Denosumab Shows Promise for Hypercalcemia of Malignancy

Denosumab, a RANKL inhibitor, shows efficacy as therapy for patients with relapsed or persistent hypercalcemia of malignancy, as evidenced by results of a recent study.

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January 10, 2015 – In patients with relapsed or persistent hypercalcemia of malignancy (HCM), denosumab treatment showed reduced albumin-corrected serum calcium (CSC) in 80% of participants in a recent open label, single arm, proof-of-concept study.

Mimi I. Hu, MD, with the University of Texas MD Anderson Cancer Center, in Houston, Texas, and colleagues reported their findings in the September 18, 2013 issue of the *Journal of the National Cancer Institute*.

Denosumab is a human monoclonal antibody which acts as a RANKL inhibitor thereby reducing bone resorption.

Previous phase III trials showed improved efficacy of denosumab in preventing HCM in patients with advanced cancer with bone involvement as compared to treatment with the biphosphonate, zoledronic acid.

The current study enrolled a total of 15 participants with solid or hematological malignancies who received intravenous biphosphonate therapy within the previous 7-30 days and showed persistent or relapsed HCM, defined as CSC of >12.5 mg/dL. Patients received 120 mg of subcutaneous denosumab weekly during weeks 1-3, once during week 5, then every 4 weeks thereafter. Researchers collected blood samples to assess CSC on predetermined days during study course.

The proportion of patients responding to denosumab therapy within 10 days of initiation of therapy served as the primary endpoint for this study. Response was defined as CSC 11.5 mg/dL or less and was noted in 12 patients (80%; 95% exact CI = 52% to 96%) by day 10, median 8 days (95% CI = 5 days to not estimable).

In evaluation of the secondary endpoints, 10 (67%; 95% exact CI = 38% to 88%) of the 12 patients who exhibited response within 10 days, showed complete response defined as CSC <= 10.8 mg/dL. Researchers also observed a median response duration of 26 days (95% CI = 7 days to not estimable).

Adverse events (AE) occurred in 14 (93%) of the study participants, with 12 (80%) experiencing serious AE's and 8 (53%) experiencing non-denosumab related fatal AE's. Nonfatal AE's did lead to study withdrawal of 7 (47%) participants. Nausea, pyrexia and cancer-related hypercalcemia each occurred in 20% of the study population. This safety profile is consistent with previous reports of denosumab therapy in advanced cancer patients.

In this patient population with persistent or relapsed HCM after biphosphonate treatment, a randomized controlled trial to compare denosumab with biphosphonate therapy was not ethically appropriate. Despite the small study size and narrow patient population, the researchers evidenced improved response duration with denosumab (26 days) as compared to biphosphonate therapy (18 days). The authors concluded that this “clinically meaningful outcome” suggests that “denosumab may offer a new treatment option for HCM in this challenging population.”

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