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Safety, Pharmacokinetics, and Pharmacodynamics of LAD191, an IL-1RAP-Targeting Monoclonal Antibody, in Adults with Hidradenitis Suppurativa: Results from Part 3 of a Phase I Study

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Introduction

LAD191 is a monoclonal antibody targeting the interleukin-1 receptor accessory protein (IL-1RAP). Parts 1 and 2 of this first-in-human (FIH) study evaluated single and multiple ascending doses of LAD191, respectively, in healthy volunteers (HV) and have demonstrated a favorable safety and tolerability profile, along with dose-proportional pharmacokinetics (PK). This Part 3 analysis aims to evaluate the safety, tolerability, PK, immunogenicity and pharmacodynamics of LAD191 among patients with hidradenitis suppurativa (HS).

Materials and Methods

This was a Phase I, randomized, 3-part, placebo-controlled study (NCT06488209). Part 3 included adult patients with HS (Hurley stage II or III). Patients were randomized to receive LAD191 or placebo, administered by subcutaneous injection once weekly for up to six doses.

Results

Five patients were randomized, of which three received LAD191 (mean age: 30.0 years; two females; Hurley stage II/III: 2/1 patients) and two received placebo (mean age: 31.0 years; all females; Hurley stage II/III: 2/0 patients). The mean International HS Severity Score (IHS4) at baseline was 30.3 in the LAD191 arm and 13.5 in the placebo arm, with a higher number of severe patients (IHS4 ≥ 11) in the LAD191 arm compared to the placebo arm (3 vs 1 patient). No treatment-emergent adverse events (TEAEs) were reported in the LAD191 arm vs three TEAEs in the placebo arm (two moderate worsenings of HS and a mild acute pharyngitis). No serious TEAEs or TEAEs leading to discontinuation were reported. Transient decreases in neutrophils count were observed in patients receiving LAD191, with spontaneous recovery noted in all cases. A trend toward lower LAD191 exposure (~25%) was observed in HS patients compared to what was previously observed in HV. The half-life of LAD191 in HS patients was 17 days and no anti-drug antibodies were detected. An improvement in HS lesion count was observed following LAD191 treatment, accompanied by reductions in serum inflammatory biomarkers, such as IL-6 and lipocalin-2.

Conclusion

LAD191 was well tolerated and demonstrated a favorable safety and PK profile in patients with HS. Moreover, LAD191 has led to downstream cytokine reduction and early signs of clinical improvement in HS, supporting

further clinical development.