapy



Kleiter I, Gahlen A, Borisow N, *et al*. Apheresis therapies for NMOSD attacks: a retrospective study of 207 therapeutic interventions. *Neurol Neuroimmunol Neuroinflamm* 2018; 5:e504.

Time to Exchange



Bonnan M, Valentino R, Debeugny S, *et al.* Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. *J Neurol Neurosurg Psychiatry* 2018; 89:346–351.

Beyond Steroids + PLEX

Case Series/Studies

- C1 esterase inhibitor
- Avastin (bevacizumab)
- Acute B cell depletion (ublituximab)
- IVIG
- Batoclimab (FcRN)

Experimental

- Sivelestat
- Alpha-1 antitrypsin

Case Reports

- Eculizumab

“Kitchen Sink”

- Combination therapy

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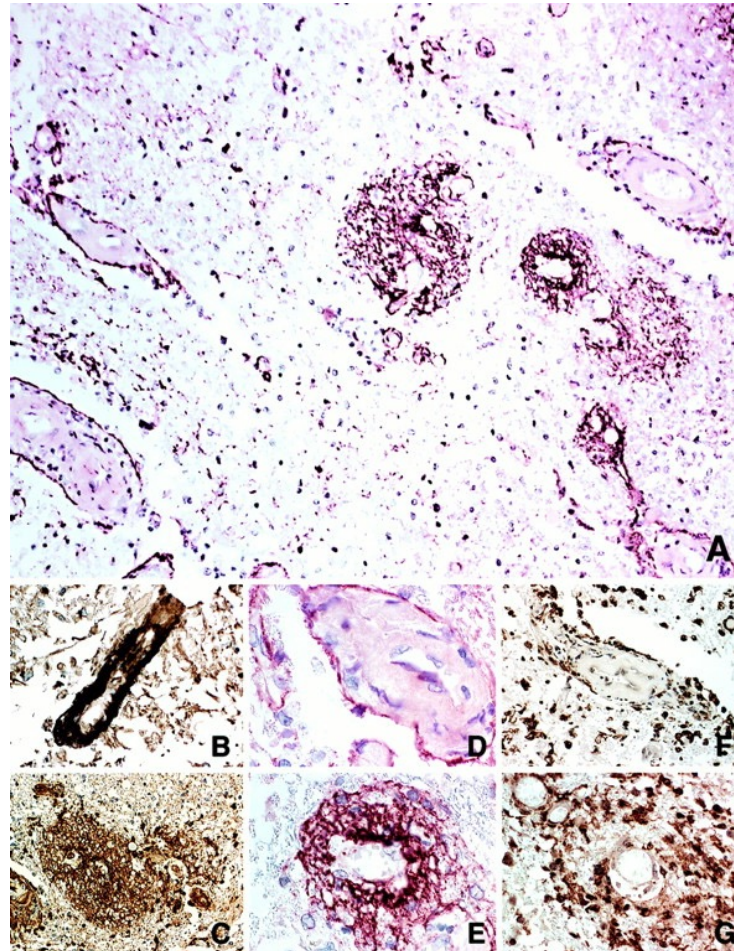
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C1-esterase inhibitor (Cinryze)



Lucchinetti CF. *Brain*. 2002
Jul;125(Pt 7):1450-61.

Cinryze Trial for Acute NMO



10

- Patients screened for eligibility

10

- Patients enrolled

10

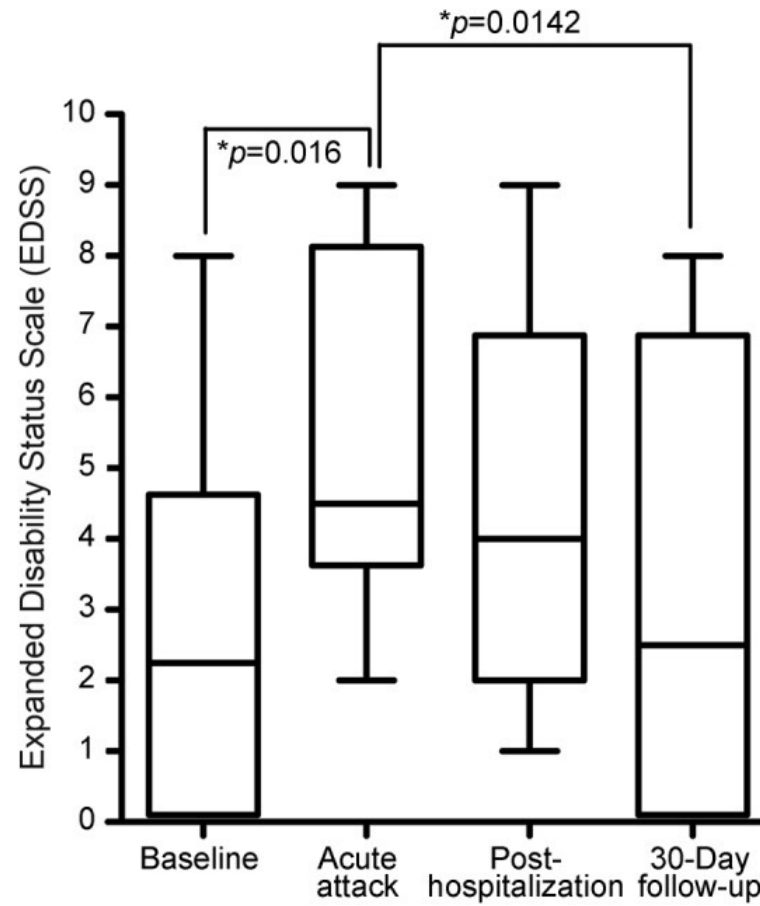
- Patients received intervention (C1-esterase inhibitor)

10

- Patients who completed the study

Levy M. *Neurol Neuroimmunol Neuroinflamm.*
2014 Apr 24;1(1):e5.

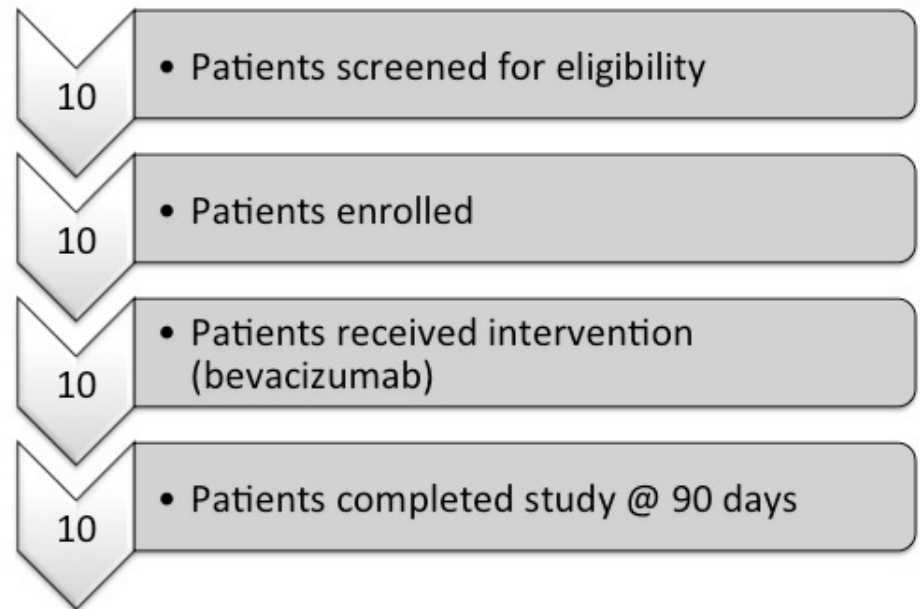
Cinryze Trial for Acute NMO



Levy M. *Neurol Neuroimmunol Neuroinflamm*. 2014 Apr 24;1(1):e5.

Blocking VEGF: Bevacizumab

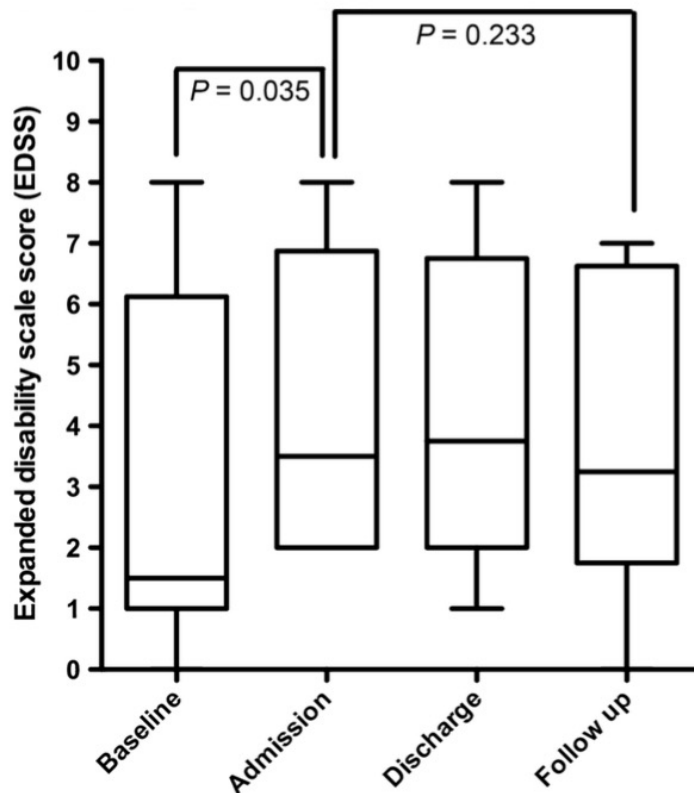
VEGF increases blood brain barrier permeability.
Blocking VEGF decreases blood brain barrier permeability.



Mealy M. *Clin Exp Neuroimmun.* 2015 Jul 28.

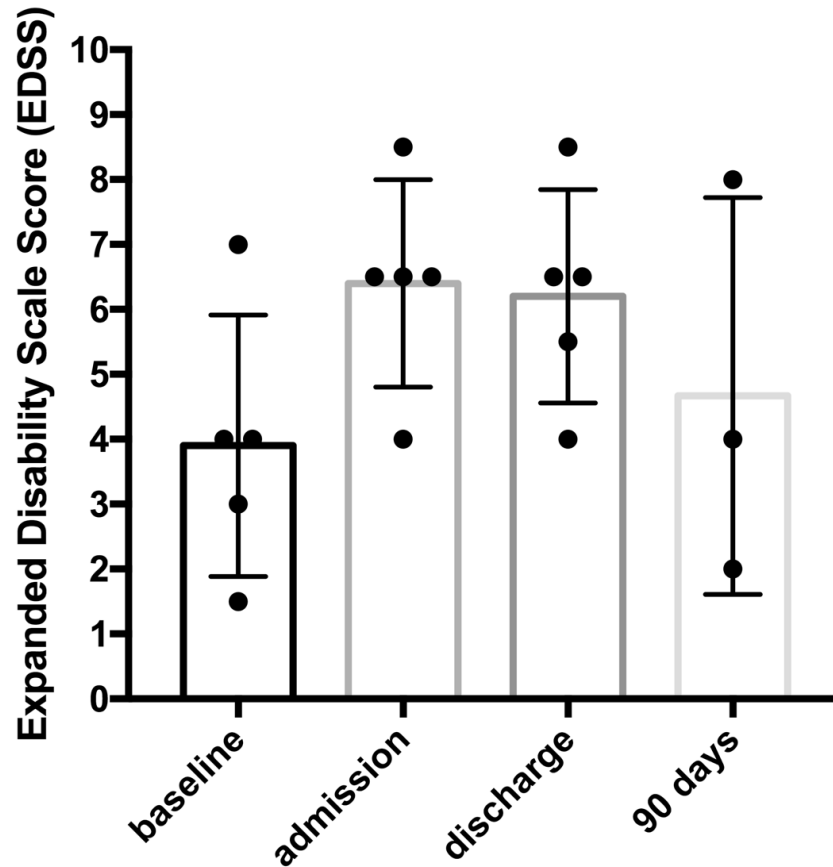
Blocking VEGF: Bevacizumab

VEGF increases blood brain barrier permeability.
Blocking VEGF decreases blood brain barrier permeability.



Mealy M. *Clin Exp Neuroimmun.* 2015 Jul 28.

Acute Trial #3: Ublituximab



Mealy M. *Medicine (Baltimore)*. 2019 Jun; 98(25): e15944.

IVIG (vs. PLEX)

Comparison of efficacy of plasma exchange versus intravenous immunoglobulin as an add-on therapy in acute attacks of neuromyelitis optica spectrum disorder

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Divjot Singh Lamba¹  | Vivek Lal² | Ratti Ram Sharma¹

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³Department of Radiodiagnosis and Imaging, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

TABLE 2 Expanded disability status scale (EDSS) score at different time points in two groups.

EDSS score at different time points	Group 1 (<i>n</i> = 29) Median (IQR)	Group 2 (<i>n</i> = 14) Median (IQR)	<i>p</i> -value Group 1 versus Group 2
Baseline	7.5 (5.5)	7.25 (5.5)	0.83
Day 10	7.0 (5)	6.5 (5.5)	0.79
3 months	6 (4)	6.0 (5)	0.85
Delta change in median score from baseline to 3 months	−1.5	−1.25	0.39
<i>p</i> -value*	0.00	0.00	–

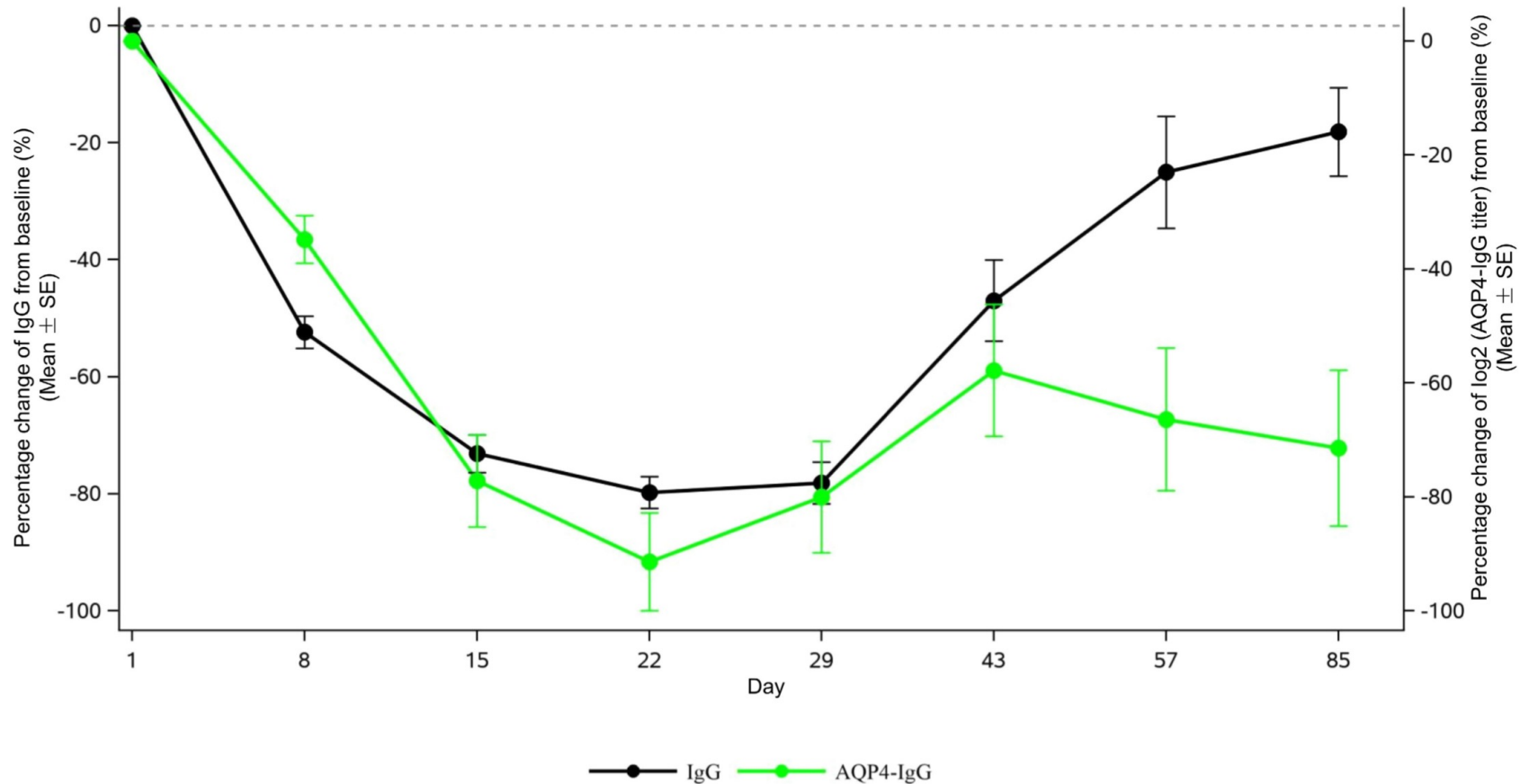
*Overall difference in score at different time points within the groups.

FcRN: Batoclimab

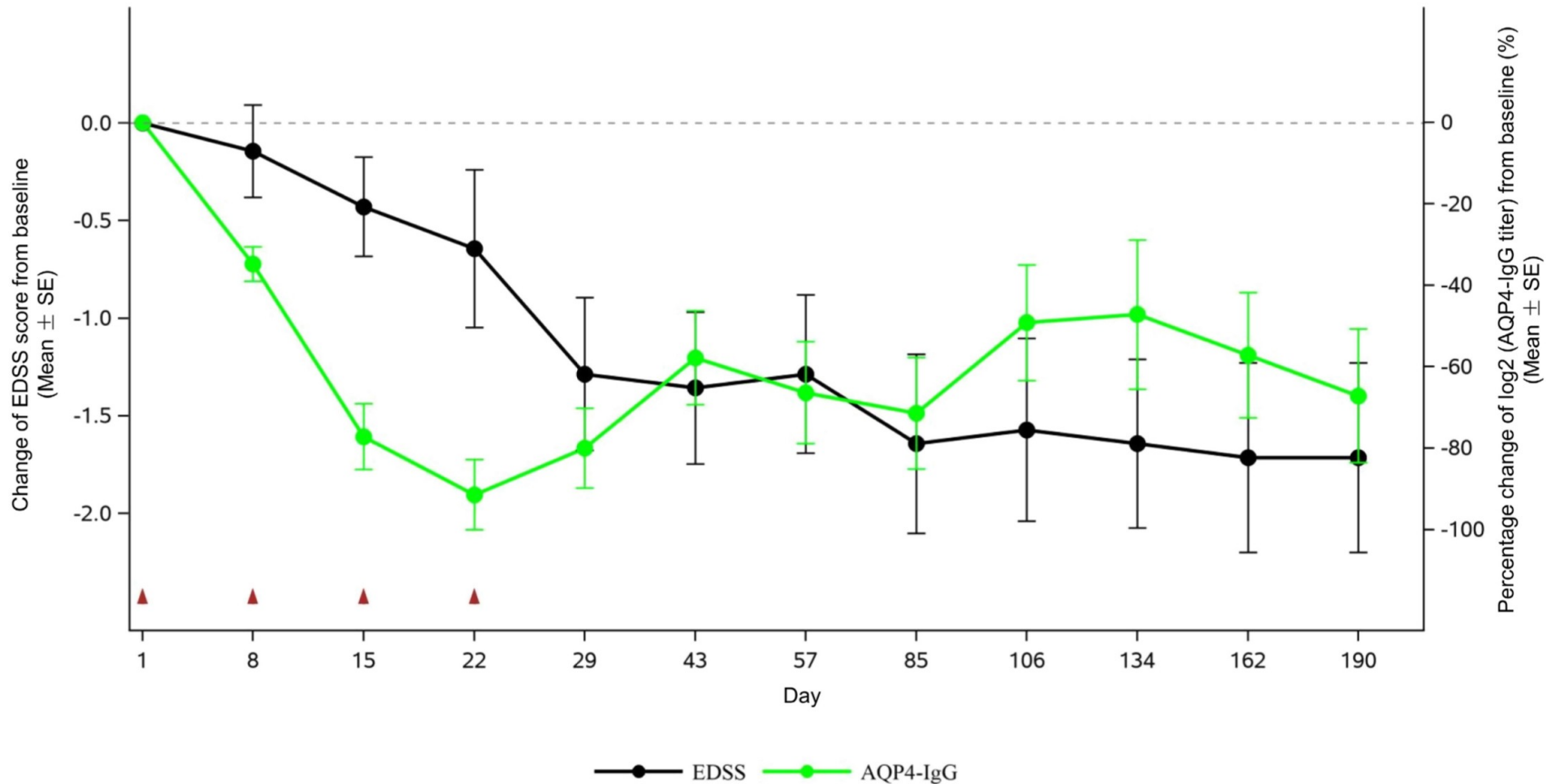
Batoclimab as an add-on therapy in neuromyelitis optica spectrum disorder patients with acute attacks

Yuge Wang¹ | Xiaonan Zhong¹ | Honghao Wang²  | Yu Peng² | Fudong Shi³ |
Dongmei Jia³ | Huan Yang⁴  | Qiuming Zeng⁴  | Chao Quan⁵ |
Jingzi ZhangBao⁵ | Michael Lee⁶ | Jun Qi⁶ | Xiaoxiang Chen⁶ |
Wei Qiu¹  | Batoclimab NMOSD Study Group

FcRN: Batoclimab



FcRN: Batoclimab



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Sivelestat

[Mult Scler.](#) Author manuscript; available in PMC 2012 Apr 5.

PMCID: PMC3319834

Published in final edited form as:

NIHMSID: NIHMS362184

[Mult Scler. 2012 Apr; 18\(4\): 398–408.](#)

PMID: [22343184](#)

Published online 2012 Feb 16. doi: [10.1177/1352458512440060](#)

Protective effect of an elastase inhibitor in a neuromyelitis optica-like disease driven by a peptide of myelin oligodendroglial glycoprotein

[Katja Herges](#),¹ [Brigit A de Jong](#),² [Ilan Kolkowitz](#),¹ [Caitlin Dunn](#),¹ [Gil Mandelbaum](#),¹ [Rose M Ko](#),³ [Alexander Maini](#),¹ [May H Han](#),¹ [Joep Killestein](#),⁴ [Chris Polman](#),⁴ [Alexandra L Goodyear](#),¹ [Jeffrey Dunn](#),¹ [Lawrence Steinman](#),¹ and [Robert C Axtell](#)¹

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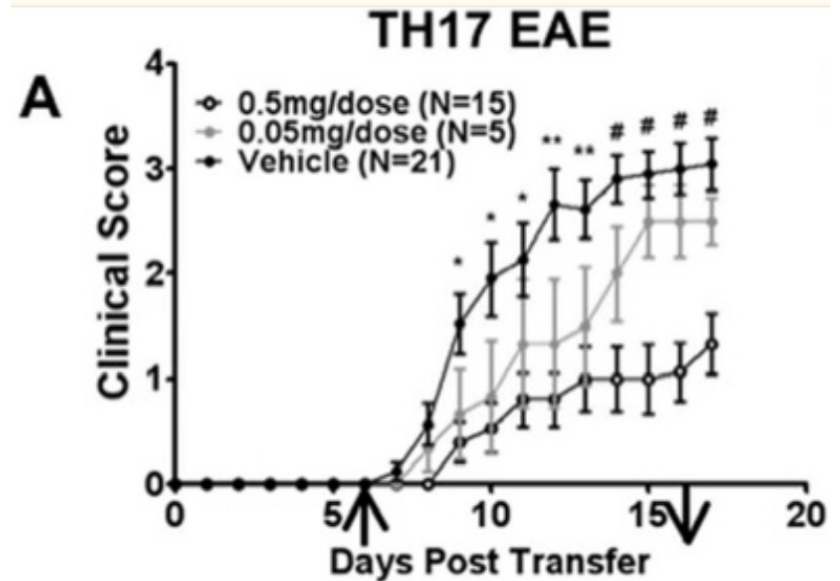
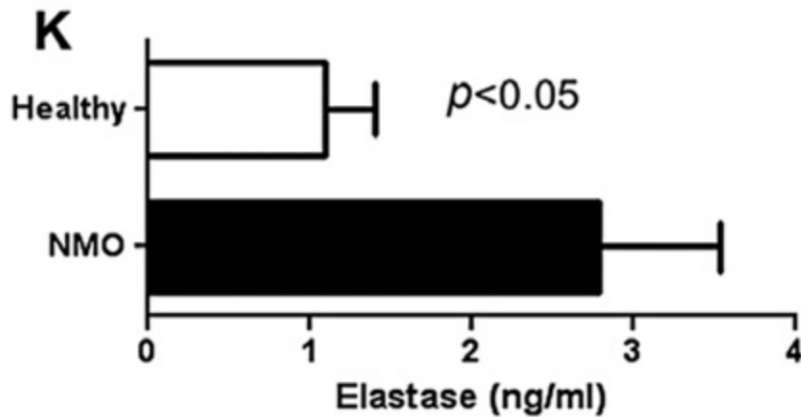
²Department of Neurology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands.

³Department of Medicine, Division of Blood and Marrow Transplantation, Stanford University School of Medicine, USA.

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Sivelestat



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Case report: Eculizumab

Eculizumab for acute relapse of neuromyelitis optica spectrum disorder: Case report



Sophie Chatterton¹



John Douglas Edward Parratt^{1,2}

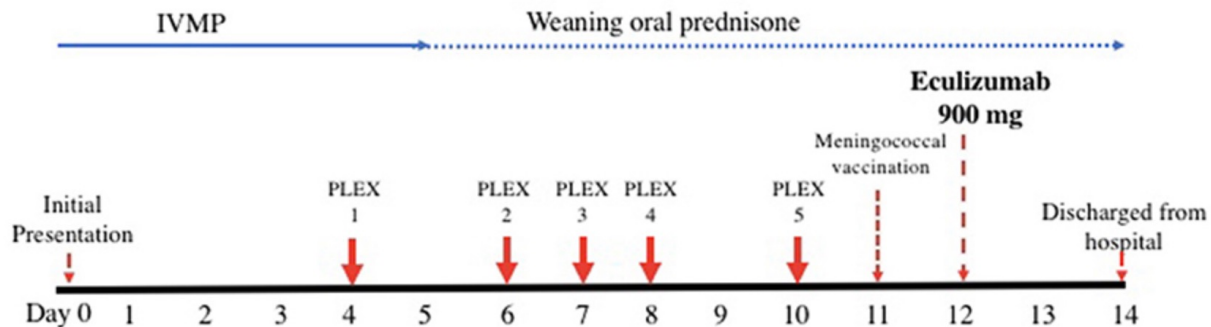


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² School of Medicine, University of Sydney, Sydney, NSW, Australia

Case report: Eculizumab



Case report: Eculizumab



The patient's visual acuity promptly improved to counting fingers with her left eye 2 days after eculizumab commencement and she was able to be discharged home after her first infusion, 2 weeks following her initial presentation. At follow-up 2 and 5 months later, she remained on maintenance eculizumab without complications and there was evidence of ongoing improvement in her left eye visual acuity but still significant loss of central vision. Given the chronicity of her right eye visual impairment, no improvement was expected or found.

Collaboration: Eculizumab cases

Do you have cases of acute NMO relapses treated with eculizumab?

Send me a text!

410-979-8297



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Combination Therapy



ZILBRYSQ[®]
(zilucoplan) Injection

