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NMO SPOTLIGHT Registry: real-world clinical outcomes with eculizumab and ravulizumab in anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD)

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INTRODUCTION

- AQP4-Ab+ NMOSD is a rare autoimmune disease of the central nervous system characterized by repeated, unpredictable relapses, leading to the accumulation of irreversible neurological disability.[1,2]
- The Alexion complement component 5 inhibitor therapies eculizumab and ravulizumab (ALXN-C5ITs) are approved to treat AQP4-Ab+ NMOSD in several countries and regions, including Europe, Japan, and the United States.[3-8]
- In the phase 3 PREVENT study, eculizumab was associated with a 94.2% reduction in NMOSD relapse risk compared with placebo.[9] In the phase 3 CHAMPION-NMOSD trial, ravulizumab demonstrated a 98.6% reduction in risk of adjudicated on-trial relapse compared with external placebo.[10]
- Real-world safety and effectiveness data are needed to complement the existing body of scientific evidence to better inform clinical practice. To fill this gap, the ongoing, Alexion-sponsored global NMO SPOTLIGHT Registry (NCT05966467) collects ALXN-C5IT real-world safety and clinical effectiveness data in adults with AQP4-Ab+ NMOSD.[11]

OBJECTIVE

- To report the first analysis of the characteristics and clinical outcomes of NMO SPOTLIGHT Registry patients with AQP4-Ab+ NMOSD treated with eculizumab or ravulizumab in real-world clinical practice.

CONCLUSIONS

- Initial NMO SPOTLIGHT Registry results are consistent with clinical trial and real-world data previously reported on eculizumab and/or ravulizumab among patients with AQP4-Ab+ NMOSD.[9,10,12]
- The annualized relapse rate (ARR) decreased from 0.50 in the 1 year prior to ALXN-C5ITs to 0.02 while receiving ALXN-C5ITs, which supports the strong clinical benefit of ALXN-C5ITs in relapse prevention.
- With a median ALXN-C5IT exposure of 40.2 months, most patients (76.7%) received no other NMOSD treatment.
- No patients experienced a meningococcal infection, and no relapses occurred within 4 weeks after receiving a vaccination, either prior to or during ALXN-C5IT treatment.

METHODS

- The NMO SPOTLIGHT Registry is designed to enroll approximately 130-200 patients (aged ≥ 18 years) with AQP4-Ab+ NMOSD in countries or regions where ALXN-C5ITs have received regulatory approval for AQP4-Ab+ NMOSD.
- The planned duration of data collection for the Registry is 5 years from enrollment of the last patient. For this analysis, data were collected from patients in the United States and Argentina, enrolled from August 2023 to the data cutoff of June 21, 2024.
- Eligible patients have NMOSD relapse and treatment history for 1 year prior to ALXN-C5IT initiation and are treated at enrollment with an ALXN-C5IT (≥ 1 dose of eculizumab within 4 weeks prior to enrollment or ≥ 1 dose of ravulizumab within 12 weeks prior to enrollment).
- NMOSD treatments, the number and characteristics of relapses (eg, type of relapses: acute myelitis, optic neuritis, other), meningococcal vaccination, and meningococcal infection data are collected retrospectively from 1 year prior to ALXN-C5IT initiation and prospectively starting at enrollment.
- Safety data are also collected prospectively from enrollment through data cutoff.
- Relapses were physician-reported and defined by the following criteria:
  - New onset of neurologic symptoms or worsening of existing neurologic symptoms.
  - Persisted for > 24 hours.
  - Preceded by ≥ 30 days of clinical stability.
  - Required acute treatment (high-dose intravenous [IV] steroids, plasma exchange, or IV immunoglobulin).

RESULTS AND INTERPRETATION

Patient characteristics

- Of the 38 patients enrolled as of the data cutoff, 30 had available data for this analysis. The majority of patients were female, with a median age at initial diagnosis of 47.0 (first quartile, third quartile [Q1, Q3]: 35.0, 57.0) years (**Table 1**).
- Median duration of exposure to eculizumab (n = 30) and ravulizumab (n = 2) was 40.2 (Q1, Q3: 24.0, 49.7) months and 1.0 (0.7, 1.3) months, respectively.

Table 1. Demographics and characteristics of NMO SPOTLIGHT Registry patients

Characteristic	Overall Registry population (N = 30)
Age at the time of informed consent, median (Q1, Q3), years	53.5 (42.0, 64.0)
Sex, n (%)	
Female	26 (86.7)
Male	4 (13.3)
Race, n (%)	
Asian	1 (3.3)
Black or African American	14 (46.7)
White	15 (50.0)
Geographic location, n (%)	
Argentina	2 (6.7)
United States	28 (93.3)
Age at first symptom onset, median (Q1, Q3), years	42.0 (27.0, 56.0)[a]
Age at initial diagnosis, median (Q1, Q3), years	47.0 (35.0, 57.0)[a]
Age at the time of ALXN-C5IT initiation, median (Q1, Q3), years	51.0 (40.0, 60.0)
Time from ALXN-C5IT initiation to enrollment, median (Q1, Q3), months	38.2 (20.1, 45.4)
ALXN-C5IT therapy received, n (%)	
Eculizumab	28 (93.3)
Eculizumab to ravulizumab switch	2 (6.7)
Most common NMOSD therapy in the 1 year prior to ALXN-C5IT (n ≥ 4), n (%)	
Rituximab	9 (30.0)
Immunosuppressive therapies	5 (16.7)
Corticosteroids	4 (13.3)
Other medication/therapies	4 (13.3)

[a]Age at first symptom onset and at initial diagnosis were unknown in 1 patient.
ALXN-C5IT, Alexion complement component 5 inhibitor therapies (eculizumab and ravulizumab); NMOSD, neuromyelitis optica spectrum disorder; Q1, first quartile; Q3, third quartile.

NMOSD relapse

- In the 1 year prior to ALXN-C5IT initiation, 10 (33.3%) patients had 15 relapses for an ARR of 0.50 (**Figure 1**).
  - More than 1 type of relapse may have occurred for a single relapse episode:
    - 6 patients had 10 acute myelitis.
    - 5 patients had 9 optic neuritis.
    - 2 patients had 2 area postrema syndrome.
    - 2 patients had 2 acute brainstem syndrome.
- While on ALXN-C5ITs, 2 (6.7%) patients had 2 relapses (acute myelitis, n = 2) for an ARR of 0.02.
- No relapses occurred within 4 weeks after a meningococcal or any other type of vaccination, either prior to or during ALXN-C5IT treatment.
- Prior to ALXN-C5IT initiation, all brain magnetic resonance imaging (MRI) and 80% of spinal MRIs performed following a relapse were consistent with relapse.
- After ALXN-C5IT initiation, all brain and spinal MRIs performed following a relapse were not consistent with relapse.

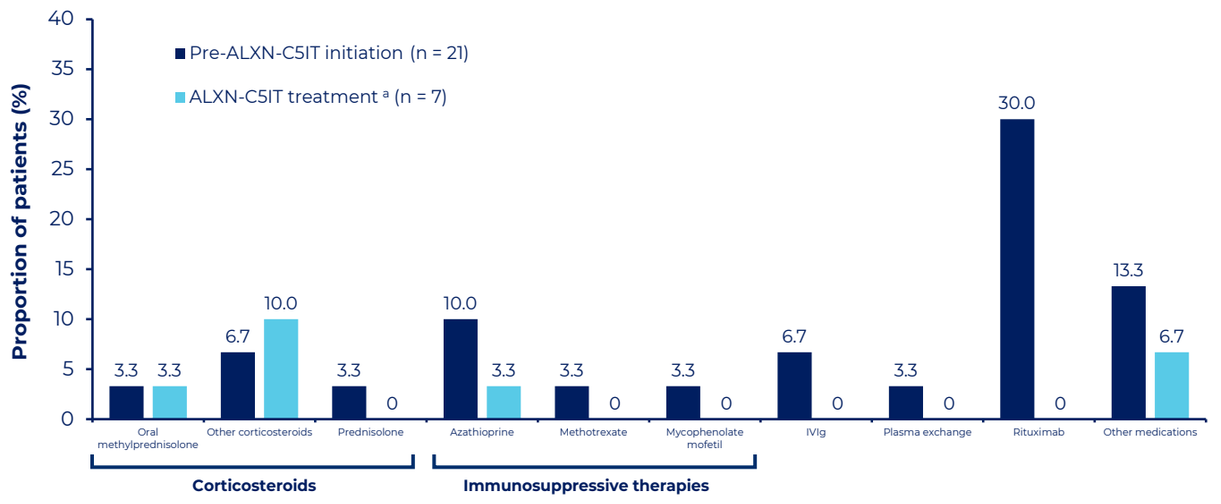
Figure 1. Incidence of relapse prior to and during ALXN- C5IT treatment (N = 30)

[a]Defined as the duration from the initiation of ALXN-C5IT treatment until its discontinuation, the date of Registry completion, lost to follow - up, or death, excluding any interruptions in treatment with eculizumab and/or ravulizumab.
ALXN-C5IT, Alexion complement component 5 inhibitor therapies (eculizumab and ravulizumab); ARR, annualized relapse rate; Q1, first quartile; Q3, third quartile

Acute and maintenance NMOSD therapies

- In the year prior to ALXN-C5IT initiation, 21/30 (70.0%) patients received treatment for NMOSD (rituximab, 30.0%; other immunosuppressive therapies, 16.7%) (**Figure 2**).
- While on ALXN-C5ITs, 7 patients received other treatments for NMOSD with corticosteroids as the most common (13.3%).
  - Twenty-three (76.7%) patients received no other treatments for NMOSD while on ALXN-C5ITs.

Figure 2. Acute and maintenance NMOSD therapies by ALXN-C5IT treatment status



[a]Defined as the duration from the initiation of ALXN-C5IT treatment until its discontinuation, the date of Registry completion, l ost to follow-up, or death, excluding any interruptions in treatment with eculizumab and/or ravulizumab.
ALXN-C5IT, Alexion complement component 5 inhibitor therapies (eculizumab and ravulizumab); IVIg, intravenous immunoglobulin; NMOSD, neuromyelitis optica spectrum disorder.

Safety

- No new safety signals were observed in patients treated with ALXN-C5ITs.
- No patients experienced a meningococcal infection.

Meningococcal vaccination

- In the year prior to ALXN-C5IT through Registry enrollment, 29 (96.7%) patients received any meningococcal vaccination (**Table 2**).
- Six of 9 patients who received rituximab in the year prior to ALXN-C5IT initiation had a median time from last rituximab discontinuation date to first meningococcal vaccination of 14.5 days.
  - Three of 9 patients were receiving rituximab at the time of a meningococcal vaccination.

Table 2. Meningococcal vaccination

Attribute	Overall Registry population (N = 30)
Received any meningococcal vaccination from 1 year prior to ALXN -C5IT initiation through data cutoff,[a] n (%)	29 (96.7)[b]
Time from latest vaccination prior to ALXN-C5IT initiation to ALXN-C5IT initiation, median (Q1, Q3), days	37.0 (15.0, 50.0)[c]
Receiving NMOSD treatment at the time of any meningococcal vaccination, n	7
Rituximab	3
Azathioprine	2
Corticosteroids, overall	2
Methotrexate	1
Time from last rituximab discontinuation date to first meningococcal vaccination	
n	6
Median (Q1, Q3), days	14.5 (-45.0, 167.0)

[a]Vaccinations received beyond 1 year prior to ALXN -C5IT initiation are not captured. [b]One patient received vaccination within 30 days after ALXN -C5IT initiation, and 3 patients received vaccination beyond 30 days after ALXN-C5IT initiation. [c]25 patients included.
ALXN-C5IT, Alexion complement component 5 inhibitor therapies (eculizumab and ravulizumab); NMOSD, neuromyelitis optica spectrum disorder; Q1, first quartile; Q3, third quartile.

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Poster

Data were previously presented at at the American Academy of Neurology (AAN) Annual Meeting, April 5-9, 2025, San Diego, CA.
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