Letter to the Editor

Burosumab: A new drug to treat hypophosphatemic rickets

Stepan Kutilek (1, 2, 3)

(1) Department of Paediatrics, Klatovy Hospital, Klatovy, Czech Republic
(2) Department of Paediatrics, Pardubice Hospital, Pardubice, Czech Republic
(3) Department of Paediatrics, Faculty of Medicine and Faculty Hospital in Hradec Kralove, Charles University, Hradec Kralove, Czech Republic

ABSTRACT

Burosumab (KRN23) is a fully human monoclonal IgG1 antibody that binds excess fibroblast growth factor 23 (FGF23) and has been successfully tested in clinical trials in children with X-linked hypophosphatemic rickets. A report enclosed in this letter gives a brief review of current knowledge on burosumab therapy.

Keywords

Burosumab, Hypophosphatemic rickets, KRN23.

LETTER

Dear Sir,

Dr. Alenazi et al. presented a patient with X-linked hypophosphatemic rickets (XLH) and gave an excellent literature overview on this topic [1]. Concerning the XLH treatment, a new investigational drug, burosumab (KRN23), which is a fully human monoclonal IgG1 antibody that binds excess fibroblast growth factor 23 (FGF23), has been successfully tested in clinical trials in XLH children and adults [2-6].

In 28 adults with XLH, monthly application of burosumab in a 4-month dose-escalation study significantly increased serum phosphate levels (S-P), renal tubular maximum reabsorption rate of phosphate/glomerular filtration rate (TmP/GFR) and 1,25(OH)2D in all subjects [2].

Furthermore, burosumab administration was associated with significantly improved patient perception of their Physical Functioning and Stiffness scores due to their disease [3].

In a phase 2, open-label study, 52 children with XLH (aged 5-12 years at baseline; previously treated by oral phosphate and active vitamin D) received burosumab subcutaneously bi-weekly or monthly. Serum phosphate levels (S-P), rickets severity score (RSS), walking ability expressed as six minute walk test (6MWT), and patient-reported pain and functional disability were assessed at baseline and at week 40. S-P increased significantly through 40 weeks. RSS improved overall by 50%. Walking ability improved from mean distance by +23 meters ($p = 0.0037$). Burosumab treatment also significantly improved pain and functional ability ($p < 0.0001$) [4]. In addition,

Correspondence to:
Stepan Kutilek
Associate Professor of Paediatric, Department of Paediatrics, Klatovy Hospital, Plzenska 929, Klatovy, Czech Republic
Email: kutilek@nemkt.cz

How to cite this article:
Kutilek S. Burosumab: A new drug to treat hypophosphatemic rickets. Sudan J Paediatr 2017;17(2):71–73
https://doi.org/10.24911/SJP.2017.2.11

these patients demonstrated increases in mean S-P, TmP/GFR and serum 1,25 dihydroxy vitamin D levels through a total of 64 weeks of treatment [6]. There was also a statistically significant improvement in RSS and radiographic Global Impreššsion of Change (RGI-C) at 64 weeks ($p < 0.0001$) together with improvement in growth velocity, 6 MWT and patient-reported pain and functional disability [6].

In an ongoing study, planned for 64 weeks, Imel et al enrolled 13 XLH children 1-4 years old with gait disturbance, tibial torsion, knee deformities and skull malformations. At baseline, all had low S-P (mean 0.8 mmol/L) and in 80% serum alkaline phosphatase activity (SALP) was elevated. Burosumab is administered every 2 weeks. After one week, mean S-P increased by 0.41 mmol/L and by 0.36 mmol/L at week 4 in the first 10 enrolled patients. Mean serum 1,25(OH)2D levels also increased after one week [5]. The children have completed 24 weeks of treatment and demonstrated increases in S-P, 1,25 (OH)2D and significant decreases in S-ALP. No serious adverse events occurred [4-6].

In conclusion, burosumab is a promising new drug in the treatment of hypophosphatemic rickets.

REFERENCES

1. Alenazi B, Molla MAM, Alshaya A, Saleh M. X-linked hypophosphatemic rickets (PHEX mutation): A case report and literature review. Sudan J Paediatr 2017; 17:61–5.
2. Imel EA, Zhang X, Ruppe MD, Weber TJ, Mark A. Klausner MA et al. Prolonged correction of serum phosphorus in adults with X-linked hypophosphatemia using monthly doses of KRN23. J Clin Endocrinol Metab 2015; 100:2565–73.
3. Ruppe MD, Zhang X, Imel EA, Weber TJ, Klausner MA, Ito T, et al. Effect of four monthly doses of a human monoclonal anti-FGF23 antibody (KRN23) on quality of life in X-linked hypophosphatemia. Bone Rep 2016; 5:158-62.
4. Imel E, Carpenter T, Linglart A, Boot A, Hogler W, Padidela R, et al. Effects of KRN23, a fully human anti-FGF23 monoclonal antibody on functional outcomes in children with X-linked hypophosphatemia (XLH). Results from a randomized, openlabel phase 2 study. 8th International Conference on Children's Bone Health (ICCBH), 10–13 June 2017, Wurzburg, Germany; 69:P063.
5. Imel E, Carpenter T, Gottesman GS, San Martin J, Mao M, Skrinar A, et al. KRN23 effects on phosphate and vitamin D dysregulation in children <5 years old with X-linked hypophosphatemia (XLH). 8th International Conference on Children´s Bone Health (ICCBH), 10-13 June 2017, Wurzburg, Germany; 45–46:OC24.
6. Ultragenyx and Kyowa Kirin International announce positive data from Paediatric Phase 2 studies of burosumab (KRN23) in X-Linked hypophosphatemia. Available at: www.ultragenyx.com [Accessed April 6, 2017].

EDITOR AND AUTHOR'S REPLY

Dear Dr. Kutilek,

Thank you for your letter addressing important up to date information about this new medication. We, Dr. Alenazi and Dr. Babiker, Assistant International Editor of Sudanese Journal of Paediatrics (SJP), are Pediatric Endocrinologists, and we are so passionate about burosumab (KRN23) as a new medicine for the rare bone disease. This December 2017, the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended a grant of conditional approval for marketing authorization of Crysvita (burosumab) in the European Union. As you concluded Dr. Kutilek, we believe that burosumab is a promising medicine that clinicians wait for a long time to manage the challenging condition of X-linked hypophosphatemic rickets (XLHPR). Not only in XLHPR, it may also be effective in treating the autosomal dominant type of hypophosphatemic rickets given its site of action in the phosphate metabolism pathway.

In fact, Dr. Alenazi's patient that was presented in the last issue of SJP represents a cohort of patients who suffers from this debilitating and crippling disease that is not free of pain and also not without

significant psychological burden on the affected children and their families. Baring this in mind, we collaborated with one of our colleagues in the United Kingdom who leads in KRN23 trials and with Kyowa Kirin pharmaceuticals, the producing company of burosumab, as well as with our local drug authority - Saudi Food and Drug Association (SFDA) - in order to facilitate "early access" of the medication to our XLHPR patients. Moreover, a regional advisory board that guide an efficient use of this new medication in the area was formulated lead by Dr. Mohammed Al Dubayee, Head of pediatric endocrine division, and coordinated by Dr. Amir Babiker, the SJP editor, both from the same institute. You may be pleased to hear that this is progressing well and hopefully burosumab will be soon available for our patients in the Middle East; namely in Saudi Arabia to start with and at least at King Abdullah Specialized Children's Hospital, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, as a centre of excellence before being widely used in the country and allover the gulf area.

Once again, kindly accept our sincere thanks for your comments regarding Dr. Alenazi's case report and literature review, and also for your contribution in this issue of SJP with the brief, yet valuable, report on burosumab.

Yours truly,

Dr. Amir Babiker, Assistant International Editor of SJP

Dr. Badi Alenazi, SJP Article Author