

board for Chugai. Dr. Fujihara has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Fujihara has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB. Dr. Fujihara has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen. The institution of Dr. Fujihara has received research support from Ministry of Health, Welfare and Labor of Japan. Dr. Fujihara has received personal compensation in the range of \$10,000-\$49,999 for serving as a speaker, chair, etc with Novartis. Dr. Fujihara has received personal compensation in the range of \$5,000-\$9,999 for serving as a speaker, chair, etc with Biogen. Dr. Fujihara has received personal compensation in the range of \$10,000-\$49,999 for serving as a speaker, chair, etc with Chugai. Dr. Fujihara has received personal compensation in the range of \$10,000-\$49,999 for serving as a speaker, chair, etc with Alexion. Dr. Fujihara has received personal compensation in the range of \$500-\$4,999 for serving as a chair, speaker with Asahi Kasei Medical. Dr. Fujihara has received personal compensation in the range of \$500-\$4,999 for serving as a speaker, chair with Teijin. Dr. Fujihara has received personal compensation in the range of \$5,000-\$9,999 for serving as a speaker with Roche. Dr. Palace has received personal compensation in the range of \$10,000-\$49,999 for serving as a Consultant for Merck Serono, Mitsubishi, UCB, Roche, Novartis, Amplo, Alexion, Chugai. Dr. Palace has received personal compensation in the range of \$10,000-\$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Argencx, Sanofi. 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of \$500-\$4,999 for serving on a Speakers Bureau for sanofi. Celia Oreja-Guevara has received personal compensation in the range of \$500-\$4,999 for serving on a Speakers Bureau for novartis. Celia Oreja-Guevara has received personal compensation in the range of \$500-\$4,999 for serving on a Speakers Bureau for alexion. Kai-Chen Wang has nothing to disclose. Shulian Shang has received personal compensation for serving as an employee of Alexion Pharmaceuticals. Shulian Shang has received stock or an ownership interest from Alexion Pharmaceuticals. Dr. Yountz has received personal compensation for serving as an employee of Alexion, AstraZeneca Rare Disease. Dr. Yountz has stock in Astra-Zeneca. Dr. Pittcock has received personal compensation in the range of \$5,000-\$9,999 for serving as a Consultant for Genentech, Inc. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Sage Therapeutics, Inc. The institution of Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Astellas. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Prime Therapeutics. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for UCB. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Roche/Genentech. The institution of Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Alexion. The institution of Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for MedImmune/Viela Bio. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB, Inc. Dr. Pittcock has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Hoffman/LaRoche AG. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Pittcock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for F. Hofman/LaRoche. The institution of Dr. Pittcock has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. The institution of Dr. Pittcock has received research support from Grifols. The institution of Dr. Pittcock has received research support from NIH. The institution of Dr. Pittcock has received research support from Viela Bio/MedImmune/Horizon. The institution of Dr. Pittcock has received research support from Alexion Pharmaceuticals. The institution of Dr. Pittcock has received research support from F. Hoffman/LaRoche/Genentech. Dr. Pittcock has received intellectual property interests from a discovery or technology relating to health care. Dr. Pittcock has received intellectual property interests from a discovery or technology relating to health care.

## A Phase 3 Efficacy and Safety Study of Ravulizumab in Adult Patients With Neuromyelitis Optica Spectrum Disorder: Study Design and Methodology

Sean Pittcock, Kerstin Allen, Yasmin Mashhoon, Marcus Yountz

### Objective

To present the design and rationale for the phase 3 trial ALXN-1210-NMO-307 (NCT04201262).

### Background

Eculizumab is a complement component 5 (C5) inhibitor approved for adults with anti-aquaporin-4 antibody-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD). Ravulizumab, which binds the same C5 epitope, has a longer half-life with an extended dosing interval (every 8 vs every 2 weeks). We designed an innovative trial without concurrent placebo exposure to assess the efficacy and safety of ravulizumab in adults with AQP4+ NMOSD.

### Design/Methods

NA.

### Results

ALXN1210-NMO-307 is an open-label, multicenter, single-arm study using the placebo group from the PREVENT trial as a comparator. Constancy with PREVENT is maintained, including similar patient populations, adjudication procedures, and endpoints. Sensitivity analyses are prespecified to account for differences in patient characteristics.

To measure confounding, an E-value is calculated for the primary endpoint (time-to-first adjudicated on-trial relapse).

Given the serious impact of NMOSD attacks, eculizumab approval precluded the use of a concurrent comparator for ethical reasons, as it would require assigning patients to placebo when effective treatments exist. A non-inferiority efficacy trial was also considered but recruiting the very large sample size to adequately power the study was not feasible for this ultra-rare disease. Thus, a standard randomized clinical trial design was used. The trial enrolled 58 adults with EDSS score = 7 to receive an infusion of ravulizumab every 8 weeks after the loading dose. The primary treatment period will end when the last enrolled patient reaches week 50 unless a predefined number of patients have an adjudicated on-trial relapse by that time. The entire treatment period will last up to ~4.5 years.

## Conclusions

ALXN1210-NMO-307 is an ongoing study evaluating the efficacy and safety of ravulizumab in patients with AQP4+ NMOSD. It is designed to be consistent with PREVENT, and robust statistical methods will address the potential impact of an external comparator.

**Disclosure:** Dr. Pittock has received personal compensation in the range of \$5,000-\$9,999 for serving as a Consultant for Genentech, Inc. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Sage Therapeutics, Inc. The institution of Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Astellas. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Prime Therapeutics. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for UCB. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Roche/Genentech. The institution of Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Alexion. The institution of Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for MedImmune/Viela Bio. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB, Inc. Dr. Pittock has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Hoffman/LaRoche AG. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genetech. Dr. Pittock has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for F. Hoffman/LaRoche. The institution of Dr. Pittock has received personal compensation in the range of \$5,000-\$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. The institution of Dr. Pittock has received research support from Grifols. The institution of Dr. Pittock has received research support from NIH. The institution of Dr. Pittock has received research support from Viela Bio/MedImmune/Horizon. The institution of Dr. Pittock has received research support from Alexion Pharmaceuticals. The institution of Dr. Pittock has received research support from F. Hoffman/LaRoche/Genentech. Dr. Pittock has received intellectual property interests from a discovery or technology relating to health care. Dr. Pittock has received intellectual property interests from a discovery or technology relating to health care. Kerstin Allen has received personal compensation for serving as an employee of Alexion Pharmaceuticals. Kerstin Allen has stock in AstraZeneca. Kerstin Allen has stock in Alexion Pharmaceuticals. Dr. Mashhoon has received personal compensation for serving as an employee of Alexion, AstraZeneca Rare Disease. Dr. Mashhoon has stock in AstraZeneca. Dr. Yountz has received personal compensation for serving as an employee of Alexion, AstraZeneca Rare Disease. Dr. Yountz has stock in AstraZeneca.

## Disease Characteristics of Seropositive Neuromyelitis Optica Spectrum Disorder in a Turkish Cohort

Samet Cam, Bade Gulec, Melih Tutuncu, Sabahattin Saip, Aksel Siva, Ugur Uygunoglu

### Objective

To determine the clinical, demographic and imaging characteristics of a Turkish cohort with aquaporin-4-antibody positive (AQP4-IgG+) neuromyelitis optica spectrum disorder (NMOSD) from a single center.

## Background

NA.

## Design/Methods

35 patients seen between January-2008 and December-2020 with a diagnosis of AQP4-IgG+NMOSD who could be studied in detail were included in the study. Inclusion criteria for patients with NMOSD diagnosis was defined according to International Consensus Diagnostic Criteria (Wingerchuk et al.2015) and all patients were confirmed for AQP4-IgG positive serology at least once by Euroimmune transfected cells assay (EU90). Demographic, clinical and MRI data were obtained retrospectively.

## Results

The female-to-male ratio was 16.5: 1. The mean age of disease onset was 26,16±10,96 years for patients with optic neuritis onset (n:12), and 43.17±11,95 for the subgroup that started with transverse myelitis (TM) (n:16), confirming a significant difference of age at onset according to the first attack type (p < 0.001). The mean age at onset in 5 patients with area postrema syndrome was 35,74±16,83. Half of the total attacks occurred within the first year of disease onset (98/196). The mean time to diagnosis was 2,98±5,78 years after the initial attack. Disease duration was 10,06±9,76 years. Cerebrospinal fluid oligoclonal bands were studied in 24 and were positive in 25%. An autoimmune rheumatologic disease comorbidity was present in 34.5% of the patients. In patients with MRI disclosing = 2 McDonald dissemination in space criteria (spinal included) was more common in TM group and correlated with a higher disability (EDSS) score.

## Conclusions

Turkish AQP4-IgG+NMOSD patients whose disease start with optic neuritis have an earlier age of onset compared to the ones with TM onset. Half of the total attacks occur within the first year of disease onset. Patients with = 2 McDonald MRI dissemination in space criteria were more common in the TM group and had a higher disability (EDSS) score.

**Disclosure:** Samet Cam has nothing to disclose. Bade Gulec has nothing to disclose. Dr. Tutuncu has nothing to disclose. Sabahattin Saip has nothing to disclose. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Novartis. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Roche. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Sanofi-Genzyme. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving as a Consultant for Biogen - TR. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Abdi Ibrahim Ilac - TR. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen - TR. Dr. Siva has received personal compensation in the range of \$500-\$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Merck Serono. The institution of Dr. Siva has received research support from Turkish MS Society. The institution of Dr. Siva has received research support from The Scientific and Technological Research Council Of Turkey - Health Sciences Research Grants. Dr. Uygunoglu has nothing to disclose.

## Nipocalimab's Selective Targeting of FcRn and IgG Clearance Preserves Key Immune Functions

Leona Ling, Steven Tyler, Christopher Beneduce, Faye Yu, Julia Brown, Sujatha Kumar, Rui Xu, Jay Duffner, William Avery

### Objective

To characterize the effect of nipocalimab, a fully human, effectorless IgG1 anti-neonatal Fc receptor (FcRn) monoclonal antibody on immune function.

# Neurology®

## A Phase 3 Efficacy and Safety Study of Ravulizumab in Adult Patients With Neuromyelitis Optica Spectrum Disorder: Study Design and Methodology

Sean Pittock, Kerstin Allen, Yasmin Mashhoon, et al.

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