P-675

Time to vaccination after rituximab (RTX) discontinuation in patients with anti–aquaporin-4 antibody–positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD): A post hoc analysis of the CHAMPION-NMOSD trial

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INTRODUCTION

- In the US, rituximab (RTX) was often prescribed off-label for patients with anti–aquaporin-4 antibody–positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD) due to a lack of approved therapies, but patients may have transitioned to ravulizumab, a complement component 5 inhibitor therapy (C5IT) that has since been approved for AQP4-Ab+ NMOSD[1]
- Vaccination against *Neisseria meningitidis (Nm)* is the primary risk-mitigating strategy for C5ITs, like ravulizumab[2,3]
  - If urgent C5IT is indicated in a patient not up to date with *Nm* vaccines, patients should be provided antibiotic prophylaxis and given *Nm* vaccines as soon as possible[2,3]
- Although meningococcal vaccines trigger a T-cell response, prior anti–B-cell therapy may attenuate part of the response to clinically relevant vaccines[4,5]
- CHAMPION-NMOSD (NCT04201262) is a global, open-label, phase 3 study evaluating ravulizumab in patients with AQP4-Ab+ NMOSD, approximately one-third of whom had prior RTX exposure
  - CHAMPION-NMOSD enrolled the greatest proportion of patients with prior RTX exposure than all other NMOSD trials (**Table 1**)

Table 1. Proportion of patients with prior RTX exposure in NMOSD trials

Trial	AQP4-Ab+ patients, n/N (%)	Treatment arm (ITT), n/N (% RTX)	Placebo arm, n/N (% RTX)	Total treatment and placebo arm, n/N (% RTX)
SakuraSky[6] (satralizumab ± ISTs)	55/83 (66)	NA[a]	NA[a]	NA[a]
SakuraStar[7] (satralizumab monotherapy)	64/95 (67.4)	8/63 (13)	4/32 (13)	12/95 (12.6)
N-MOmentum[8-10] (inebilizumab)	213/230 (92.6)	13/174 (7.47)	4/56 (7.1)	17/230 (7.4)
PREVENT[11-12] (eculizumab ± ISTs)	143/143 (100)	26/96 (27.1)	20/47 (42.6)	46/143 (32.2)
CHAMPION-NMOSD[13] (ravulizumab ± ISTs)	58/58 (100)	21/58 (36.2)	NA[b]	21/58 (36.2)

[a]The use of anti-CD20 agents, including RTX, was not permitted during the trial and for 6 months before baseline.
[b]The placebo group from the PREVENT trial was used as the control group in the CHAMPION-NMOSD trial.
AQP4-Ab+, anti–aquaporin-4 antibody–positive; **ITT**, intent-to-treat; **IST**, immunosuppressive therapy; **NA**, not available; **NMOSD**, neuromyelitis optica spectrum disorder; **RTX**, rituximab.

OBJECTIVE

- To report the time from last RTX dose to the first administered meningococcal vaccine in patients from the CHAMPION-NMOSD trial who were previously treated with RTX

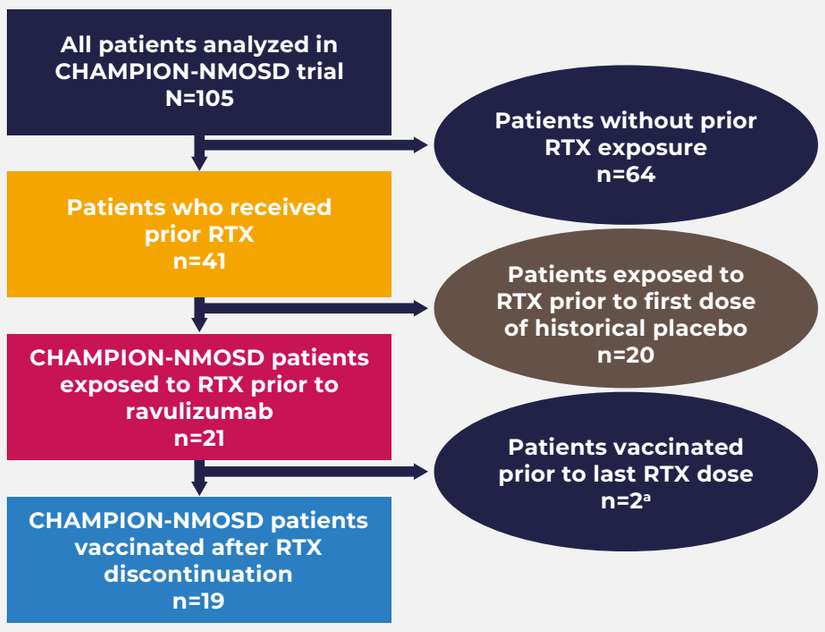
CONCLUSIONS

- Most patients received a meningococcal vaccination ≤6 months after their last dose of RTX, with MenACWY and MenB vaccines administered at the same visit
- In patients with initial *Nm* vaccination after RTX exposure who eventually received ravulizumab, there were no NMOSD attacks or reports of meningococcal infection

METHODS

- A post hoc analysis was conducted among patients previously exposed to RTX in the CHAMPION-NMOSD trial (treatment period up to March 2022)
  - Per the study protocol, patients receiving RTX treatment within ≤3 months were excluded from screening in the CHAMPION-NMOSD study
  - Patients on ravulizumab who received meningococcal vaccinations (MenACWY or MenB) after their last RTX dose were included (n=19; **Figure 1**)
- Clinical laboratory parameters, vaccine administration, and time to first meningococcal vaccination and ravulizumab dose post-RTX are summarized

Figure 1. CONSORT diagram



[a]One patient received 4 vaccinations prior to RTX, with the last being a tetravalent vaccination 1.5 years (day −930) before the last RTX dose (day −384); another patient received both tetravalent and MenB vaccinations 22 days (day −245) before the last RTX dose (days −237 and −223); day 0=ravulizumab initiation.
CONSORT, Consolidated Standards of Reporting Trials; **NMOSD**, neuromyelitis optica spectrum disorder; **RTX**, rituximab.

RESULTS AND INTERPRETATION

- Patients were primarily White (63.2%), North American (68.4%), and female (94.7%; **Table 2**)
- Of the 14 patients who had laboratory results after their last RTX dose but prior to the following meningococcal vaccination, 13 patients (92.9%) had lymphocyte counts within normal limits; specific lymphocyte cell types were not measured in this study

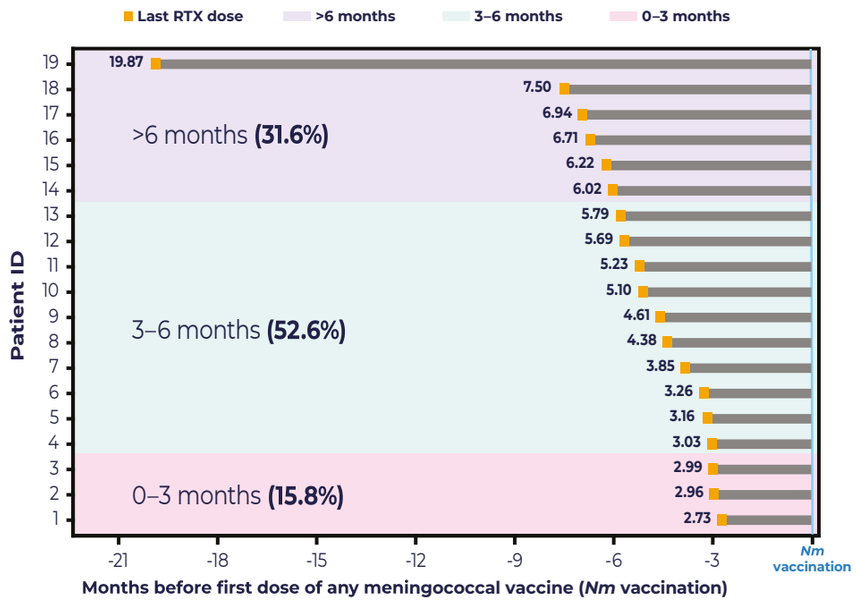
Table 2. Baseline demographics and clinical characteristics

Characteristic	Prior RTX use subgroup with subsequent Nm vaccination: Ravulizumab (n=19)
Sex, female, n (%)	18 (94.7)
Race, n (%)	
Asian	2 (10.5)
Black	3 (15.8)
White	12 (63.2)
Unknown/other	2 (10.5)
Region, n (%)	
North America[a]	13 (68.4)
Europe[b]	4 (21.1)
Asia-Pacific[c]	2 (10.5)
Age, median (IQR: quartile 1–3), years	
At first dose study drug	47 (43, 62)
At initial clinical presentation	44 (32, 61)
Historical annualized relapse rate in 24 months prior to screening, median (IQR)	1.72 (0.96, 2.25)
Time from last RTX dose to first study drug dose, median (IQR), months	6.32 (5.3, 7.3)

[a]Countries in North America included Canada and USA; [b]Countries in Europe included Spain and Italy; [c]Countries in Asia-Pacific included Australia and Korea
IQR, interquartile range; ***Nm***, *Neisseria meningitidis*; ***RTX***, *rituximab.*

- Most patients (68.4%) received their first meningococcal vaccinations either 0–3 months (15.8%) or 3–6 months (52.6%) after the last dose of RTX prior to ravulizumab (**Figure 2**)

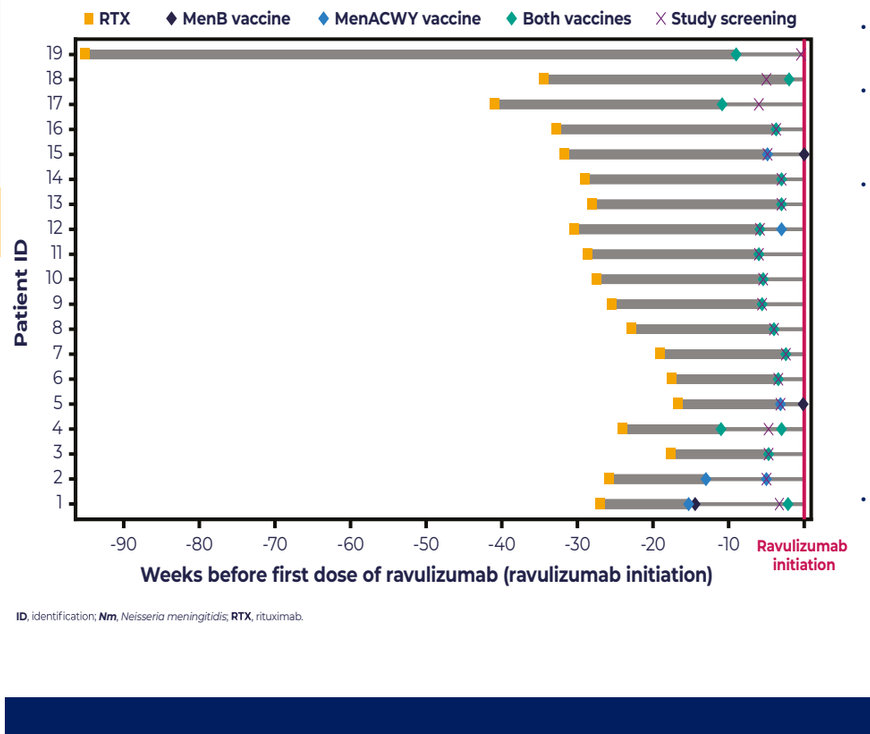
Figure 2. Vaccination time profiles: Last RTX dose to first *Nm* vaccination



Vaccination time profiles are shown from longest to shortest.
ID, identification; ***Nm***, *Neisseria meningitidis*; **RTX**, rituximab.

- Most patients (84.2%) received both MenACWY and MenB vaccinations at the same visit; 4 patients (21.1%) received multiple doses of either vaccine (**Figure 3**)

Figure 3. *Nm* vaccination profiles by vaccination type



ID, identification; ***Nm***, *Neisseria meningitidis*; **RTX**, rituximab.

Table 3. *Nm* vaccination characteristics

Characteristic	Prior RTX use subgroup with subsequent *Nm* vaccination: Ravulizumab (n=19)
Time from last RTX dose to first meningococcal vaccination, median (IQR), months	5.1 (3.2, 6.2)
Vaccination 0–3 months since last RTX dose, n (%)	3 (15.8)
Vaccination 3–6 months since last RTX dose, n (%)	10 (52.6)
Vaccination ≥6 months since last RTX dose, n (%)	6 (31.6)
Meningococcal vaccinations administered prior to first dose of ravulizumab, n (%)	19 (100)
At least 1 tetravalent (MenACWY) vaccination dose, n (%)	19 (100)
At least 1 serogroup B (MenB) vaccination dose, n (%)	18 (94.7)
Both vaccine types administered at same visit, n (%)	16 (84.2)
At least 2 MenACWY or MenB vaccination doses, n (%)	4 (21.1)

- All patients received ≥1 meningococcal vaccine ≥2 weeks prior to ravulizumab initiation (**Table 3**)
- In patients with initial *Nm* vaccination after RTX exposure who eventually received ravulizumab, there were no NMOSD attacks or reports of meningococcal infection
- Two vaccinated patients in CHAMPION-NMOSD developed meningococcal infections
  - One patient who received RTX 13 months prior to ravulizumab was vaccinated 1.5 years before RTX. This patient received a booster during the trial and experienced a meningococcal infection (serogroup B) without sequelae and continued in the study[13]
  - One patient without RTX exposure experienced a meningococcal infection (serogroup W-135) without sequelae and withdrew from the study after recovering[13]
- Two vaccinated patients in CHAMPION-NMOSD, 1 of whom had been treated with RTX, experienced a physician-reported relapse within 4 weeks of meningococcal vaccination; both were screen failures[14]

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Poster

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