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Long-Term Comparative Efficacy of Inebilizumab in the AQP4+ Subpopulation from the N-MOmentum Open-Label Extension Versus Azathioprine and Immunosuppressive Therapies and Versus Placebo in Patients with NMOSD

Bruce Cree * 1, Beatrice Suero 2, Sarah Walsh 2, Romain Marignier 3, John Lindsey 4, Ho Jin Kim 5, Dewei She 6, Daniel Cimbora 6, Kristina Patterson 6, Friedemann Paul 7,

1 UCSF Weill Institute for Neurosciences, San Francisco, United States 2 Eversana, Burlington, Ontario, Canada 3 Pierre Wertheimer Hospital, Bron, France, 4 UTHealth Houston (The University of Texas Health Science Center at Houston), Houston, United States, 5 Research Institute and Hospital of National Cancer Center, Goyang, South Korea, 6 Horizon Therapeutics, Deerfield, United States, 7 Max Delbrück Center for Molecular Medicine, Berlin, Germany

Introduction:

Inebilizumab (INEB), an anti-CD19 B cell-depleting antibody, is approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults seropositive for aquaporin-4 antibody (AQP4+). N-MOmentum (NCT02200770) consisted of a 28-week randomized-controlled period (RCP) and an optional open-label extension (OLE) (>2 years) in which all participants received treatment with INEB.

Objectives/Aims:

To evaluate the long-term comparative efficacy of INEB over N-MOmentum OLE vs azathioprine and other immunosuppressive therapies (AZA/IST) and vs PBO in participants with NMOSD.

Methods:

Two historical comparator groups (HCGs) derived using data from published NMOSD studies were used to evaluate the comparative efficacy of INEB (N=208) over the OLE. The first group consisted of participants who received AZA/IST (N=132), and the second group consisted of participants who received PBO only (N=106). Hazard ratios (HR) for INEB vs HCGs were estimated using a Cox proportional hazards (PH) regression. Time to NMOSD attack was analysed using parametric and flexible survival (spline) models that were fit to INEB and HCGs. Model selection was determined by testing the PH and accelerated failure time assumptions as well as assessing Akaike’s information criterion/Bayesian information criterion, visual fit, estimated attack-free survival at 4 years, and clinical validation.

Results:

The HR for time to NMOSD attack for the N-MOmentum PBO group compared to the PBO groups was 1.15; (95% CI: 0.67–1.91; P value = 0.58). The HRs for time to NMOSD attack for INEB vs AZA/IST and PBO groups were 0.29 (95% CI: 0.17, 0.42; P < 0.001) and 0.15 (95% CI: 0.10, 0.21; P < 0.001), respectively. A time-varying spline with two internal knots and normal linear predictor provided the best fit. At 4 years, the model estimated an attack-free survival of 77% (95% CI: 71, 83) for INEB, 36% (95% CI: 27, 46) for AZA/IST, and 12% (95% CI: 7, 20) for PBO. Results indicate a greater difference in efficacy for INEB vs PBO compared to AZA/IST vs PBO, suggesting a significant reduction in risk of attack for INEB vs both AZA/IST and PBO.

Conclusion:

INEB was associated with a statistically significant improvement in time to onset of an NMOSD attack and provided a long-term attack-free survival benefit over the OLE compared to the relative short-term benefit.
observed with AZA/IST. That the PBO treated group from the RCT had a similar attack risk as the historical PBO controls supports the validity of using historical datasets for these comparisons.

**Disclosures:**

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