Congress: ANA 2022

Word limit (Title + abstract body): ≤400 (400/400)

Title word limit: 25 (18/25)

CIELO: A Randomized, Double-Blind, Placebo-controlled, Phase 3 Basket Study of Satralizumab in Patients with NMDAR- or LGI1-antibody Encephalitis

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Abstract body word count: (381)

Background:

Autoimmune encephalitis (AIE) refers to a group of rare, severe, antibody-mediated neurological diseases characterized by prominent neuropsychiatric symptoms, the most common subtypes being anti-N-methyl-D-aspartic acid-receptor (NMDAR)-antibody and leucine-rich-glioma-inactivated-1 (LGI1)-antibody AIE.

Currently, no approved therapies for AIE exist. Evidence suggests T cells, B cells, and interleukin-6 (IL-6) play key roles in AIE pathogenesis. Satralizumab, a monoclonal, recycling antibody targeting the IL-6 receptor, was engineered to provide sustained suppression of IL-6 signalling.

Objective:
CIELO is a randomized, double-blind (DB), placebo-controlled basket study evaluating the efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of satralizumab in participants with NMDAR or LGI1 AIE.

Study design:
CIELO will enroll approximately 102 participants aged ≥12 years with NMDAR AIE and 50 participants aged ≥18 years with LGI1 AIE from 12 countries. Participants, who must have an onset of AIE symptoms ≤9 months before randomization, will be classified into “new onset” or “incomplete responder” groups defined by time since initial acute first-line therapy and whether they received prior immunotherapy treatment. CIELO comprises a 52-week DB primary treatment period (Part 1). Participants will be randomized in a 1:1 ratio to receive either satralizumab or placebo, administered subcutaneously at Weeks 0, 2, 4, and every 4 weeks thereafter as monotherapy or in addition to background immunosuppressants; corticosteroids must be tapered from Week 4. Following Part 1, participants can enter an optional extension period (Part 2) and continue randomized DB study treatment, receive open-label satralizumab, or discontinue study treatment and continue follow-up assessments.

Endpoints:
The primary endpoint in both cohorts is the proportion of participants with a modified Rankin scale (mRS) score improvement ≥1 from baseline without use of rescue therapy at Week 24. Key secondary endpoints are time to mRS improvement ≥1 from baseline without use of rescue therapy, time to rescue therapy, time to seizure freedom without rescue therapy, and Week 24 values for: Montreal cognitive assessment score; Rey auditory verbal learning test score (LGI1 cohort); mRS score (0–6; NMDAR cohort); and change from baseline in clinical assessment scale of encephalitis (CASE) score. Safety outcomes include the incidence, seriousness, and severity of adverse events. Additionally, patient-reported outcomes, satralizumab’s PK/PD profile, and longitudinal biomarker assessments will be evaluated.

Conclusions:
The CIELO study will provide efficacy, safety, PK, and PD data for satralizumab in participants with NMDAR and LGI1 AIE.

This study is funded by F. Hoffmann-La Roche. Medical writing assistance was provided by Reece Bracewell, MBiolSci, of ApotheCom, London, UK, and was funded by Roche.