Role for Novel Drug Sotatercept in Multiple Myeloma Treatment?

By Leah Lawrence [2]

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The novel experimental drug sotatercept increased bone mineral density and bone formation in patients with osteolytic lesions of multiple myeloma who had not used bisphosphonates, a phase II study showed. In addition, sotatercept resulted in increased hemoglobin levels suggesting that it could be used as an erythropoietic agent in the future.

“Sotatercept treatment increased biomarkers of bone formation and lumbar bone mineral density, and appeared to produce clinical responses in heavily pretreated multiple myeloma patients with osteolytic bone lesions,” wrote Kudrat M. Abdelkadyrov, MD, PhD, of the Russian Research Institute of Hematology and Blood Transfusion, and colleagues. “By decoupling pathological bone remodeling, sotatercept may be able to direct bone remodeling balance more in favor of bone formation, and may potentially have a role in countering the osteolytic bone lesions associated with myeloma.”

According to the study published in the British Journal of Haematology, patients with multiple myeloma often develop skeletal abnormalities and bone pain. Although standard treatment for these symptoms is bisphosphonates, the drugs can be associated with transient or sometimes serious side effects. Therefore, new treatments for skeletal-related events in patients with multiple myeloma are needed.

Sotatercept is a recombinant activin receptor type IIA IgC-Fc fusion protein used in the treatment of anemia and bone loss. Prior research has shown that the drug may prevent continued loss of bone and that it has resulted in increases in hemoglobin, hematocrit, and red blood cell counts in patients with myeloma.

This phase II study included 30 patients with newly diagnosed or relapsed multiple myeloma who were randomly assigned 4:1 to four 28-day cycles of sotatercept or placebo. Patients also received six cycles of combination oral melphalan, prednisolone, and thalidomide (MPT). The patients were heavily pretreated. Forty-three percent were anemic.

All 30 patients received at least one dose of sotatercept; 25% of the patients assigned sotatercept received all four cycles and 87% of patients completed the study.

Seventy-one percent of patients had at least one dose interruption, mainly due to hemoglobin levels that were greater than 110 g/L. One patient had a dose interruption due to grade 2 hypertension. In addition, 58% of patients assigned sotatercept had a grade 3/4 adverse event compared with 17% of patients assigned placebo. Grade 4 adverse events for patients treated with sotatercept were neutropenia, granulocytopenia, and atrial fibrillation.

All patients assigned to sotatercept had an increase in hemoglobin levels. The researchers observed a trend of higher hemoglobin levels in patients assigned the investigational drug compared with placebo, suggesting a dose-related effect.

“An exploratory analysis of maximum mean change in percentage from baseline in ‘bone specific’ alkaline phosphatase (bALP) levels in patients, stratified by bisphosphonate use at baseline, suggested a dose-related effect in patients not receiving bisphosphonates,” the researchers wrote. Overall, serum bALP levels increased by more than 30% in 45.8% of patients assigned sotatercept and in 50% of patients assigned placebo. Among those patients who received the full four cycles of treatment a 30% increase in bALP at one or more point in time was seen in 83.3% of patients. In patients not taking bisphosphonates a 30% increase was seen in 57.1% of patients assigned sotatercept and 66.7% of patients in the placebo group. However, these rates were lower in patients receiving bisphosphonates: 30% of patients assigned sotatercept and 33.3% in patients assigned placebo.

Hip bone mineral density increased in patients assigned 0.1 mg/kg and 0.3 mg/kg sotatercept
compared with placebo and with patients assigned 0.5 mg/kg sotatercept. Increases in lumbar spine bone mineral density were also seen for the 0.1 mg/kg and 0.3 mg/kg groups; however, patients assigned to 0.5 mg/kg sotatercept had decreased lumbar bone mineral density. Again, bone mineral density levels were more likely to increase among patients who had undergone all four cycles of sotatercept.

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