Satralizumab Treatment in Adult Patients With AQP4-IgG–Seropositive Neuromyelitis Optica Spectrum Disorder: A Case Series

CSR04

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BACKGROUND

- Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune neuroinflammatory disease that primarily affects the optic nerves and spinal cord and can lead to sensory and motor impairment, vision loss and permanent neurological disability[1]
- Satralizumab is a humanized monoclonal recycling antibody against the interleukin 6 (IL-6) receptor with demonstrated safety and efficacy in patients with NMOSD in 2 randomized, placebo-controlled Phase III clinical trials (SAkuraSky [NCT02028884] and SAkuraStar [NCT02073279])[2,3]; the safety and efficacy were sustained over the long-term in the open-label extension (OLE) periods[4,5]
  - The long-term safety and efficacy of satralizumab continue to be monitored in the ongoing SAkuraMoon (NCT04660539) OLE study evaluating patients who have completed the SAkuraSky and SAkuraStar OLE periods
  - A small number of patients in SAkuraSky and SAkuraStar received prior rituximab (>6 months prior to study entry as mandated by the study protocol), with outcomes comparable to those in the overall study population[2,3]
- The US Food and Drug Administration (FDA) approved satralizumab for use in adult patients with aquaporin-4–positive (AQP4-IgG+) NMOSD in 2020, but real-world data are limited

OBJECTIVE

- To describe the experience with satralizumab in adult patients with AQP4-IgG+ NMOSD

METHODS

- Case information for patients with AQP4-IgG+ NMOSD who had received satralizumab for ≥6 months was obtained from US healthcare professionals
  - Healthcare professionals were asked to provide information for all patients in their practice who received satralizumab and provided consent
  - All cases (regardless of the clinical outcomes or the patient's experience) that fit the inclusion criteria were included in the publication
- Patient characteristics, examination findings, diagnostic test results, treatment response and reported adverse events were recorded
- All patients provided consent for the publication of their case information

RESULTS

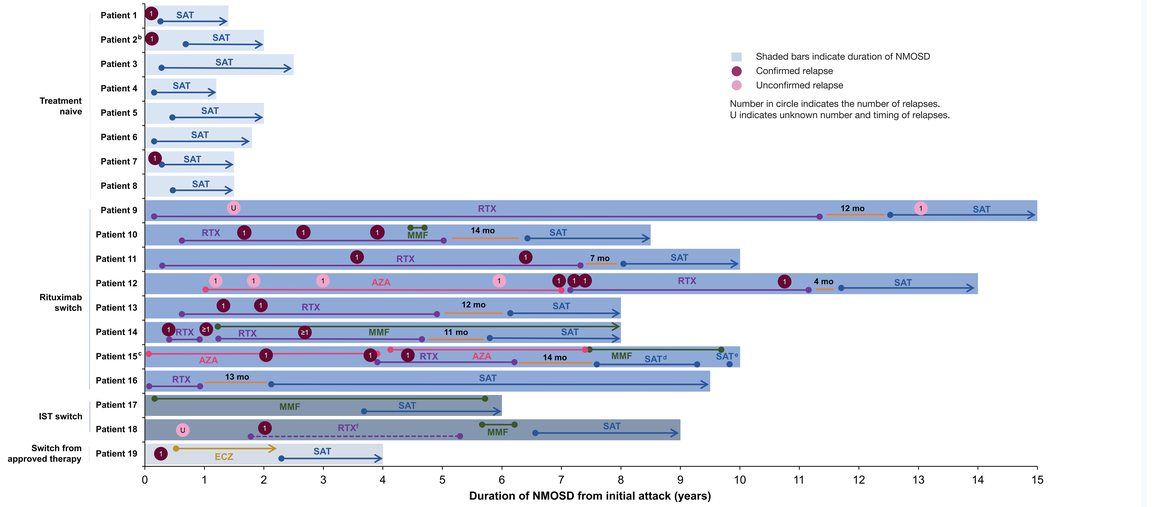
- A total of 19 patients aged 23 to 74 years were included; 8 self-identified as White, 7 as Black and 4 as Hispanic (**Table**)
- NMOSD disease duration ranged from 1 to 15 years
- Eight patients were preventive-treatment naive, 8 had received rituximab (1 with concomitant mycophenolate mofetil [MMF] and 1 with azathioprine and MMF), 2 received MMF alone and 1 received eculizumab before initiating satralizumab
  - The most common reasons for initiation of satralizumab were new diagnosis (n=8), intolerance of previous treatment (n=5) and inadequate disease control/relapse (n=3)
  - In the 8 patients who switched from rituximab to satralizumab, the interval between therapies ranged from 4 to 14 months
- As of March 2023, patients had received satralizumab for 13 to 88 months (**Figure**)
  - Almost all (18 of 19) patients were relapse free with satralizumab
    - One patient (Patient 9) experienced relapse symptoms characterized by increased paresthesia in all 4 limbs, which did not lead to treatment discontinuation. There were no objective findings on neurological examination; brain and cervical/thoracic MRI showed no new or enhancing lesions
  - Overall, all patients maintained disease control with satralizumab, with few adverse events reported
    - One patient (Patient 15) temporarily and then permanently discontinued satralizumab due to asymptomatic neutropenia
    - One patient (Patient 19) temporarily paused satralizumab for 1 dose due to transient neutropenia

Table. Demographic and clinical characteristics of and safety events in patients with AQP4-IgG+ NMOSD who received satralizumab

Category	Patient	Age, years	Sex	Race and ethnicity[a]	Comorbid or previous autoimmune disease	Disease phenotype	EDSS score[b]	Reason for initiation of satralizumab	Laboratory abnormalities and AEs considered possibly related to satralizumab[c]	Other laboratory abnormalities and AEs[c]
Treatment naive	1	74	F	White	Myasthenia gravis	Optic	4	Newly diagnosed	None noted	None noted
	2	60	F	Hispanic	Hypothyroidism	Optic	4	Newly diagnosed	Slight elevation in ALT, which resolved; slight elevation in triglycerides and cholesterol	Elevated glucose related to diabetes and prednisone use; tinea corporis related to prednisone use
	3	67	F	White	Positive anti-dsDNA but no clinical SLE	Spinal	6.5	Newly diagnosed	None noted	None noted
	4	65	F	Black	Possible MOGAD[d]	Optic	4	Newly diagnosed	Mild lymphopenia, which resolved	None noted
	5	66	F	Hispanic	None	Spinal	1	Newly diagnosed	Mild leukopenia and thrombocytopenia; mild worsening of hyperlipidemia	None noted
	6	31	F	Black	None	Spinal	6.5	Newly diagnosed	Mild leukopenia	No change in baseline hyperlipidemia
	7	41	F	White	Sjogren syndrome	Opticospinal	NA	Newly diagnosed	Transient abdominal bloating after injection	None noted
	8	62	F	White	Hypothyroidism	Optic	NA	Newly diagnosed	None noted	None noted
Rituximab switch	9	53	F	White	Autoimmune lymphocytic colitis	Spinal	3	Hypogammaglobulinemia and recurrent infections	Mild elevation in total cholesterol and LDL. Levels returned to normal with rosuvastatin treatment	Herpes zoster considered related to long-standing rituximab use, hypogammaglobulinemia and concomitant budesonide use
	10	23	F	Hispanic	None	Opticospinal	8	Intolerance to rituximab	Asymptomatic, slight reduction in platelet count, which resolved	None noted
	11	69	F	White	SLE	Opticospinal	3	Hypogammaglobulinemia and recurrent infections	None noted	Upper respiratory infection, which resolved
	12	39	F	Black	None	Optic	4.5	Inadequate disease control/relapse	None noted	None noted
	13	31	F	Black	None	Opticospinal	2	Inadequate disease control/relapse	None noted	None noted
	14	51	F	White	Myasthenia gravis	Opticospinal	NA	Inadequate disease control/relapse	None noted	None noted
	15	39	F	Black	SLE	Spinal	5.5	Persistent lymphopenia (complicated by multiple ISTs)	Neutropenia[e]	Total leukopenia
	16	26	M	White	ADEM	Spinal	6.5	Insurance reasons	None noted	None noted
IST switch	17	67	M	Hispanic	Hypothyroidism	Spinal	6.5	Switch to FDA-approved treatment with goal of tapering MMF	None noted	Leukopenia, low C4 complement, elevated LDL, slightly elevated GGT levels
	18	29	F	Black	None	Opticospinal	NA	Intolerance to MMF	None noted	Hypogammaglobulinemia but present post rituximab
Switch from approved therapy	19	55	F	Black	None	Spinal	NA	Preferred less frequent treatment	Contact dermatitis and postinflammatory hypopigmentation of the foot and neutropenia, which resolved[f]	None noted

ADEM, acute disseminated encephalomyelitis; AE, adverse event; ALT, alanine aminotransferase; AQP4, aquaporin-4; dsDNA, double-stranded DNA; EDSS, Expanded Disability Status Scale; F, female; FDA, US Food and Drug Administration; GGT, gamma-glutamyltransferase; IgG, immunoglobulin G; IST, immunosuppressive therapy; LDL, low-density lipoprotein; M, male; MMF, mycophenolate mofetil; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; NA, not available; NMOSD, neuromyelitis optica spectrum disorder; SLE, systemic lupus erythematosus.
[a]Race reported as Black or African American is referred to as Black, and ethnicity reported as Hispanic or Latino/Latina is referred to as Hispanic. [b]At time of switch to satralizumab. [c]All AEs were reported to US Drug Safety as required. [d]Confirmed AQP4-IgG-positive NMOSD using the cytometric bead array assay from Mayo Clinic Laboratories. [e]Initial neutropenia episode did not resolve until both satralizumab and then MMF were discontinued. The first satralizumab discontinuation was for 7 months. Satralizumab was resumed, but neutropenia recurred after initial loading dose, and satralizumab was discontinued. At the time of the most recent follow-up, which was 1 month later, neutropenia was persistent and satralizumab was permanently discontinued. [f]Resulted in temporary discontinuation of satralizumab.

Figure. Timeline of NMOSD treatments and suspected or confirmed relapses[a]



AZA, azathioprine; ECZ, eculizumab; IST, immunosuppressive therapy; MMF, mycophenolate mofetil; NMOSD, neuromyelitis optica spectrum disorder; RTX, rituximab; SAT, satralizumab; SLE, systemic lupus erythematosus.
[a]Only relapses after initial attack are indicated in this figure. All patients had an initial attack. [b]Duration of NMOSD based on time since NMOSD diagnosis. The patient first presented with optic neuritis in 1997, but she received no preventive treatment and was symptom free until February 2021. Patient also receives prednisone. [c]Patient also receives prednisone for SLE. [d]Satralizumab was discontinued for 7 months due to neutropenia. [e]Satralizumab was resumed after MMF was discontinued, and neutropenia resolved. After initial loading dose, neutropenia recurred and satralizumab was discontinued. [f]Exact timing and duration of rituximab treatment unknown. The duration was estimated to be 2 to 4 years.

LIMITATIONS

- The limitations of this presentation are those inherent to case reports, including the small number of patients, partially missing data and the retrospective design
- The duration of treatment with satralizumab was shorter than the duration of previous NMOSD treatment in all patients; thus, comparison of the number of relapses with each treatment should be evaluated with caution
- Despite these limitations, this case series provides valuable real-world data on patients with AQP4-IgG+ NMOSD who received satralizumab after previous treatment with biologics, including long-term rituximab, and conventional ISTs. Future studies of a larger number of patients will help to further elucidate the clinical response to satralizumab in patients with NMOSD

CONCLUSIONS

- In this ongoing retrospective case series, satralizumab was effective and well tolerated in patients with NMOSD, including those with concomitant autoimmune comorbidities, who switched due to ineffectiveness and/or poor tolerability of their previous treatment
- As of March 2023, almost all (18 of 19) patients were relapse free after switching to satralizumab
  - The one patient relapse reported was not confirmed radiographically and did not lead to treatment discontinuation
- No major safety events were reported in any of the patients after switching to satralizumab, and almost all (18 of 19) patients continue to receive satralizumab
  - One patient permanently discontinued satralizumab due to asymptomatic neutropenia
- These outcomes align with the long-term safety and efficacy outcomes with satralizumab in the Phase III SAkura clinical trials

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DISCLOSURES

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Scan this QR code or visit https://forms.gle/PT3BTmJhaoKnUp9Z8 to contribute cases from your practice to this ongoing case series

A PDF of this poster can be downloaded by scanning the QR code or visiting https://bit.ly/3LN2FLI

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