P301

# Infection in NMOSD: An Analysis of the Patterns of Infections in SAkuraMoon (an Open-label Study to Evaluate the Long-term Safety and Efficacy of Satralizumab▼) with Post-marketing Data and US-based Health Claims Data

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## INTRODUCTION

- Satralizumab (SAT), an interleukin-6 receptor (IL-6R) inhibitor, was approved for the treatment of AQP4-IgG+ neuromyelitis optica spectrum disorder (NMOSD) based on the positive results of the SAkura studies[1,2]
- The rate of adverse events (AEs) and serious AEs, including infections, was comparable between the placebo and SAT groups in the double-blind period (DBP) of the pivotal studies[3]
- The majority of patients from the SAkura studies rolled over to SAkuraMoon, an open-label study to evaluate the long-term safety of SAT
- Given that long-term use of ISTs and other IL-6R inhibitors have been associated with risk of infection,[4-6] continued evaluation of the patterns of infection in the NMOSD population outside of a controlled setting is warranted

## OBJECTIVES

- To evaluate the pattern of infection following long-term SAT treatment in the SAkura studies and to compare the post-marketing (PM) experience to real-world data (RWD) from a US claims database

## METHODS

- Analyses were based on: a) **SAkura clinical trials:** combined data from SAkuraSky, SAkuraStar and SAkuraMoon, from patients' first dose in the DBP or open-label extension period to the clinical cut-off date (CCOD) of 31 Jan 23; b) **SAT PM experience data:** retrospective analysis of the Periodic Benefit–risk Evaluation Reports (6-month intervals) between 1 Jun 20 (first approval) to 31 May 23; c) **US PharMetrics claims RWD:** retrospective analysis of data from patients with NMOSD between 1 Jan 17 to 31 Oct 22
- AEs were identified as infections when coded to the MedDRA system organ class 'Infections and Infestations' in the SAkura studies and PM reports. In the US PharMetrics claims database, infections were defined when ≥1 International Classification of Diseases, Tenth Revision (ICD-10) code for an infection was used, and ≥1 ICD-10 code for an infection listed on the same administrative claim as an inpatient visit established a serious infection
- Data for defined follow-up (FU) periods were used to establish incidence rates of infection/serious infection per 100 patient-years (IR/100 PY) in the SAkura studies. Cumulative incidence (%) of infection/serious infection were calculated for SAT PM data and US claims RWD

## RESULTS

- Baseline demographics of patients from these analyses are shown in **Table 1**
- Patients in the SAkura studies had a median baseline EDSS score of 3.5
- 87.1% of patients in the US claims RWD had a Charlson Comorbidity Index score of 0–1 (EDSS score information not available)

**Table 1:** Baseline demographics

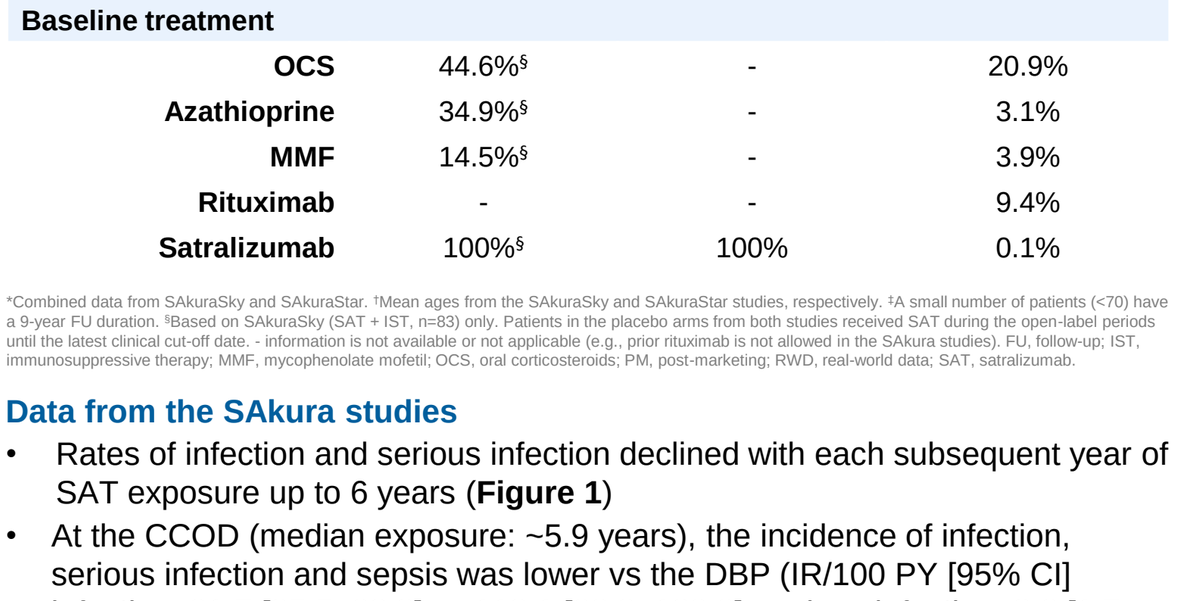
| | SAkura studies* | SAT PM data | US claims RWD |
|---|---|---|---|
| **No. of patients** | 166 | 2,951 | 2,872 |
| **Mean age (years)** | 40.8, 45.3† | - | 45.3 |
| **Duration of follow-up** | 6 years‡ | 3 years | 4 years |
| **Baseline treatment** | | | |
| **OCS** | 44.6%§ | - | 20.9% |
| **Azathioprine** | 34.9%§ | - | 3.1% |
| **MMF** | 14.5%§ | - | 3.9% |
| **Rituximab** | - | - | 9.4% |
| **Satralizumab** | 100%§ | 100% | 0.1% |

*Combined data from SAkuraSky and SAkuraStar. †Mean ages from the SAkuraSky and SAkuraStar studies, respectively. ‡A small number of patients (<70) have a 9-year FU duration. §Based on SAkuraSky (SAT + IST, n=83) only. Patients in the placebo arms from both studies received SAT during the open-label periods until the latest clinical cut-off date. - information is not available or not applicable (e.g., prior rituximab is not allowed in the SAkura studies). FU, follow-up; IST, immunosuppressive therapy; MMF, mycophenolate mofetil; OCS, oral corticosteroids; PM, post-marketing; RWD, real-world data; SAT, satralizumab.

### Data from the SAkura studies

- Rates of infection and serious infection declined with each subsequent year of SAT exposure up to 6 years (**Figure 1**)
- At the CCOD (median exposure: ~5.9 years), the incidence of infection, serious infection and sepsis was lower vs the DBP (IR/100 PY [95% CI] infection: 91.7 [85.5, 98.3] vs 113.1 [98.8, 129.0]; serious infection: 2.6 [1.7, 3.9] vs 4.1 [1.8, 8.0]; and sepsis: 0.56 [0.2, 1.3] vs 1.01 [0.1, 3.7])
- The incidence of serious infection was higher in patients with a baseline EDSS score ≥4.0 vs an EDSS score <4.0 (17.3% vs 5.6%, respectively)

**Figure 1:** IR/100 PY of infection and serious infection by year of exposure **(A)** and incidence of serious infection vs baseline EDSS scores **(B)**




Note, 1 case did not report EDSS score at baseline.
EDSS, Expanded Disability Status Scale; GI, gastrointestinal; IR/100 PY, incidence rate per 100 patient-years; LRTI, lower respiratory tract infection; UTI, urinary tract infection.

## RESULTS (cont'd)

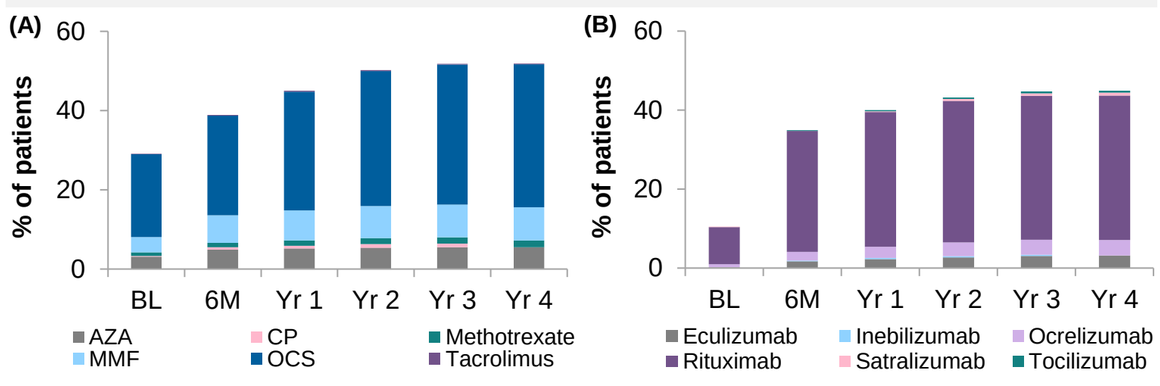
### Data from SAT PM experience

- With up to 3 years of SAT exposure, the cumulative incidence of infection, serious infection and sepsis was 7.3%, 3.8% and 0.6%, respectively
- The incidence of serious infection and sepsis was higher in patients aged >65 years vs patients aged 18–65 years (serious infection: 5.2% [37/710] vs 3.1% [67/2,139]; sepsis: 1.4% [10/710] vs 0.3% [7/2,139], respectively)
- 58.8% (10/17) of patients with sepsis had a baseline EDSS score ≥4 (5 cases unreported). ISTs were concomitant medications in 76.5% (13/17) of patients (4 cases unreported). Three sepsis cases were fatal

### Data from US claims RWD

- Oral corticosteroids (36.1%) and rituximab (36.6%) were the most commonly used ISTs and biologic treatments over a 4-year FU period, respectively. Only 0.7% of patients received SAT at 4-year FU (**Figure 2**)
- At 4-year FU, the cumulative incidence (%) of infection, serious infection and sepsis was 67.3%, 8.4% and 4.4%, respectively

**Figure 2:** Use of ISTs (**A**) and biologics (**B**) among patients with NMOSD in US claims RWD

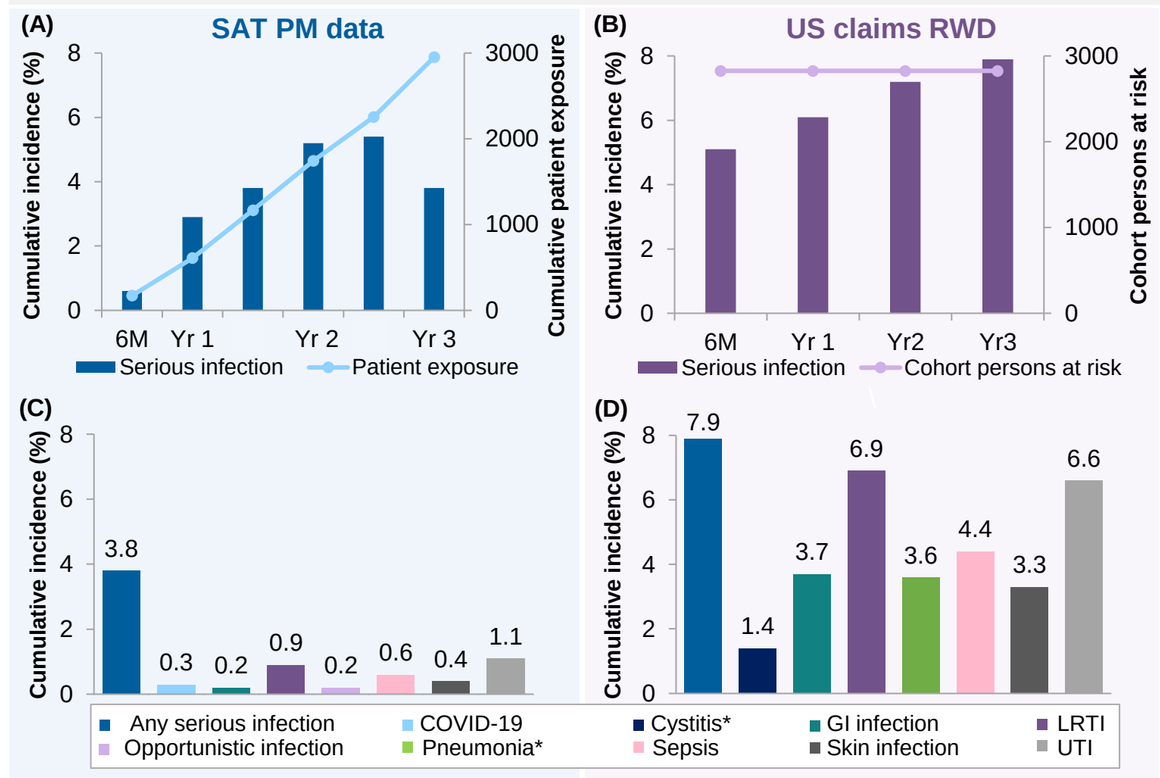



AZA, azathioprine; BL, baseline; CP, cyclophosphamide; IST, immunosuppressive therapy; MMF, mycophenolate mofetil; NMOSD, neuromyelitis optica spectrum disorder; OCS, oral corticosteroids; RWD, real-world data.

### Data from the SAT PM experience and US claims RWD

- In the SAT PM data, the cumulative incidence of serious infection was consistently lower than US claims RWD over a 3-year period (3.8% vs 7.9% at 3-year FU) (**Figure 3A–B**)
- The most common types of serious infection in both the SAT PM data and US claims RWD were urinary tract infections, lower respiratory tract infections and sepsis (**Figure 3C–D**)

**Figure 3:** Cumulative incidence of patients with serious infection (**A–B**) and types of serious infection (**C–D**) in SAT PM data and US claims RWD




*In satralizumab, pneumonia and cystitis are part of the LRTI and UTI baskets, respectively. GI, gastrointestinal; LRTI, lower respiratory tract infection; PM, post-marketing; RWD, real-world data; SAT, satralizumab; UTI, urinary tract infection.

## LIMITATIONS

- Direct comparisons of infection rates should be interpreted with caution due to differences in study design and populations
- Low rates of non-serious infection in the SAT PM data is likely due to under-reporting

## CONCLUSIONS

- The US claims RWD indicates that infection is a major comorbidity in NMOSD, independent of IL-6R inhibitor treatment
- The rate of infection, serious infection and sepsis was consistently lower in SAT-treated patients compared to the US claims RWD (where >99% of patients were not receiving SAT)
- EDSS score ≥4.0, age >65 years and IST use were major covariates of serious infection and sepsis in SAT-treated patients

## REFERENCES

1. Yamamura T, et al. *N Engl J Med* 2019;381:2114–24; 2. Traboulsee A, et al. *Lancet Neurol* 2020;19:402–12; 3. Yamamura T, et al. *Mult Scler Relat Disord* 2022;66:104025; 4. Dooley MA, et al. *N Engl J Med* 2011;365:1886; 5. Singh JA, et al. *BMC Med* 2016;14:137; 6. Pawar A, et al. *Ann Rheum Dis* 2019;78:456–64.

## DISCLOSURES

**BMG** received consulting fees from Alexion, Novartis, EMD Serono, Viela Bio, Genentech/Roche, Greenwich Biosciences, Axon Advisors, Rubin Anders, ABCAM, Signant, IQVIA, Sandoz, Druggability Technologies, Genzyme, and Immunovant. He receives contracted research fees from Clene Nanomedicine. He receives royalties from UpToDate. **KF** received grants from Ministry of Education of Japan, Ministry of Health, Welfare and Labour of Japan; received personal fees from Roche/Chugai, Alexion, Viela Bio, Biogen, Eisai, Mitsubishi Tanabe, Novartis, Astellas, Takeda, UCB, Merck Biopharma, AbbVie, and Asahi Kasei. **BW** reports consulting fees from UCB Biosciences, Mitsubishi Tanabe, Genentech, and Roche, and speaking fees from Genentech, Roche, and Novartis; he participated on the Attack Adjudication Committee for Alexion and Horizon Therapeutics (formerly MedImmune/Viela Bio). He reports personal fees from Chugai. He has a patent NMO-IgG for diagnosis of neuromyelitis optica with royalties received from RSR Ltd., Oxford University, Hospices Civils de Lyon, and MVZ Labor PD Dr. Volkmannund Kollegen GbR. **FP** received personal fees for speaking activities or serving on advisory boards from Alexion, Almirall, Bayer, Biogen, Bristol, Janssen, Merck, Novartis, Roche, and Sanofi. He further received research grants from Alexion, Almirall, Biogen Global, Merck, Novartis, Roche, FIS, Italian Health Ministry, University of Catania, and Reload Onlus Association. **IK** has received personal compensation for consulting, serving on a scientific advisory board, speaking or other activities from Alexion, Almirall, Bayer, Biogen, Hexal, Horizon, Merck, Neuraxpharm, Roche/Chugai, and Sanofi. **JLB** reports payment for consultation from MedImmune/Viela Bio; personal fees from AbbVie, Alexion, Antigenomycs, Beigene, Chugai, Clene Nanomedicine, EMD Serono, Genentech, Genzyme, Mitsubishi Tanabe, Novartis, Reistone Bio, Roche, Imcyse, and TG Therapeutics; grants from the National Institutes of Health, Novartis, Alexion, and Mallinckrodt; speaker bureau for Alexion, and has a patent for Aquaporumab issued. **JP** has received support for scientific meetings and honoraria for advisory work from Merck Serono, Novartis, Chugai, Alexion, Roche, Medimmune, Argenx, Vitaccess, UCB, Mitsubishi, Amplo, Janssen, and grants from Alexion, Argenx, Roche, Medimmune, and Amplo Biotechnology. Patent ref P37347WO and licence agreement for Numares multimarker MS diagnostics Shares in AstraZeneca. Her group has been awarded an ECTRIMS fellowship and a Sumaira Foundation grant to start later this year. A Charcot fellow worked in Oxford 2019-2021. Acknowledges partial funding to the trust for highly specialised services for NHS England. On the medical advisory boards of the Sumaira Foundation and MOG project charities, is a member of the Guthy Jackson Foundation Charity and on the Board of the European Charcot Foundation and the steering committee of MAGNIMS and the UK NHSE IVIG Committee and chairman of the NHSE neuroimmunology patient pathway and ECTRIMS Council member on the educational committee since June 2023. On the ABN advisory groups for MS and neuroinflammation and neuromuscular diseases. **MT, KB, AB, IN** and **GK** are full-time employees of F. Hoffmann La-Roche Ltd. **TY** Served on scientific advisory boards for Chugai, Roche, Biogen Japan, Biogen MA, Novartis, and Mitsubishi Tanabe; received research grants from Chugai, Novartis, Biogen Japan, Chiome Bioscience, Sanofi, UCB Japan, and Mebix; received speaker honoraria from Chugai, Biogen Japan, Novartis, Mitsubishi Tanabe, Takeda, Miyarisan, Alexion, Sumitomo, and Teijin.

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▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPc for information on the reporting of suspected adverse reactions or report to your local Roche Drug Safety contact at: https://www.roche.com/solutions/pharma/safety-reporting. The clinical trials from which data were included were conducted with informed written consent from participating patients, with the approval of the ethics committee or institutional review board for each participating study site and in accordance with the Helsinki Declaration of 1964, as revised in 2013. The PM data and US PharMetrics claims databases from which data were included only used de-identified patient data; therefore, informed consent for this analysis was not needed.

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