EXPERIENCE OF 6-MONTHS OF BUROSUMAB THERAPY IN FIVE SIBLINGS WITH X-LINKED HYPOPHOSPHATEMIC RICKETS IN THE STATE OF KUWAIT

S. AL SHAMMARI1, A. AL ENEZI1, G. SAMEER1 and N. FAWZY2
1: Al Jahra Hospital, Al Jahra, Kuwait

INTRODUCTION
X-linked hypophosphatemic rickets (XLH) is a genetic disorder, characterized by hypophosphatemia and caused by a mutation in the phosphate regulating endopeptidase homolog, x-linked (PHEX) gene which leads to overexpression of fibroblast growth factor 23 (FGF23).1,2

Conventional therapy with the supplementation of oral phosphate and vitamin D analogs does not treat the underlying cause of the disorder and is associated with high failure rates and long-term adverse effects such as hyperparathyroidism and nephrocalcinosis.3,4 Patients are also known to suffer from gastrointestinal symptoms due to the multiple doses needed to achieve therapeutic response, leading to reduced treatment compliance and poor tolerability.3 Conventional therapy stimulates FGF23 levels and thereby renal phosphate wasting, resulting in a vicious circle, which further limits its efficacy.4

Burosunab is a fully human IgG1 monoclonal anti-FGF23 antibody that addresses the underlying pathophysiology of XLH and demonstrates significant clinical improvement in related symptoms. It was approved by the FDA in 2018 and is indicated for the treatment of XLH in adult and pediatric patients 6 months of age and older.3,4

AIM
The aim of this prospective observational study was to assess the effect of 6 months of burosunab treatment in XLH patients from a Kuwaiti family.

METHODS
The study collected and analyzed data for 5 XLH patients treated at Al Jahra hospital, Kuwait. All patients were female, aged 2-5 years at diagnosis and 7-20 years at burosunab initiation. Biochemical parameters including fasting serum phosphate, tubular maximum reabsorption of phosphate to glomerular filtration rate (TmP/GFR), serum calcium, alkaline phosphatase (ALP) and active vitamin D were collected at baseline (prior to burosunab treatment) and every 4 weeks during the first 6-months of treatment. X-rays were also performed at baseline and at 6-months.

Burosunab was initiated at a starting dose of 0.8 mg/kg for the three pediatric patients and 1 mg/kg for the two adult patients, following a washout period of one week after cessation of conventional therapy.

RESULTS
All patients treated with burosunab experienced improvements in the biochemical parameters following 6-months of treatment (Table 1).

Table 1: Effect of burosunab in XLH patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline 1</th>
<th>Baseline 2</th>
<th>Baseline 3</th>
<th>Baseline 4</th>
<th>Baseline 5</th>
<th>Baseline 6</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum phosphate (mmol/L)</td>
<td>0.57</td>
<td>0.69</td>
<td>0.90</td>
<td>0.95</td>
<td>0.82</td>
<td>1.03</td>
<td>0.73</td>
</tr>
<tr>
<td>TmP/GFR (mL/min/1.73m²)</td>
<td>1.00</td>
<td>0.79</td>
<td>0.69</td>
<td>0.79</td>
<td>0.86</td>
<td>0.86</td>
<td>0.57</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>81.40</td>
<td>58.85</td>
<td>58.85</td>
<td>58.85</td>
<td>58.85</td>
<td>55.0</td>
<td>55.0</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.20</td>
<td>9.20</td>
<td>9.20</td>
<td>9.20</td>
<td>9.20</td>
<td>9.20</td>
<td>9.20</td>
</tr>
</tbody>
</table>

All patients showed improvement in serum phosphate levels at 6-months of burosunab treatment, compared to the baseline (Figure 1). Also, all patients had reduction in the ALP (mean 81.40 to 58.85 levels) (Figure 2) and the TmP/GFR values improved (mean +0.06 mol/L) in 3 patients for which data was available.

CONCLUSIONS
Six-months of burosunab treatment led to clinical, biochemical and radiological improvements in these 5 XLH siblings from the State of Kuwait.

REFERENCES

ACKNOWLEDGEMENTS
Medical Writing support was provided by Linda Mascarenhas from Connect Communications, Dubai, UAE and funded by Kyowa Kirin Pharma

CONTACT INFORMATION
Dr Sameer Al Shammari, Consultant, Department of Endocrinology, Al Jahra Hospital, Kuwait. Email: lafit8@yahoo.com