Real World Experience of Burosumab Therapy in Children with X-linked Hypophosphaetemic 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 hypophosphatemia (XLH). We explored the effects in a clinical setting, considering biochemistry, growth, deformity, functionality, quality of life, pain and fatigue.

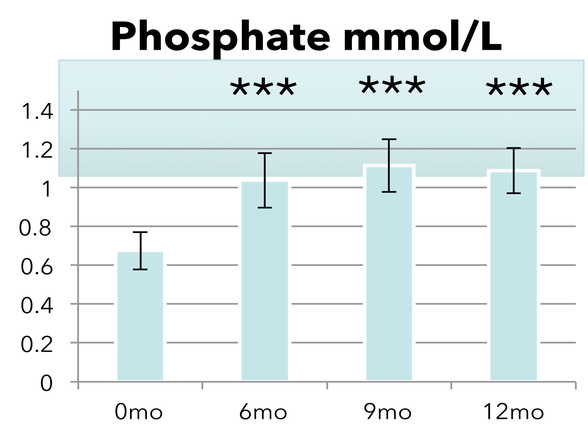
Methods

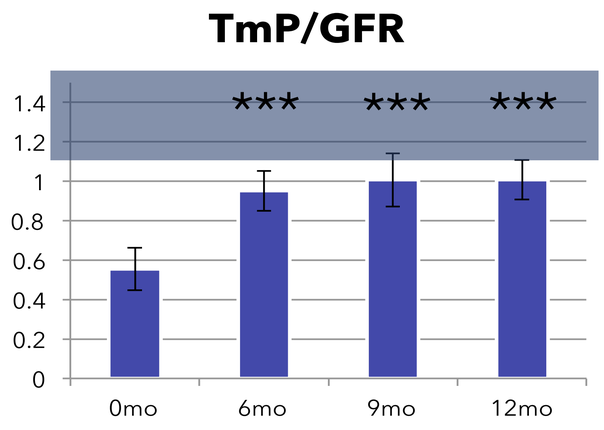
Clinical, biochemical, and questionnaire data were reviewed at 6 and 12 months for 8 children with XLH starting burosumab. Functionality was assessed with 6-minute walk test (6MWT) and Timed Up and GO (TUG). Questionnaires included: Core Paediatric Quality of Life Inventory (PedsQL-Core), Paediatric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

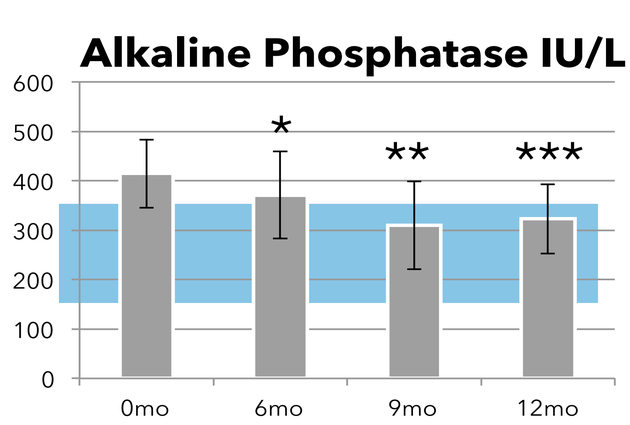
Results

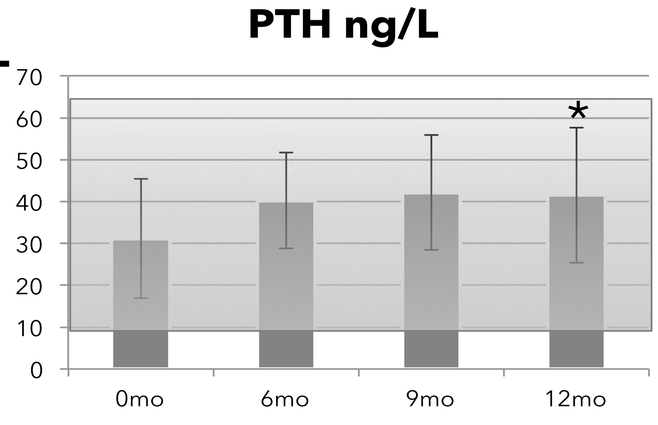
Characteristic	Baseline	6 month	12 month	P value*
Age (Median, Range)	5.5 years, 19 months - 11 years			-
Gender M/F	Females 50% (n=4)			-
Serum Phosphate Mean±SD 1.0-1.9mmol/L	0.7±0.1	1.0±0.2	1.1±0.2	<0.001
Serum alkaline phosphatase Mean±SD 163-375IU/L	415±73	371±79	323±70	<0.001
Urine Tmp/GFR** Mean±SD 1.15-2.44[1]	0.82±0.07	0.92±0.04	1.19±0.18	<0.001
Parathyroid hormone Mean±SD 10-65ng/L	31±14	40±12	42±16	<0.05
Urine calcium:creat ratio Mean±SD 0.05-0.60	0.44±0.21	0.34±0.26	0.37±0.23	=0.5
Starting dose mg (Range dose mg/kg)	10 (0.3- 1.0)	10-30 (0.6-1.7)	10-40 (0.6-2.0)	-
Height Z-scores	-2.60±0.81	-	-2.44±0.79	<0.05
TUG (N=5,seconds)	5.7±0.5	-	4.8±0.6	<0.05
6MWT (N=4,metres)	258±75	-	447±53	=0.05

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







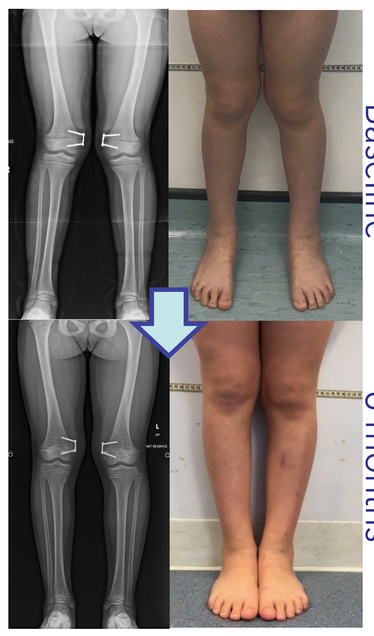


** p<0.05, **p<0.01, ***p<0.001 (as compared to baseline)*

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

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.

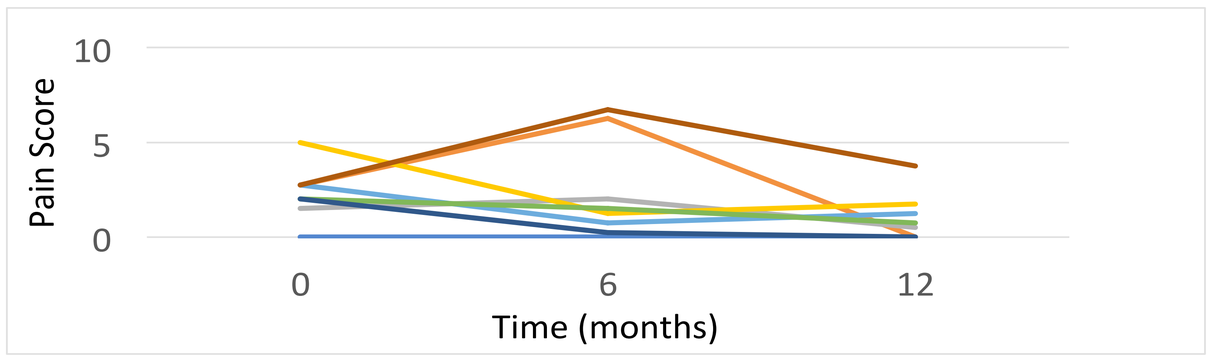


Lower Limb Deformity:

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).

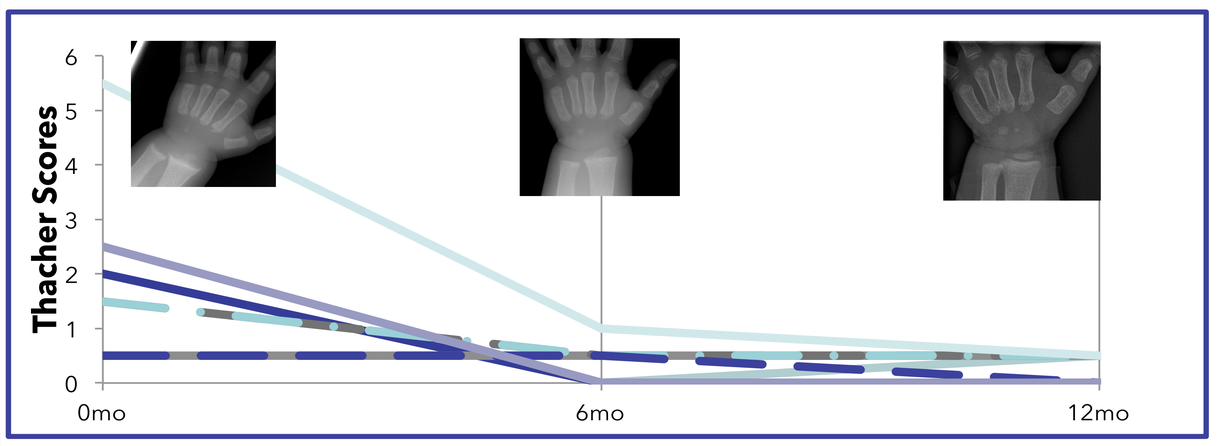


Quality of Life:

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 sometimes because of pain & fatigue – 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.

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Bone, growth plate and mineral metabolism

Jessica Sandy

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