**INTRODUCTION**

Burosumab is an investigational fully human immunoglobulin G1 monoclonal antibody that specifically inhibits serum fibroblast growth factor 23 (FGF23) (Figure 1). FGF23 is a hormone that plays a crucial role in the regulation of serum phosphate levels. Clinical studies have demonstrated the efficacy and safety of burosumab in patients with X-linked hypophosphatemia (XLH), a rare, lifelong, debilitating, and disfiguring bone disease mediated by high levels of circulating fibroblast growth factor-23 (FGF23) (23).

**Skeletal deformity and growth impairment begin in early childhood, and some studies suggest earlier initiation of treatment with phosphate and active vitamin D may lead to better height outcomes.**

Burosumab is an investigational fully human immunoglobulin G1 monoclonal antibody that specifically targets FGF23 and inhibits its activity (Figure 2).

**METHODS**

- In BURUX-012, 25 children (aged 1–12 years) received burosumab subcutaneously (SC) every 2 weeks for 48 weeks (Figure 3). Here, we summarize findings from the week 48 interim analysis.
- **Radiographs:** Hologic (Bedford, MA, USA) Hologic Discovery™ PQ scanner (23).
- **Serum:** Sampled weekly at each visit (23).
- **Bone biopsy:** Biopsy samples were collected from the tibia at baseline (23).
- **Efficacy analysis:** All patients who received 2 doses of burosumab were included in the safety population (Figure 4).

- **Safety:** Adverse events (AEs).

**RESULTS**

- **Absence of hyperphosphatemia:** A low incidence of hyperphosphatemia, defined as serum phosphorus (mg/dL) >4.5 (baseline -25%; P<0.0001) and 40 (-36%; P<0.001) (Supplemental Table S1).
- **Reduced serum alkaline phosphatase:** A statistically significant decrease in alkaline phosphatase (U/L, 0-1000) was observed from baseline to week 40 (mean percent change from baseline, -48% [-37, -56%; P<0.0001]) (Figure 5).
- **Reduced radiographic rickets:** At baseline and week 40, all 13 subjects achieved substantial healing of rickets, defined as a Radiographic Global Improvement of Change (RGI-C) Global score of +2.0 (Figure 6).
- **Increased serum 1,25(OH)2D:** A statistically significant increase in 1,25(OH)2D (pg/mL) was observed from baseline to week 40 (mean percent change from baseline, +155% [107, +217%; P<0.0001]) (Figure 7).

**CONCLUSIONS**

**The Efficacy of Burosumab (KRN23), a Fully Human Anti-FGF23 Monoclonal Antibody, on Phosphate Metabolism and Rickets in 1 to 4-Year-Old Children with X-linked Hypophosphatemia (XLH)**

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**Intended outcomes:** Efficacy and safety.

**Intervention:** Open-label SC Burosumab.

**Participants:** 13 children with XLH, age 1–4 years, who had radiographic rickets at baseline or 2 consecutive measurements were below normal range.

**Primary comparison:** Open-label SC Burosumab vs baseline.

**Primary index outcome/endpoint:** Primary index outcome: Increased serum 1,25(OH)2D.

**Secondary index outcomes/endpoints:** Radiographic Global Improvement of Change (RGI-C) Global score was improved from baseline to week 40.

**Study sample size:** 13 children.

**Study duration:** 48 weeks.

**Study design:** Phase 2 Study Design.

**Study completion date:** June 2017.

**Trial registration:** NCT02570502.

**Presented at MO 0695, Denver, CO, USA**

February 2017, Denver, CO, USA

**Additional Safety &**

Presented at MO 0695, Denver, CO, USA

**DISCLOSURES**

- This study was supported by Ultragenyx Pharmaceutical Inc. Inc. in partnership with Kyowa Kirin International plc. Catherine Woods, PhD, an employee of Ultragenyx Pharmaceutical Inc., provided medical writing support.

- There were no instances of hyperphosphatemia and no clinically meaningful changes observed in serum PTH, serum or urine calcium, hematology, or urine biochemical parameters.

- These findings are consistent with previous studies investigating burosumab for XLH and suggest that early use of burosumab may result in positive clinical outcomes in children with XLH.

**REFERENCES**

