Evaluating the Economic Value of Monoclonal Antibodies for AQP4+ NMOSD in the US Using Attack-Free Survival over a 5-Year Horizon

EE489

Rosemarie Walch[1], Justin R Abbatemarco[2], Moushmi Singh[3], Therese Aubry de Maraumont[4], Kim Rand[5], Martin Dalziel[6], Dustin Cavida[4], Istvan M Majer[7], Robert C Sergott[8]

[1]Memorial Healthcare, Owosso, MI, USA; [2]Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland, OH, USA; [3]Amgen, Uxbridge, UK; [4]Amgen Inc., Thousand Oaks, CA, USA; [5]Maths in Health, Klimmen, Netherlands; [6]Oxford PharmaGenesis, Oxford, UK; [7]Amgen Europe GmbH, Global HEOR, Rotkreuz, Switzerland; [8]William H. Annesley, Jr., EyeBrain Center, Thomas Jefferson University, and Wills Eye Neuro-Ophthalmology, Philadelphia, PA, USA

INTRODUCTION

- Aquaporin-4–positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease of the central nervous system characterized by attacks that can lead to cumulative and permanent disability. The occurrence and timing of attacks vary across patients and cannot be predicted at the individual level.[1]
- Attacks are the primary driver of disability and are associated with increased healthcare utilization and costs. Consequently, durable attack prevention is a key determinant of clinical and payer decision-making, alongside considerations of treatment burden and costs.[2]
- Several US Food and Drug Administration (FDA)-approved monoclonal antibody therapies are available for long-term attack prevention, targeting different pathways and varying in dosing schedules and cost profiles, including inebilizumab (anti-CD19),[3] satralizumab (anti-IL6),[4] eculizumab and ravulizumab (complement C5 inhibitors).[5,6]
- These therapies have been evaluated in separate randomized controlled trials (RCTs) with differences in attack-adjudication and study populations limiting direct comparisons. Robust indirect treatment comparisons (ITCs) are therefore needed to estimate attack-free survival across treatments and inform economic evaluation outcomes, including attack-free life-years (AFLYs) and associated costs.

OBJECTIVES

- To compare incremental NMOSD AFLYs and associated costs over 5 years versus placebo (no relapse prevention therapy) for FDA-approved therapies in adult patients with AQP4+ NMOSD, using AFLY as a measure of sustained attack prevention.

METHODS

Data

- A systematic literature review identified three relevant placebo-controlled RCTs, N-MOmentum (inebilizumab),[7] SAkuraStar (satralizumab),[8] and PREVENT (eculizumab),[9] and one single-arm trial, CHAMPION-NMOSD (ravulizumab).[10]

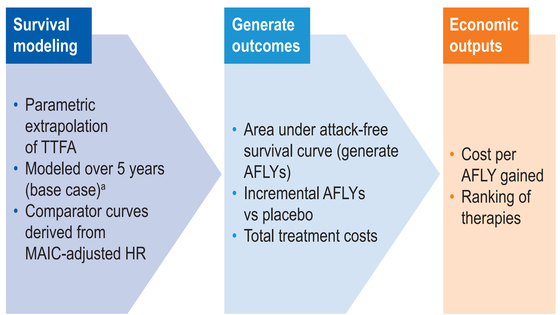
Indirect treatment comparison

- An evidence synthesis feasibility assessment concluded that N-MOmentum, SAkuraStar and PREVENT were sufficiently comparable for inclusion in an anchored ITC. However, CHAMPION-NMOSD was excluded because it was a single-arm trial with no internal comparator.
- Anchored matching-adjusted indirect comparisons (MAICs) were conducted to adjust for important cross-trial differences in baseline characteristics, consistent with methodological guidance.[11]
- Investigator-determined attacks were used due to heterogeneity in adjudication criteria and to better reflect routine clinical practice.
- Individual patient-level data from N-MOmentum were weighted to match published baseline characteristics from the comparator trials SAkuraStar and PREVENT. Matching variables considered were age at diagnosis, age at baseline, sex, race/ethnicity, Expanded Disability Status Scale (EDSS) score, and annualized attack rate (AAR) based on availability, clinical relevance, and methodological guidance. Of these, age at diagnosis, AAR, and EDSS score were selected for the base case analyses.
- Hazard ratios (HRs) for investigator-determined time to first attack were estimated using weighted Cox proportional hazard models to inform the comparative survival modeling.
- Robustness of the MAICs was assessed using alternative sets of matching variables.

Attack-free survival modeling

- AFLYs were calculated as the area under the attack-free survival curve, reflecting time lived without a first investigator-determined attack (**Figure 1**).
- Parametric survival models were fitted to time to attack data in N-MOmentum to model and extrapolate attack-free survival. For inebilizumab, pooled data from the randomized control period (RCP) and open-label extension (OLE) were used to leverage the longest available follow-up and improve the plausibility of extrapolations. Placebo extrapolation was based on RCP data only, as patients crossed over to inebilizumab in the OLE.

Figure 1. Analytical Framework



[a]Extrapolated to 15 years in scenario analysis.
AFLY, attack-free life-year; HR, hazard ratio; MAIC, matching-adjusted indirect comparison; TTFA, time to first attack.

- The generalized gamma (inebilizumab) and the exponential (placebo) models were selected for the base case analysis based on statistical fit and clinical plausibility.
- Attack-free survival curves for satralizumab and eculizumab were derived by applying MAIC-adjusted HRs to the modeled inebilizumab curve.
- Analyses were conducted over a 5-year time horizon with a half-cycle correction.

Costs

- Analyses were conducted from a US payer perspective using 2025 wholesale acquisition cost. No treatment discontinuation was assumed in the base case.
- FDA-approved dosing regimens were applied, with year 1 versus subsequent costs reflecting loading and maintenance phases.
- Administration costs were included for intravenous therapies (inebilizumab and eculizumab), while subcutaneous satralizumab was assumed to incur no administration cost.

Outcomes

- Primary outcomes were incremental AFLYs versus placebo and incremental costs per AFLY gained versus placebo, evaluated over a 5-year time horizon (base case) and up to 15 years to account for life-long therapy (scenario analysis).
- Additional scenario analyses assessed alternative attack-free survival input data from N-MOmentum (RCP only), parametric models, inclusion of healthcare resource use (HCRU) costs, treatment discontinuation, alternative MAIC specifications, unadjusted comparisons, biosimilar pricing assumptions for eculizumab (up to 30% lower than the originator[12]), and exclusion of half-cycle correction.

RESULTS

Indirect treatment comparisons

- The estimated HR for time to first attack was 0.328 (95% confidence interval [CI] 0.125–0.862) for inebilizumab vs satralizumab, and 1.004 (95% CI 0.351–2.872) for inebilizumab vs eculizumab (**Table 1**).
- Results were consistent across alternative matching scenarios, with no change in relative treatment ranking. Precision varied across scenarios (reflecting differences in effective sample size) with inclusion of AAR and age at diagnosis having the greatest impact on comparative estimates (**Table 1**).

Economic evaluation – base case

- The 5-year per-patient treatment costs were $1,542,734 for inebilizumab, $1,167,638 for satralizumab, and $3,418,052 for eculizumab.
- Incremental AFLYs versus placebo were 3.2 for inebilizumab, 3.2 for eculizumab, and 1.8 for satralizumab.
- Cost per AFLY gained was lowest for inebilizumab ($487,927), followed by satralizumab ($646,756) and eculizumab ($1,079,916) (**Table 2**).

Table 1. Anchored MAIC Results, Time to First Attack

Matching variables	ESS	HR	95% CI	*P*-value
Inebilizumab vs satralizumab[a]				
Base case analysis (age at diagnosis, AAR, EDSS)	163.9	0.328	0.125–0.862	0.024
Unadjusted comparison	200.0	0.529	0.210–1.337	0.178
Age at baseline, AAR, EDSS	164.2	0.372	0.141–0.984	0.046
Age at diagnosis, EDSS	194.9	0.508	0.201–1.208	0.151
Age at diagnosis, AAR	164.3	0.323	0.123–0.848	0.022
Inebilizumab vs eculizumab[b]				
Base case analysis (age at diagnosis, AAR, EDSS ≥ 4)[c]	87.1	1.004	0.351–2.872	0.993
Unadjusted comparison	165.0	1.353	0.556–3.291	0.505
Age at baseline, AAR, EDSS ≥ 4	79.8	1.753	0.574–5.353	0.324
Age at diagnosis, EDSS ≥ 4	142.3	1.316	0.527–3.284	0.556
Age at diagnosis, AAR	87.5	0.972	0.339–2.784	0.958

[a]N-MOmentum data were restricted to AQP4-seropositive patients with EDSS ≤ 6.5 to align patient selection criteria in SAkuraStar. [b]N-MOmentum data were restricted to AQP4-seropositive patients with EDSS ≤ 7.0 and ≥ 2 relapses to align patient selection criteria in PREVENT. [c]EDSS definition differs by comparator because EDSS high (≥ 4.0) was used to match the PREVENT reporting style.
Notes: RCP data from N-MOmentum were used to inform the MAIC, preserving a randomized comparison. *P*-values are reported for descriptive purposes only.
AAR, annualized attack rate; AQP4, aquaporin-4; CI, confidence interval; EDSS, Expanded Disability Status Scale; ESS, effective sample size; HR, hazard ratio; MAIC, matching-adjusted indirect comparison.

Economic evaluation – scenario analyses

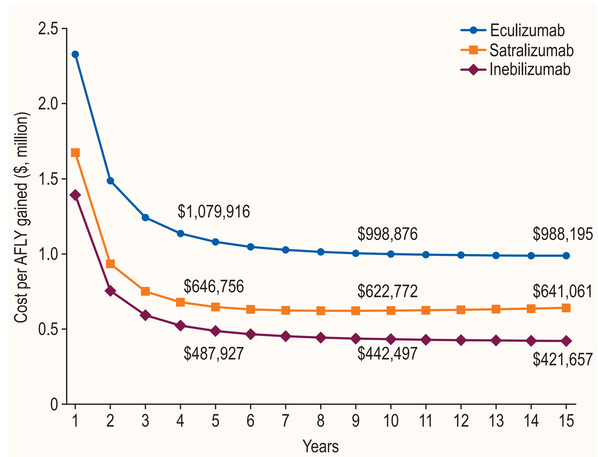
- Results were consistent across all scenario analyses, with inebilizumab consistently having the lowest and eculizumab the highest cost per AFLY gained (**Table 2**).
- Findings were robust to alternative time horizons (up to 15 years, **Figure 2**), survival inputs, parametric models, MAIC specifications, inclusion of HCRU costs, and removal of half-cycle correction.
- Assuming a 30% price reduction for eculizumab biosimilars reduced cost per AFLY gained but did not change the overall ranking.

Table 2. Scenario Analyses, Cost per AFLY Gained

Scenario	Cost per AFLY gained ($)		
	Inebilizumab	Eculizumab	Satralizumab
Base case	487,927	1,079,916	646,756
Using only RCP data from N-MOmentum for inebilizumab survival extrapolations	554,765	1,227,208	991,764
Including treatment discontinuation	398,149	841,299	506,907
Including HCRU costs	482,340	1,074,333	638,729
Using alternative matching variables[a]	487,927	966,923–1,089,221	467,974–655,652
Using biosimilar eculizumab costs[b]	487,927	755,924	646,756
Using the exponential distribution for the extrapolation of time to attack	474,118	1,049,499	567,320
Using the generalized gamma distribution for the extrapolation of time to attack	475,745	1,052,982	618,998
No half-cycle correction	492,791	1,090,683	653,045

[a]Based on range of MAIC matching scenarios presented in **Table 1**. [b]Assuming up to a 30% price reduction for eculizumab.
Scenario analyses were conducted using the same modeling framework as the base case. Cost per AFLY gained is defined as incremental cost versus placebo divided by incremental AFLYs.
AFLY, attack-free life-year; HCRU, healthcare resource use; MAIC, matching-adjusted indirect comparison; RCP, randomized controlled period.

Figure 2. Cost per AFLY Gained



AFLY, attack-free life-year.

LIMITATIONS

- Although the MAIC approach is consistent with methodological guidance,[11] results are subject to inherent limitations, including reduced effective sample size after weighting, potential residual confounding due to unobserved cross-trial differences, and reliance on published aggregate data to inform matching.
- Concomitant immunosuppressive therapy use in PREVENT may confound comparisons.
- Differences in study design and attack adjudication methods across trials may affect comparability; investigator-determined attacks were used to improve comparability.
- Extrapolation of attack-free survival beyond observed data introduced uncertainty; however, scenario analyses suggested a limited impact on results.
- The model captures time to first attack only and does not account for recurrent attacks.

CONCLUSIONS

- This analysis provides payer-relevant comparative evidence on the long-term value of monoclonal antibody therapies for AQP4+ NMOSD in the US.
- AFLY represents a clinically meaningful and decision-relevant outcome, capturing sustained attack prevention aligned with payer priorities.
- Following MAIC adjustment and parametric survival modeling, inebilizumab was associated with a lower cost per AFLY gained versus comparators, indicating greater value for money.

REFERENCES

1. Siriratnam P et al. *Autoimmun Rev* 2023;22:103465.
2. Wingerchuk DM et al. *J Manag Care Spec Pharm* 2022;28:S3-S27.
3. UPLIZNA (inebilizumab-cdon) Prescribing Information. Viela Bio, 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761142s000lbl.pdf (Accessed April 10, 2026).
4. ENSPRYNG (satralizumab-mwge) Prescribing Information. Genentech, 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761149s000lbl.pdf (Accessed April 10, 2026).
5. SOLIRIS (eculizumab) Prescribing Information. Alexion Pharmaceuticals, 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125166s431lbl.pdf (Accessed April 10, 2026).
6. ULTOMIRIS (ravulizumab-cwvz) Prescribing Information. Alexion Pharmaceuticals, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761108s026s031lbl.pdf (Accessed April 10, 2026).
7. Cree B et al. *The Lancet* 2019;394:1352-63.
8. Traboulsee A et al. *Lancet Neurol* 2020;19:402-12.
9. Pittock SJ et al. *N Engl J Med* 2019;381:614-25.
10. Pittock SJ et al. *Ann Neurol* 2023;93:1053-68.
11. Phillippo DM et al. *Res Synth Methods* 2020;11:568-72.
12. Abdelaziz A et al. *JAMA Netw Open* 2025;8:e2542937.

DISCLOSURES

RW, JRA, and RCS declare that this research was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.
MS, TAdM, DC, and IMM are employees of Amgen.
KR is a director of Maths in Health.
MD is an employee of Oxford PharmaGenesis.

ISPOR 2026; Philadelphia, PA; May 17–20, 2026

This study was funded by Amgen.