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Extrapolation of impact on individual patient outcomes in neuromyelitis optica spectrum disorder due to relapse reduction from ravulizumab and other novel biologic treatments

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INTRODUCTION

- Anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease of the central nervous system characterized by repeated, unpredictable relapses, leading to accumulation of irreversible neurological disability, including visual impairment, motor disability, paralysis, and increased overall risk of mortality.[1,2]
- Patients with NMOSD who experience relapses have worse outcomes, use more healthcare resources, and incur higher costs than patients without relapses, leading to substantial clinical, economic, and psychological burdens.[2-4]
- Ravulizumab, satralizumab, and inebilizumab are approved for the treatment of patients with AQP4-Ab+ NMOSD in multiple countries and regions[5-13]; however, data are limited on the long-term consequences of relapse reduction in patients with AQP4-Ab+ NMOSD receiving biologic therapies.

OBJECTIVE

- To develop a model using real-world data and extrapolate the long-term impact of ravulizumab, satralizumab, and inebilizumab on individual symptoms and outcomes resulting from relapse reduction in patients with AQP4-Ab+ NMOSD.

CONCLUSIONS

- This 5-year modeling study illustrates the substantial risk of permanent disability associated with relapses, even among patients with AQP4-Ab+ NMOSD receiving some biologic treatments.
- In the model, patients treated with ravulizumab had the lowest proportion of patients with relapse-associated symptoms and average number of relapse-associated outcomes compared with satralizumab, inebilizumab, and placebo with or without immunosuppressive therapy (IST).
- Timely treatment with a highly effective preventive therapy such as ravulizumab may avoid irrevocable deterioration of NMOSD symptoms.

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Poster

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METHODS

- The data for individual symptoms and outcomes based on the number of previous relapses were drawn from the Adelphi Real World NMOSD Disease Specific Programme™ (DSP).
  - The DSP is a cross-sectional, multinational, retrospective survey of physicians and their patients conducted in routine clinical practice and provides real-world data for disease burden and management.
  - Data for this analysis were collected in France, Germany, Italy, Spain, and the United Kingdom between January 2023 and June 2023.
  - Physicians included in the analysis were neurologists actively involved in the management and treatment of ≥ 1 patient with AQP4-Ab+ NMOSD.
  - Eligible patients were aged ≥ 18 years with a current diagnosis of AQP4-Ab+ NMOSD and currently not participating in a clinical trial.
- The relapse risk for ravulizumab versus satralizumab and inebilizumab was drawn from an indirect treatment comparison using a network meta-analysis.[14]
- Based on the relapse risks, a Markov cohort model was utilized to extrapolate the average risks of individual relapse-associated symptoms or outcomes over a 5-year time horizon for ravulizumab, satralizumab, inebilizumab, and placebo with or without IST.
- Disease progression or worsening of symptoms was assumed to be driven by the number of relapses a patient experienced.[1,2]
  - The changes in relapse-associated symptoms or outcomes were assessed up to 3 relapses (> 3 relapses were conservatively assumed to have no additional effect on symptoms).
- Symptoms and outcomes with statistically significant differences between the number of relapses and sufficient sample size (> 30 patients) were included in the analysis.

RESULTS AND INTERPRETATION

Relapse-associated symptoms

- Physician-reported data from the Adelphi database were available for 433 patients with AQP4-Ab+ NMOSD, of whom 128 (29.6%) had ≥ 1 relapse as of data collection.
  - The proportion of patients with symptoms generally increased with the number of relapses (**Table 1**).

Table 1. Key symptoms by number of relapses[a]

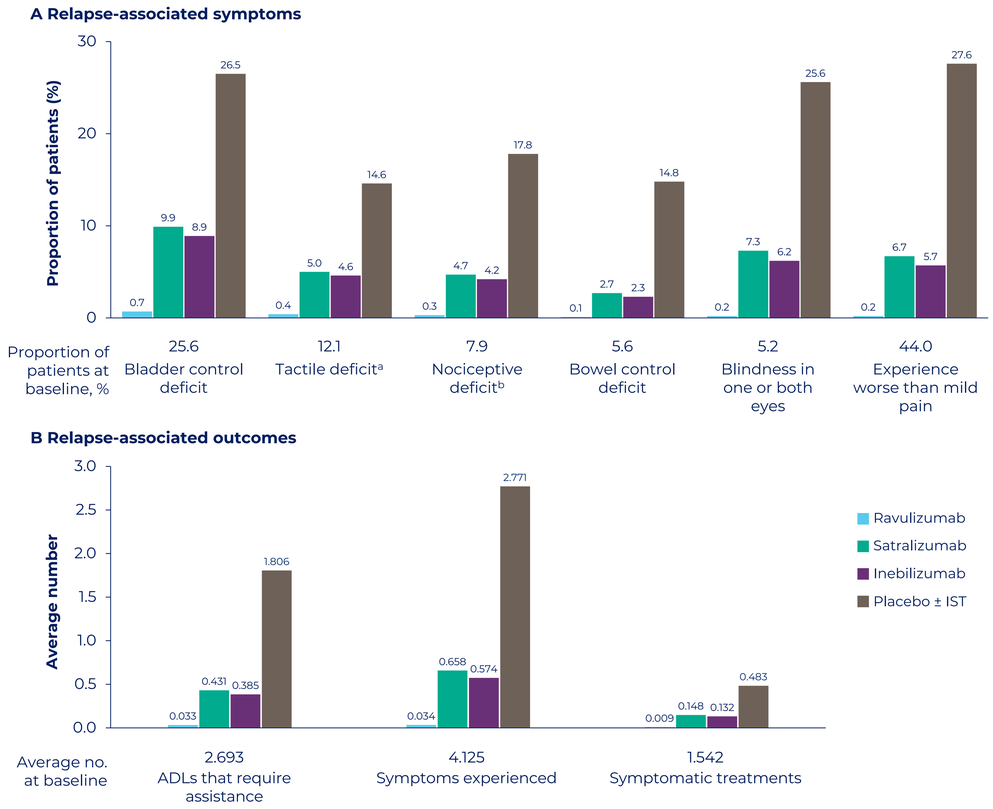
		Number of relapses				
Symptom, n (%)	Overall (N = 433)	0 (n = 305)	1 (n = 82)	2 (n = 24)	3+ (n = 22)	*P* value[b]
Decreased visual acuity	218 (50.3)	154 (50.5)	34 (41.5)	13 (54.2)	17 (77.3)	0.0264
Bladder control deficit	134 (30.9)	78 (25.6)	33 (40.2)	10 (41.7)	13 (59.1)	0.0008
Tactile deficit[c]	66 (15.2)	37 (12.1)	17 (20.7)	4 (16.7)	8 (36.4)	0.0095
Nociceptive deficit[d]	46 (10.6)	24 (7.9)	11 (13.4)	4 (16.7)	7 (31.8)	0.0038
Bowel control deficit	32 (7.4)	17 (5.6)	7 (8.5)	2 (8.3)	6 (27.3)	0.0081
Blindness in one eye	29 (6.7)	13 (4.3)	5 (6.1)	7 (29.2)	4 (18.2)	0.0001
Blindness in both eyes	10 (2.3)	3 (1.0)	3 (3.7)	0	4 (18.2)	0.0007

[a]Data obtained from Adelphi Real World NMOSD DSP. [b]Calculated using Fisher exact test to assess significant differences in the proportion of patients across relapse groups. [c]Decreased touch reception. [d]Decreased pain reception. DSP, Disease Specific Programme; NMOSD, neuromyelitis optica spectrum disorder.

Modeled changes in relapse-associated symptoms and outcomes after 5 years of treatment

- At 5 years, ravulizumab had the lowest proportion of patients with relapse-associated symptoms and outcomes compared with satralizumab, inebilizumab, and placebo with or without IST (**Figure 1**).

Figure 1. Change from baseline in relapse-associated symptoms and outcomes at 5 years

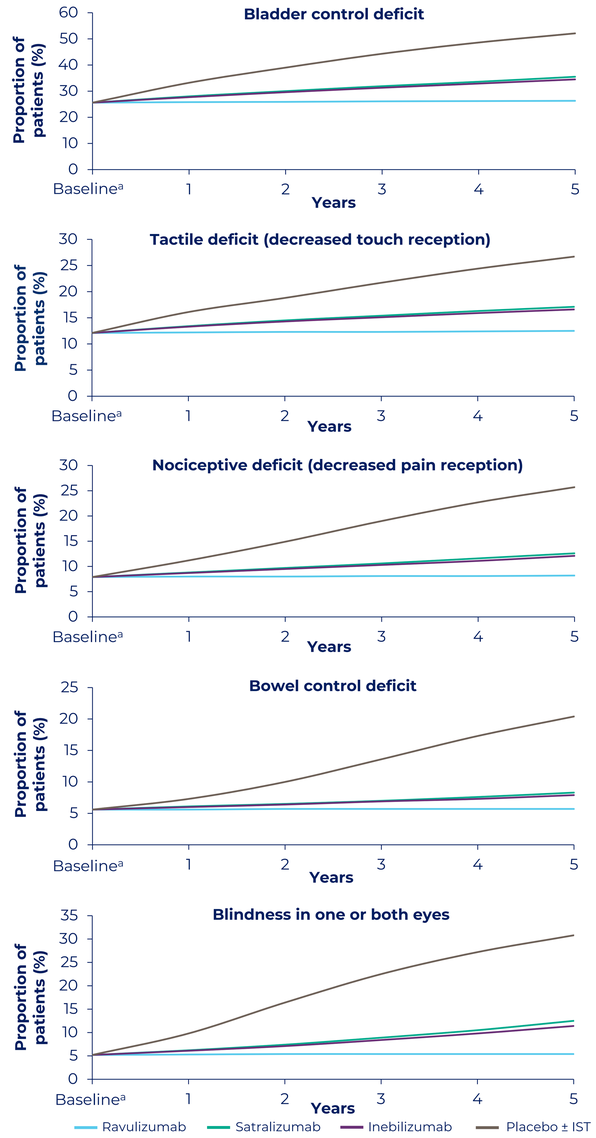


[a]Decreased touch reception. [b]Decreased pain reception. ADL, activities of daily living; IST, immunosuppressive therapy.

Modeled changes over time in key relapse-associated symptoms

- Differences between ravulizumab and other treatments in the proportion of patients with relapse-associated symptoms generally emerged within 2 years and increased over the course of 5 years (**Figure 2**).

Figure 2. Key relapse-associated symptoms across 5 years



[a]Indicates proportion of patients with the symptoms before treatment initiation. IST, immunosuppressive therapy.

Study limitations

- Because this analysis combined data from different sources (Adelphi database and a network meta-analysis) and methods (Markov model), numbers from the study show the general trend in the outcomes expected over time.
- It was assumed that all relapses among patients on any treatment are equally likely to cause symptoms.