A Randomized, Double-Blinded, Placebo-Controlled, Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of XmAb7195

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INTRODUCTION

The clinical utility of blocking the interaction of IgE with basophils and mast cells has been established in models relevant to allergic asthma.

Clinical trials of the humanized monoclonal antibody (mAb) XmAb7195 have demonstrated a correlation between its basophil and asthmaspecific symptom control and supporting that greater suppression of the IgE may result in better clinical outcomes.

XmAb7195 is a humanized, anti-IgE mAb that is being developed for the treatment of atopic dermatitis (AD), allergic asthma, and AD. The antibody variable region has been engineered to increase affinity for human IgE relative to murine antibodies. XmAb7195 shows a reduced potential for triggering FcyR-mediated AD, and has shown improved human IgE binding to mouse cells and to inhibit the differentiation of IgE positive cells.

METHODS

STUDY DESIGN

This was a randomized, placebo-controlled, ascending dose study of safety, tolerability, and pharmacokinetics of XmAb7195. Patients with atopic dermatitis were enrolled in Part 1. Referred to the Table 1: Subject Disposition.

RESULTS

Table 1: Subject Disposition

- Part 1: 40 healthy subjects, single IV administration of XmAb7195 (0.3, 0.6, 1.2, 3.0, and 6.0 mg/kg) were investigated in Cohorts 1, 2, 3, 4, and 5, respectively.
- Part 2: 16 subjects with elevated total IgE administration of XmAb7195 (40 mg/kg) were investigated in Cohorts 1.0 mg/kg and further doses.
- Part 3: 16 healthy subjects, two sequential IV doses of XmAb7195 (0.3 mg/kg and 1.0 mg/kg) were administered in Day 7 and 5 at 0.3 mg/kg a Day 7 and 5 mg/kg.

Table 2: Subject Demographics and Baseline Characteristics

- All subjects were enrolled in the study and were randomized to each of the 4 study arms.
- Baseline levels of IgE were similar across the 3 parts of the study.

SAFETY

- Urticaria (pruritus and hives) occurred in 10 subjects with onset during the infusion.
- AConclusions: XmAb7195 was generally well tolerated when administered as a single IV infusion with transient, asymptomatic systemic symptoms occurring in 2.0% (3) of 150 subjects.

PHARMACOKINETICS

- XmAb7195 exposure increased in a slightly greater than proportional manner with doses between 0.3-3.0 mg/kg.
- XmAb7195 was rapidly cleared from the circulation, with a median half-life of 0.5-1.0 hr (median 0.8 hr).
- There were no significant differences in clearance, volume of distribution or half-life between subjects with FcγRIIA (+) or FcγRIIA (-) genotypes.

REFERENCES


ACKNOWLEDGEMENTS

This study was supported by PAREXEL International.