P.044

Efficacy, safety, and tolerability of efgartigimod in AChR-Ab– patients with Generalized Myasthenia Gravis: interim analysis of ADAPT/ADAPT+

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Background: Efgartigimod, a human IgG1 antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor blockade. Patients with anti-acetylcholine receptor antibody–negative (AChR-Ab–) generalized myasthenia gravis (gMG) comprise 15%-20% of the gMG population and have limited approved treatment options. We evaluated long-term safety and efficacy of efgartigimod in AChR-Ab– patients from ADAPT/ADAPT+ (open-label extension). Methods: ADAPT evaluated safety and efficacy of efgartigimod versus placebo in AChR-Ab+ (n=129) and Ab– (n=38) patients with gMG. This integrated analysis includes 37 AChR-Ab– patients who received ≥1 dose of efgartigimod in ADAPT/ADAPT+ through October 2020 (median[-range] follow-up: 453[85-721] days). Responder status was defined as ≥2-point (MG-ADL) and ≥3-point (QMG) improvement for ≥4 consecutive weeks (with first improvement ≤1 week after last infusion). Results: Among AChR-Ab– patients in ADAPT (cycle 1), 68.4% (13/19) efgartigimod-treated were MG-ADL responders (placebo, 63.2% [12/19]), and 52.6% (10/19) were QMG responders (placebo, 36.8% [7/19]). In the integrated ADAPT/ADAPT+ analysis (cycle 1), AChR-Ab– patients improved from baseline in MG-ADL/QMG scores, with consistent improvements across multiple subsequent cycles. No clinically meaningful differences in safety or efficacy outcomes between AChR-Ab+ and Ab– patients occurred. Conclusions: Long-term treatment (median >1 year) with efgartigimod was well tolerated and associated with clinically meaningful improvements in MG-ADL/QMG scores in AChR-Ab– patients.

P.045

Safety profile overview of Efgartigimod Clinical Trials in participants with diverse Diverse IgG-Mediated Autoimmune Diseases

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Background: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces IgG autoantibody levels through FcRn blockade. This study reports safety of efgartigimod across IgG-mediated disorders. Methods: The safety of intravenous efgartigimod was evaluated in 204 efgartigimod-treated subjects with generalized myasthenia gravis (phase 3 ADAPT and 3-year open-label extension ADAPT+ trials), primary immune thrombocytopenia (phase 3 ADVANCE trial), or pemphigus (open-label phase 2 trial). These studies examined different efgartigimod doses (10–25 mg/kg), including cyclical dosing in generalized myasthenia gravis and continuous weekly dosing in primary immune thrombocytopenia and pemphigus. Results: Across all indications and doses studied, efgartigimod demonstrated a consistent safety profile, with treatment-emergent adverse event (TEAE) rates comparable to placebo (ADAPT, 77.4% efgartigimod/84.3% placebo; ADVANCE, 93.0% efgartigimod/95.6% placebo; and 85% in the pemphigus study). Most TEAEs were mild to moderate in severity. Discontinuation rates due to adverse events were consistently low (ADAPT, 3.6% efgartigimod/3.6% placebo; ADVANCE, 3.5% efgartigimod/2.2% placebo; and 3% of pemphigus study participants). In ADAPT+, no increases in TEAEs or infections occurred with additional efgartigimod dosing (≤19 cycles). Conclusions: Efgartigimod was well tolerated across indications and doses studied. Most TEAEs, including infections, were mild or moderate in severity and did not increase in frequency with recurrent dosing.

P.046

Real-world survival effectiveness of edaravone in amyotrophic lateral sclerosis: a propensity score weighted, registry-based, Canada-wide cohort study

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Background: ALS is a progressive neurodegenerative disease without a cure and limited treatment options. Edaravone, a free radical scavenger, was shown to slow disease progression in a select group of patients with ALS over 6 months; however, the effect on survival was not investigated in randomized trials. The objective of this study is to describe real-world survival effectiveness over a longer timeframe. Methods: This retrospective cohort study included patients with ALS across Canada with symptom onset up to three years. Those with a minimum 6-month edaravone exposure between 2017 and 2022 were enrolled in the interventional arm, and those without formed the control arm. The primary outcome of tracheostomy-free survival was compared between the two groups, accounting for age, sex, ALS-disease progression rate, disease duration, pulmonary vital capacity, bulbar ALS-onset, and presence of frontotemporal dementia or C9ORF72 mutation using inverse propensity treatment weights. Results: 182 patients with mean ± SD age 60±11 years were enrolled in the edaravone arm and 860 in the control arm (mean ± SD age 63±12 years). Mean ± SD time from onset to edaravone initiation was 18±10 months. Tracheostomy-free survival will be calculated. Conclusions: This study will provide evidence for edaravone effectiveness on tracheostomy-free survival in patients with ALS.