Real World Experience of Burosumab Therapy in Children with X-linked Hypophosphataemic Rickets - 12 month follow-up data

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Background
Burosumab, a monoclonal antibody targeting fibroblast growth factor 23, is now available for clinical use in children with X-linked hypophosphataemia (XLH). We explored the effects in a clinical setting, considering biochemistry, growth, deformity, functionality, quality of life, pain and fatigue.

Methods
Clinical, biochemical, and questionnaire data were reviewed at 6 and 12 months for 8 children with XLH starting burosumab. Functionality was assessed with 6-minute walk test (6MWT) and Timed Up and GO (TUG). Questionnaires included: Core Paediatric Quality of Life Inventory (PedsQL-Core), Paediatric Quality of Life multidimensional fatigue scale (PedsQL-Fatigue), and Brief Pain Index Pain Severity Score (PSS).

Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>6 month</th>
<th>12 month</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Median, Range)</td>
<td>5.5 years, 19 months - 11 years</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gender M/F Females 50% (n=4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Serum Phosphate Mean±SD</td>
<td>1.0-1.9mmol/L</td>
<td>0.7±0.1</td>
<td>1.0±0.2</td>
<td>1.1±0.2</td>
</tr>
<tr>
<td>Serum alkaline phosphatase</td>
<td>Mean±SD</td>
<td>163-375IU/L</td>
<td>415±73</td>
<td>371±79</td>
</tr>
<tr>
<td>Urine TmP/GFR** Mean±SD</td>
<td>1.15-2.44*</td>
<td>0.82±0.07</td>
<td>0.92±0.04</td>
<td>1.19±0.18</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>Mean±SD</td>
<td>10-65ng/L</td>
<td>31±14</td>
<td>40±12</td>
</tr>
<tr>
<td>Urine calcium:creatin ratio</td>
<td>Mean±SD</td>
<td>0.05-0.60</td>
<td>0.44±0.21</td>
<td>0.34±0.26</td>
</tr>
<tr>
<td>Starting dose mg (Range dose mg/kg)</td>
<td>10-50</td>
<td>(0.3-1.0)</td>
<td>(0.6-1.7)</td>
<td>(0.6-2.0)</td>
</tr>
<tr>
<td>Height Z-scores</td>
<td></td>
<td>-2.60±0.81</td>
<td>-2.44±0.79</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TUG</td>
<td>(N=4,seconds)</td>
<td>5.7±0.5</td>
<td>-</td>
<td>4.8±0.6</td>
</tr>
<tr>
<td>6MWT</td>
<td>(N=4,metres)</td>
<td>258±75</td>
<td>-</td>
<td>447±53</td>
</tr>
</tbody>
</table>

*12 months compared to baseline, paired t tests
**Calculated ratio of renal tubular maximum phosphate reabsorption

Motor function:
All patients functionally evaluated had improvements in both TUG scores and 6MWT distances. 12-month distances were still 63-183m below norms for age/gender.

Lower Limb Deformity:
Six children had lower limb deformity; varus(N=3), valgus(N=2), windswept(N=1). The most severely affected patient (intermalleolar distance=10cm) noted progression at 6 months with slight improvement by 12 months. All others noticed improvement at 12 months with reduced intercondylar/intermalleolar distances.

Pain/Fatigue:
One child reported no pain. 12 month PSS decreased for 6 patients and slightly increased for one. Mean±SD PSS was 2.3±1.3 at baseline and 1.0±1.2 at 12 months (maximum score 10). Mean±SD PedsQL-Fatigue scores were 64±19 at baseline improving to 76±17 at 12 months (maximum score 100,P=0.2).

Quality of Life:
Mean±SD PEDsQL-Core score improved from 69±17 at baseline to 81±15 at 9 months, however decreased back to 67±17 by 12 months (N=7, maximum score 100). This is despite verbal reports of improvements and may reflect a shift in expectation.

Radiology
Thacher scores improved in all but one patient (whose score remained the same). Mean±SD scores were 2.0±1.5 at baseline and 0.4±0.3 at 12 months (p=0.02).

Family comments:
"Thank you very much for this magic medicine"
“It has not only changed (my child’s) life, it has changed mine also"
“My son inherited XLH from me, I had to carry him to school... now he literally skips to school!"

Conclusion
In a real-world setting, burosumab can improve biochemistry, growth, deformity, pain and function in children with XLH.

References:
1. Kemp H. Measurement of TmP/GFR.Blood Sciences Department of Clinical Biochemistry, Bristol NHS Trust.

Poster presented at:
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**Calculated ratio of renal tubular maximum phosphate reabsorption

Phosphate mmol/L

Alkaline Phosphatase IU/L

PTH ng/mL

TmP/GFR

Thacher Scores

Poster presented at: