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LETTER TO THE EDITOR

Appropriate dosing of burosumab in tumor-induced osteomalacia

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To the Editor:

We appreciated the recently published paper of Crotti and coworkers in which the authors reported a patient with tumor-induced osteomalacia (TIO) treated with burosumab for over 2 years for a tumor located in the pre-sacral region that recurred 18 months after excision [1]. Recurrence was associated with decline of serum phosphate (SP) and increase of serum FGF23. After 4 years of treatment with calcitriol and phosphorus supplements without SP normalization, burosumab was started "at the dose of 0.3 mg/kg/month." The starting dose of burosumab used in this patient was the same used in two previous trials on TIO adult patients [2, 3]. However, in these studies, the overall effects were not completely satisfactory. For example, tubular reabsorption of phosphate remained low, mean SP was barely in the normal range, fractures persisted after 2 years of treatment, new fractures developed, and the osteoid surface/bone surface remained elevated. In addition, pain relief was moderate in one study[2] and absent in the other[3]. As noted by Hartley and Collins [4], these findings contrast with the effects of burosumab (starting dose, 1 mg/kg/month) in adults with X-linked hypophosphatemia (XLH), in which, compared to TIO, baseline SP and intact FGF23 are higher and lower, respectively, and normalization of SP and fracture healing occur faster [4, 5]. In the patient described by Crotti and coworkers [1], burosumab at the starting dose of 0.3 mg/kg/month failed to normalize SP and, when increased to 0.6 mg/kg/month, the patient showed a "new and persistent decline of SP" that resolved in 2 months after the increase of the dose to 0.8 mg/kg/month[4]. It is likely that, in TIO patients with unresectable/unlocalizable tumors, higher doses are required at the onset to achieve the desired effects (i.e., normalization of SP and resolution of symptoms). Doses up to 2 mg/kg Q2W have been approved for these patients [4].

Declarations

Conflict of interest Salvatore Minisola served as a speaker for Abiogen, Bruno Farmaceutici, Diasorin, Kyowa Kirin, UCB. He also served in the advisory board of Eli Lilly, Kyowa Kirin, UCB. All other authors have no conflict of interest to declare.

References

1. Crotti C, Zucchi F, Alfieri C, Caporali R, Varenna M (2022) Long-term use of burosumab for the treatment of tumor-induced osteomalacia. Osteoporos Int 4:1–6. https://doi.org/10.1007/s00198-022-06516-6
2. Jan de Beur SM et al (2021) Burosumab for the treatment of tumor-induced osteomalacia. J Bone Miner Res 36:627–635. https://doi.org/10.1002/jbmr.4233
3. Imanishi Y et al (2021) Interim analysis of a phase 2 open-label trial assessing burosumab efficacy and safety in patients with tumor-induced osteomalacia. J Bone Miner Res 36:262–270. https://doi.org/10.1002/jbmr.4184
4. Hartley IR, Collins MT (2021) Burosumab for tumor-induced osteomalacia: not enough of a good thing. J Bone Miner Res 36:2453–2454. https://doi.org/10.1002/jbmr.4318
5. Insogna KL et al (2018) A randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy of burosumab, an anti-FGF23 antibody, in adults with X-linked hypophosphatemia: week 24 primary analysis. J Bone Miner Res 33:1383–1393. https://doi.org/10.1002/jbmr.3475

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