CORRESPONDENCE

RE: Denosumab for Patients With Persistent or Relapsed Hypercalcemia of Malignancy Despite Recent Bisphosphonate Treatment

Jason Adhikaree, Yvette Newby, Santhanam Sundar

Affiliation of authors: Academic Oncology Department, Nottingham City Hospital, Nottingham, UK (JA, YN, SS).
Correspondence to: Jason Adhikaree, Academic Oncology Department, Nottingham City Hospital, Hucknall Road, Nottingham, UK NG5 1PB (e-mail: jadhikaree@doctors.org.uk).

We read with interest the correspondence by Tsuda et al. (1) on the article by Hu et al. (2). Tsuda et al. advocate the need to monitor patients for hypocalcemia when denosumab therapy is used for hypercalcema of malignancy (HCM) refractory to intravenous bisphosphonates (1).

Our experience in an ovarian cancer patient strongly supports their concerns. Our 66-year-old patient was originally diagnosed with ovarian cancer in 2001 and treated surgically with a total abdominal hysterectomy and bilateral salpingectomy and oophorectomy, followed by adjuvant carboplatin and paclitaxel. She relapsed in 2012 and was rechallenged with chemotherapy and required regular bisphosphonate treatment from November 2012 for paraneoplastic hypercalcemia. However, she became bisphosphonate resistant and was treated with denosumab when her adjusted serum calcium level rose to 3.21 mmol/L (August 2013). The following day, her adjusted calcium decreased to 2.72 mmol/L, and by day 14 her adjusted calcium was 2.55 mmol/L, the first time her adjusted calcium had fallen into normal range in 12 months. The serum calcium remained normal for many months with just one injection of Denosumab given concurrently with her chemotherapy. By day 89, her adjusted calcium went up to 2.85 mmol/L and a second administration of denosumab was given and again normalization of serum calcium was achieved. By day 190, her adjusted calcium was again 3.04 mmol/L and a third denosumab treatment provided (Figure 1A). She subsequently became severely hypocalcemic (adjusted calcium 1.5 mmol/L), combined with pronounced hypophosphatemia (level 0.32 mmol) and low magnesium (0.36 mmol/L). The patient was symptomatic and required two hospital admissions to address her electrolyte imbalance.

This case serves as a precautionary warning that whilst denosumab is beneficial in controlling bisphosphonate refractory HCM, it can render patients substantially hypocalcemic without substantial renal impairment (Figure 1B). Patients on Denosumab should therefore have their blood monitored regularly, and replacement calcium should be administered to those patients who develop hypocalcemia despite previously being hypercalcemic.

References

Figure 1. A) Adjusted Calcium mmol/L post–denosumab treatment. B) Creatinine umol/L post–denosumab treatment.