A phase 1b/2a single dose ascending dose study to evaluate the safety, tolerability, and pharmakokinetics of an RSV-neutralizing antibody, clesrovimab, in pre-term and full-term infants

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Background

Clesrovimab is an investigational RSV-neutralizing monoclonal antibody for the prevention of RSV lower respiratory tract infection in infants.

Methods

This phase 1b/2a, double-blind, randomized, placebo-controlled study enrolled healthy preterm and full-term infants 2 weeks to 8 months of age. Participants were randomized 4:1 within 5 panels (pre-term: 20, 50, 75 or 100-mg, full-term: 100 mg) to receive 1 dose of clesrovimab or placebo. Safety was evaluated by the proportion of participants with adverse events (AEs). Pharmacokinetics, serum neutralizing antibodies, and anti-drug antibodies were analyzed through 1 year. RSV-associated endpoints, as determined by RT-PCR and the presence of symptoms, were evaluated through Day 150 postdose.

Results

Overall, 183 participants were randomized; 181 received treatment. The proportions of participants with solicited injection-site adverse events (AEs), solicited systemic AEs, and serious AEs were generally comparable across all clesrovimab groups and placebo. Clesrovimab serum concentrations increased proportionally with dose and displayed a geometric mean apparent half-life of 44.9 days. Of the participants receiving clesrovimab, 13.1% and 22.8%, were positive for ADA through Days 150 and 365 postdose, respectively, with no apparent impact in PK. SNA titers increased in a dose-dependent manner. The incidences of RSV-associated endpoints were lower in infants in the combined clesrovimab dose groups and the 100 mg dose group, compared with the placebo group.

Conclusion

Single doses of clesrovimab were generally well tolerated in infants, the antibody displayed an extended half-life, and the incidence of RSV-associated disease endpoints were lower in clesrovimab group compared to placebo.