**Assessment of Quality of Life Data After Four Monthly Subcutaneous (SC) Doses of a Human Monoclonal Anti-FGF23 (Fibroblast Growth Factor 23) Antibody (KRN23) in Adults with X-linked Hypophosphatemia (XLH)**

**KRN23 is a recombinant human IgG1 monoclonal antibody which binds to FGF23, blocking its biologic activity. Both intact and fragment FGF23 polyepitopes are immunologically related with KRN23 doses were 0.05 to 0.1 mg/kg. In the 24-week study, the 4-week self-reported SF36 showed general health using 8 underlying scales (Table 1). The 8 scales were then used to compute Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.**

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**Methods**

**Demographics and Baseline Characteristics**

- Twenty-eight patients were enrolled in the study and 26 patients completed the 24-week study.
- One patient withdrew after three doses (injection site reaction).
- The enrolled population ranged in age from 19 to 80 (mean 41.9; range 10-80 years).
- Mean body mass index was 24.3 kg/m².
- Characteristics were similar in the completor population (N=26).
- Mean SF-36v2 and EQ-5D were within the normal range. Mean 1.25(OH)2D was within the normal range (Table 3).

**PRO Results**

**Figure 1. Mean PRO Scores at Baseline and Endpoint Among completers (n=26)**

**Table 3. Patient Baseline Disease Characteristics (n=26)**

**Table 2. WOMAC Scale**

**Table 1. SF-36v2 Scale**

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**Responders**

- **Figure 2 displays the number of patients who were classified as "better," "same," or "worse" according to the established MIC (Minimally Important Change) for each PRO scale.**

For each scale, at least some of the patients were classified as "better," ranging from five cases [19%] for SF, pain, and stiffness. For nearly all the scales, a few patients did "worse" (one case [4%] for BP to five cases [19%] for SF, pain, and stiffness). The WOMAC Physical Functioning scale was the only one to register no "worse" cases. For many scales, the ratio of "better" to "worse" may suggest a treatment benefit. The SF-36v2 PF scale, for example, showed a 3.1 ratio of patients to "worse" patients to "worse." The WOMAC Physical Functioning categorized 9 patients as "better" and none as "worse," whereas the SF-36v2 PF with its higher level of functioning, also categorized 5 patients as "better" but also identified 3 cases as "worse." This suggests that in the XLH population, the form of the WOMAC scale are better targeted to the level of functioning of XLH patients, where treatment appeared to have its greatest impact.

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**Figure 3. Burden of Disease Compared to a General Population in United States (US)**

**Compare with General US Population**

- This series of analyses compared the SF-36v2 scores of the completor XLH patient population to an age- and gender-matched general US population (N=4,040). (Figure 3)
- At baseline, mean BP (P<0.0001), PF (P<0.0001), RP (P<0.005), and MCS (P<0.0165) and PCS (P<0.0071) scores were far below the general US population norm, while all other scales did not show a statistically significant difference.
- Changes in disease burden from baseline to endpoint with KRN23 treatment were positive for all SF-36v2 domains, suggesting alleviation of disease burden over time.
- At endpoint, the MH (P<0.0003) and MCS (P=0.006) scale became significantly lower than the norm; mean MCS (P=0.004), SF (P=0.0102), and PF (P=0.001) remained significantly below the norm; and the other domains remained without statistically significant difference from the norm.

**Disease Burden Analysis**

- Figure 4. Burden of Disease Compared to a General Population

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**Figure 5. Burden of Disease Compared to a General Population**

**Compare with Asthma Population**

- Figure 4 shows mean SF-36v2 scale scores for XLH patients at baseline and endpoint relative to patients with asthma (N=343).
- Results mirror those from the general US population, although at a generally higher level of magnitude. Although asthma patients are on the whole less healthy than the general healthy population, their condition does not resemble XLH.
- Their burden relative to XLH follows the same pattern as that of the US population.
- Results support the discriminant validity of SF-36v2 used in an XLH population.

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**Figure 6. Burden of Disease Compared to a General Population**

**Compare with Osteoarthritis Population**

- This series of analyses compared the SF-36v2 scores of the completor XLH patient population to an age- and gender-matched osteoarthritis population (N=583); (Figure 5).
- At baseline, the disease burden for the XLH patients when compared to the general US population (Figure 3) showed a different profile relative to that for patients with osteoarthritis.
- GH (P<0.0003), RP (P<0.0327), and SF (P<0.0116) scores for XLH patients were significantly higher than those of the osteoarthritis population at baseline, indicating better health; all other scores did not show statistically significant differences.
- At mean SF-36v2 scale scores for XLH patients increased (improved) relative to those for osteoarthritis patients at endpoint, showing significant improvement across all PF and RE: RP (P<0.0001; PF (P<0.0001), BH (P<0.0004), VT (P<0.006), SF (P<0.0002), MH (P<0.0081), PCS (P<0.0072), and MCS (P<0.015).

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**Summary**

- All 10 SF-36v2 scales showed higher mean scores at the end of treatment compared to baseline, with statistically significant improvements observed for 3 measures (RP, BP, and PCS). When corrected for multiplicity, RP remained statistically significant.
- All 3 WOMAC scales showed lower mean scores (indicating HRQL improvement) at the end of treatment compared to baseline, with statistically significant improvements observed for 2 measures (Physical Functioning and Stiffness). SF-36v2 and WOMAC appear to be appropriate measures of HRQL in XLH patients and therefore applicable for use in future clinical trials with XLH patients.
- Results should be interpreted cautiously due to the open-label study design without placebo or active comparator control.
- In conclusion, treatment with KRN23 for 4 months resulted in significantly improved patient physical functioning using SF-36v2 and WOMAC as HRQL instruments.