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Long-Term Eculizumab in AQP4+ NMOSD: Relapse-Risk Reduction and Safety in PREVENT and its Completed Open-Label Extension

Achim Berthele, Dean Wingerchuk, Kazuo Fujihara, Jacqueline Palace, Michael Levy, Ho Jin Kim, Ichiro Nakashima, Celia Oreja-Guevara, Kai-Chen Wang, Shulian Shang, Marcus Yountz, Sean Pittock

Objective

NA.

Background

Eculizumab is well tolerated and significantly reduces relapse risk versus placebo in patients with aquaporin-4 immunoglobulin G-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD). We report eculizumab's long-term relapse-risk-reduction efficacy and safety in AQP4+ NMOSD during PREVENT (NCT01892345) and its completed open-label extension (OLE; NCT02003144).

Design/Methods

After receiving eculizumab or placebo during PREVENT, adults with AQP4+ NMOSD could enter the OLE (eculizumab maintenance dose, 1200 mg/2 weeks, with/without concomitant immunosuppressive therapy). Combined PREVENT and OLE (final data cut, 12 July 2021) data were analysed.

Results

During PREVENT and/or the OLE, 137 patients received eculizumab for a median (range) of 183.4 (0.1–342.0) weeks (3.5 years) and a total of 449.2 patient-years (Table 1). The estimated proportion of adjudicated relapse-free patients at week 216 (4.1 years) was 92.9% (95% CI: 85.9–96.5%; Figure). Nine patients experienced 10 adjudicated relapses (seven during the OLE, including one since the last interim analysis; Table 2). The adjudicated annualized relapse rate was 0.022 (95% CI: 0.012–0.041; Table 1). Rates of treatment-related adverse events and serious adverse events (SAEs)/100 patient-years were 165.3 and 7.0, respectively, versus 167.5 and 24.5 with placebo in PREVENT. The most common SAE was urinary tract infection (5.1% of patients). The serious infection rate was 10.5/100 patient-years with no meningococcal infections. No patients died during the OLE.

Conclusions

The proportion of relapse-free patients remained high (92.9%) through 4.1 years' eculizumab treatment. Long-term eculizumab was well tolerated with no new safety signals. These long-term data confirm eculizumab's sustained benefit/risk profile in AQP4+ NMOSD.

Disclosure: Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Bayer. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Celgene. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Merck. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Novartis. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Biogen. Achim Berthele has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Alexion. Dr. Wingerchuk has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Viela Bio. Dr. Wingerchuk has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Wingerchuk has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Wingerchuk has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen. Dr. Wingerchuk has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon. Dr. Wingerchuk has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Mitsubishi Tanabe. Dr. Wingerchuk has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB Pharma. Dr. Wingerchuk has received personal compensation in the range of $10,000-$49,999 for serving as an Editor, Associate Editor, or Editorial Advisory Board Member for Wolters Kluwers. The institution of Dr. Wingerchuk has received research support from Alexion. Dr. Fujihara has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Abbvie. Dr. Fujihara has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Merck Boipharma. Dr. Fujihara has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Japan Tobacco. 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 Novartis. 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 Mitsubishi-Tanabe. Dr. Fujihara has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring

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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, 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.

Long-Term Eculizumab in AQP4+ NMOSD: Relapse-Risk Reduction and Safety in PREVENT and its Completed Open-Label Extension

Achim Berthele, Dean Wingerchuk, Kazuo Fujihara, et al.

Neurology 2022;99;S3-S4
DOI 10.1212/01.wnl.0000903068.75712.b8