Conclusions

- The estimated proportion of participants with improvement on the alternative multicompontent endpoint was highest for 10 mg/kg opicinumab compared with placebo and the other opicinumab doses.
- Similarly, the hazard ratio for time to improvement was highest for 10 mg/kg opicinumab, vs. the other arms.
- Additional study, particularly of the 10 mg/kg dose, is necessary to further characterize the potential treatment effects of opicinumab in patients with pre-existing disability.
- More details on the SYNERGY study are provided in posters P0327, P0316, and oral presentation P0330.004.

Introduction

- Opicinumab (anti-LINGO-1) is a novel cell-based neuroprotective agent previously assessed in the RENOA (Phase 2a; NCT00707181), trial of participants with a first episode of optic neuritis.
- SYNERGY (Phase 2b; NCT03480231) was designed to assess the efficacy and safety of escalating doses of opicinumab, vs. placebo, in participants with relapsing-remitting multiple sclerosis (RRMS), secondary progressive MS (SPMS), or primary progressive MS (PPMS), who were to be treated concurrently with intramuscular (IM) interferon (IFN) beta-1a.
- Double-blind, randomized to 3 mg/kg were treated as a monoclonal antibody with low backflow/borther penetration (superficial fluid radioactivity: 0.1%).
- Additional prespecified analyses of improvement in pre-existing disability (including using an alternative endpoint minus the 3% Second Baseline Auditory Serial Add (PASAT-3)) may provide further evidence for the potential benefit of opicinum in patients with relapsing MS.

Objectives

- To further investigate the potential benefit of opicinum in SYNERGY participants using prespecified analyses of neuroreparative treatment in pre-existing disability.

Methods

- SYNERGY was a randomized, placebo-controlled, double-blind, parallel-group study (Figure 1).
- Participants were 18-58 years of age, had active RRMS or SPMS, and on Expanded Disability Status Scale (EDSS) scores 3.0-6.0.
- The primary endpoint was the percentage of participants with improvement in disability and neurophysiologic and/or cognitive function over 72 weeks measured by a multicenter endpoint comprising: EDSS, Timed 25-Foot Walk Test (T25FW), 9-Hole Peg Test (9HPT; dominant and nondominant hand), and PASAT-3.
- Improvement was defined as: ≥1.0-point decrease in EDSS compared with baseline (0.58–2.68).
- An additional prespecified analysis included confirmed improvement and time to confirmed improvement as:
  - An alternative multicompontent endpoint comprising physical components of the primary endpoint: EDSS, T25FW, and 9HPT (dominant and nondominant hand).
  - This was proposed to remove PASAT-3 as a previous analysis of double-blind scores showed minimal if any improvement by MCI.

Results

- Four hundred eighty-two participants were randomized and dosed; efficacy was assessed in 412 participants (6 were excluded from the efficacy analyses due to good clinical practice violations).
- The SYNERGY prespecified primary endpoint used a linear trend test across 5 arms was not met due to a dose response consistent with the inverted U-shaped dose response and Cox proportional hazards models were used to analyze time to improvement.

Figure 1. SYNERGY study design

- Two or more of the individual physical components of the primary endpoint.
- To capture individual improvement across ≥1 component.
- A logistic regression model was used to analyze improvement probability. Kaplan-Meier curves were used to display distribution of time to improvement and Cox proportional hazards models were used to analyze time to improvement.

Figure 2. Proportion of participants with improvement on the alternative multicompontent endpoint (EDSS, T25FW, 9HPT)

- The estimated proportion of participants with improvement on the alternative multicompotent endpoint was highest for 10 mg/kg opicinumab compared with placebo and the other opicinumab doses.
- Similarly, the hazard ratio for time to improvement was highest for 10 mg/kg opicinumab, vs. the other arms.
- Additional study, particularly of the 10 mg/kg dose, is necessary to further characterize the potential treatment effects of opicinumab in patients with pre-existing disability.
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Figure 3. Time to improvement on the alternative multicompontent improvement endpoint

- The estimated proportion of participants with improvement on the alternative multicompotent endpoint was highest for 10 mg/kg opicinumab compared with placebo and the other opicinumab doses.
- Similarly, the hazard ratio for time to improvement was highest for 10 mg/kg opicinumab, vs. the other arms.
- Additional study, particularly of the 10 mg/kg dose, is necessary to further characterize the potential treatment effects of opicinumab in patients with pre-existing disability.
- More details on the SYNERGY study are provided in posters P0327, P0316, and oral presentation P0330.004.

Figure 4. Confirmed improvement responders on individual components of the primary endpoint (EDSS, T25FW, 9HPT, PASAT-3)