Managing Myeloma

Denosumab for Bone Disease in NDMM

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Welcome to *Managing Myeloma*. My name is Dr. Noopur Raje, and I am a Professor of Medicine at Harvard Medical School and the Director of the Center for Multiple Myeloma at Massachusetts General Hospital in Boston, Massachusetts. Today, I will be reviewing the results of an international randomized double-blind trial that evaluated the efficacy and safety of denosumab compared to zoledronic acid in newly diagnosed multiple myeloma patients. The background of this trial was based on a smaller trial we did which included a subset of approximately 200 multiple myeloma patients. That trial, despite showing a benefit in terms of skeletal-related events, had a survival disadvantage. We then carried out this very large randomized international trial. It is 1700 plus patients, with the idea of making sure that we included in the randomization stratification for the kind of treatment myeloma patients receive; the kind of risk stratification in terms of ISS staging; whether or not they would get a transplant; whether they get new drugs versus not. We did here a double-blind randomized trial wherein patients received denosumab at a dose of a 120 mg subcutaneously every 4 weeks versus zoledronic acid at the recommended dose of 4 mg intravenously. What we found in this trial was the skeletal-related events, whether a patient had denosumab or zoledronic acid, ended up being equivalent. We also found a progression-free survival (PFS) benefit in terms of nearly 10 months of a PFS advantage to patients getting denosumab versus zoledronic acid. When we looked at overall survival, we did not see any differences in overall survival in patients receiving either denosumab or zoledronic acid. When we looked at a landmark analysis in this trial, what we found was that SREs were significantly lower in patients who were getting denosumab versus those who got zoledronic acid. This trial, therefore, demonstrates to us that we have a new active bone-targeted agent in addition to zoledronic acid. It is in fact safer in patients with renal dysfunction, and the progression-free survival benefit with denosumab is something which needs to be investigated further. Thank you for viewing this activity.