Effects of Burosumab (KRN23), a Human Monoclonal Antibody to FGF23, in Patients with Tumor-Induced Osteomalacia (TIO) or Epidermal Nevus Syndrome (ENS)

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INTRODUCTION

- Tumor-induced osteomalacia (TIO) and epidermal nevus syndrome (ENS) are rare diseases characterized by excess fibroblast growth factor 23 (FGF23), hypophosphatemia secondary to phosphaturia, and impaired active vitamin D synthesis. As a result, patients with TIO and ENS have bone pain, osteomalacia, fractures, and muscle weakness.

- TIO is usually caused by small, slowly growing, FGF23-secreting tumors. As more tumors, with or without skeletal defects, the source of the excess FGF23 in ENS-associated osteomalacia is unclear.

METHODS

- UX023-T201 is an open-label, single-arm, dose-finding, Phase 2 clinical trial investigating the safety and efficacy of burosumab for TIO and ENS (Figure 2).

RESULTS

- In patients with TIO (Table 1), a 25% increase in bone mineral density (BMD) was observed at 24 weeks as compared to baseline (P=0.0025). The mean change in serum phosphorus (mg/dL) was 0.49 ± 0.13 at 24 weeks (P<0.0001).

- In patients with ENS (Table 2), a 25% increase in bone mineral density (BMD) was observed at 24 weeks as compared to baseline (P=0.0007). The mean change in serum phosphorus (mg/dL) was 0.35 ± 0.12 at 24 weeks (P<0.0001).

SUMMARY & CONCLUSIONS

- In patients with TIO or ENS, burosumab improved mean serum phosphorus levels at 24 weeks.

DISCLOSURES

- All patients experienced an adverse event (AE) and 3 patients experienced a serious adverse event (SAE) during the study.

Figure 1. Burosumab Proposed Mechanism of Action

Table 1. Bone Turnover Characteristic TIO ENS Median (range) Median (range) P-value

Table 2. Bone Histomorphometry Results

Table 3. Week 48 Safety Summary

Table 4. Week 48 Safety Summary

Figure 2. UX023-T201 Study Design

Figure 3. Improvements in Serum Phosphorus, TmP/GFR, and 1,25(OH)2D

Figure 4. Increase in Markers of Bone Turnover

Figure 5. Changes in Fatigue, Pain, and Muscle Strength

Figure 6. Improvement in Fatigue, Pain, and Muscle Strength

Figure 7. Summary of Results

Figure 8. Summary of Results