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

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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.[5] Conventional therapy stimulates FGF23 levels and thereby renal phosphate wasting, resulting in a vicious circle, which further limits its efficacy.[6]

Burosumab 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.[7,8]

AIM

The aim of this prospective observational study was to assess the effect of 6-months of burosumab 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 burosumab 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 burosumab treatment) and every 4 weeks during the first 6-months of treatment. X-rays were also performed at baseline and at 6-months.

Burosumab 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 burosumab experienced improvements in the biochemical parameters following 6-months of treatment (Table 1).

Table 1: Effect of burosumab in XLH patients

Patient #	Laboratory parameter	Baseline (Dose 1)	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6
1	Serum phosphate (mmol/L)	0.90	1.15	1.23	1.10	1.17	1.25
	TmP/GFR (mmol/L)	1.15	1.21	1.48	NA	1.21	1.25
	ALP (IU/L)	729	623	666	412	465	446
2	Serum phosphate (mmol/L)	0.86	1.06	0.98	1.03	1.01	0.91
	TmP/GFR (mmol/L)	0.97	1.00	1.12	NA	1.03	1.00
	ALP (IU/L)	437	400	398	341	344	375
3	Serum phosphate (mmol/L)	0.66	1.11	1.06	1.03	1.00	0.99
	TmP/GFR (mmol/L)	1.28	1.41	1.37	1.35	1.33	1.31
	ALP (IU/L)	179	172	146	141	152	163
4	Serum phosphate (mmol.L)	0.57	0.73	0.86	0.83	0.85	0.87
	TmP/GFR (mmol/L)	1.36	1.48	1.33	1.35	1.39	1.42
	ALP (IU/L)	181	170	168	165	160	157
5	Serum phosphate (mmol.L)	0.69	0.79	1.04	0.95	1.01	0.82
	TmP/GFR (mmol/L)	1.28	1.36	1.39	1.38	1.40	1.37
	ALP (IU/L)	176	168	146	148	152	154

Abbreviations: NA - not available or not performed; ALP alkaline phosphate; TmP /GFR tubular maximum re absorption to glomerular filtration rate

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

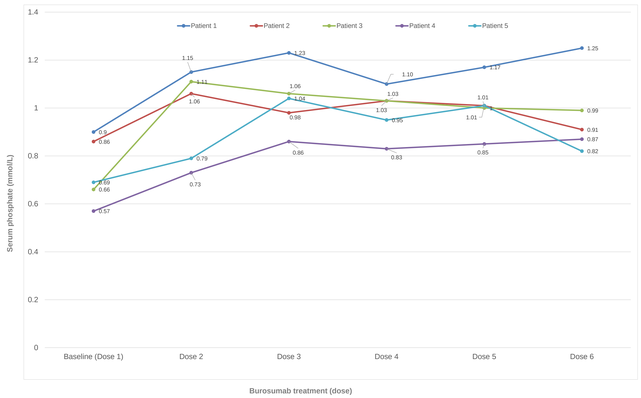

Figure 1: Serum phosphate at 6 months of burosumab treatment

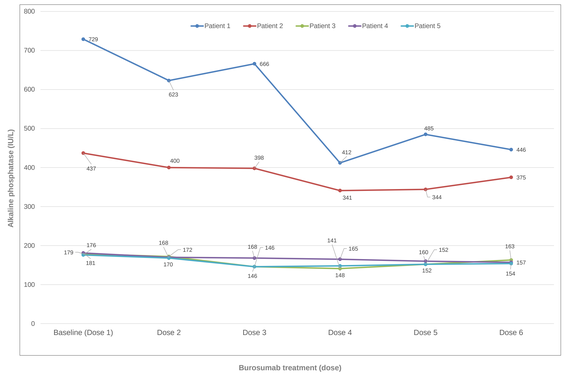

Figure 2: Alkaline phosphatase at 6 months of burosumab treatment

The X-ray evaluation indicated marked improvements in rickets (Figure 3).

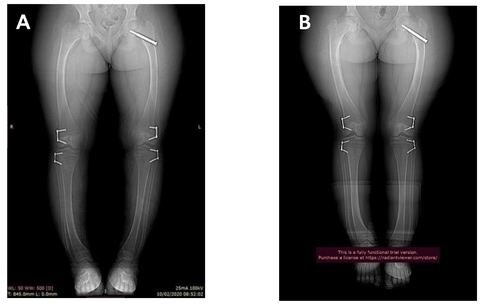

Figure 3: Radiological improvement with burosumab treatment in Patient 1

(A) Baseline lower extremity X-ray at baseline showed bilateral genu varus and and widening and cupping in the medial aspect of the distal femur
(B) Lower extremity X-ray after 6 months of burosumab treatment showed almost healed rickets in the proximal tibia and lateral aspect of the distal femur

Burosumab treatment led to improved overall quality of life in these patients. All of them reported increased active mobility and improved musculoskeletal pain, eliminating the need for daily pain medications. Furthermore, there were no treatment-related adverse events recorded.

CONCLUSIONS

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

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