KRN23 is an investigational fully human IgG1 monoclonal antibody designed to specifically bind to and inhibit excess FGF23.

Rickets: an Investigational Nonequivalent Interleukin-21 Receptor Antagonist for the Treatment of X-Linked Hypophosphatemia

INTRODUCTION

X-linked hypophosphatemia (XLH) is a rare, lifelong, disorders characterized by low serum phosphorus levels and high circulating fibroblast growth factor 23 (FGF23) levels. Patients with XLH, including those with XLH1, develop rickets, which is a significant cause of morbidity and mortality, especially in early childhood.

The trial evaluating the effects of KRN23, a fully human anti-FGF23 monoclonal antibody on the radiographic, biochemical, and clinical outcomes of adult patients with XLH was conducted under a protocol approved by the Institutional Review Board (IRB) at each participating site. The study followed the Declaration of Helsinki and Good Clinical Practice guidelines. All patients provided written informed consent prior to study entry.

A Randomized, Open-label Phase 2 Study of KRN23, a Fully Human Anti-FGF23 Monoclonal Antibody, in 52 Children with X-Linked Hypophosphatemia (XLH): 40-Week Results


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Objective: This 40-week study evaluated the safety, tolerability, and efficacy of KRN23, an investigational fully human IgG1 monoclonal antibody designed to specifically bind to and inhibit excess FGF23.

METHODS

KRN23 dosing: 45.5 mg/dose/week (Q2W) or 91 mg/dose/week (Q4W) for patients weighing ≥ 40 kg, and 91 mg/dose/week (Q2W) or 182 mg/dose/week (Q4W) for patients weighing < 40 kg. The study comprised two randomized, double-blind, placebo-controlled phases: 12 weeks of treatment followed by an open-label extension phase in which all patients received KRN23 for 28 weeks (total of 40 weeks).

RESULTS

Patients with XLH had substantial healing of rickets at Week 64. Mean LS Mean Change from Baseline in Rickets Severity Score (RSS) at Week 40 was −1.0 ± 0.5 vs −1.7 ± 0.7 at Week 64.

CONCLUSIONS

KRN23 was well tolerated and demonstrated radiographic and clinical benefit in all 40-week patients treated with Week 64 periods. KRN23 treatment resulted in a significantly greater improvement in rickets scores compared with placebo for all patients and for patients weighing ≥ 40 kg. Further studies are warranted to confirm the findings in a larger population of patients with XLH.