



Arthritis News

Media Contact: Tammy McCoy
(404) 633-3777 (until Oct. 15)
(210) 582-7010 (Oct. 16–Oct. 21)
tmccoy@rheumatology.org

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SEMI-ANNUAL THERAPY MAY PROVE EFFECTIVE IN DECREASING BONE RESORPTION FOR POSTMENOPAUSAL PATIENTS

SAN ANTONIO, TEXAS—A novel treatment administered semiannually to postmenopausal women with low bone density appears to rapidly inhibit the bone resorption process, resulting in improvements in bone mineral density at 12 months, according to research presented this week at the American College of Rheumatology annual scientific meeting in San Antonio, Texas.

Bone is living tissue that is in constant regeneration. This means tissues that form bone are constantly being created and resorbed by the body. During adolescence and early adulthood, bone growth resulting in peak bone density is due to the significantly greater new bone formation as compared to bone resorption. With aging and the loss of estrogen post menopause, the balance between bone resorption and new bone formation shifts. More bone is lost than can be replaced, leaving bones thinner and structurally weaker. This results in osteoporosis and fragility fractures.

Researchers recently studied a new treatment antibody, AMG 162, that binds to a receptor protein on the surfaces of osteoclasts—the cells that function in the absorption and removal of bone tissue. AMG 162, which is still in clinical trials, may prevent bone loss resulting in osteoporosis and the bone erosions that lead to rheumatoid arthritis.

To assess AMG 162's effectiveness when administered every six months, researchers conducted a year-long test of different doses of the antibody use in 411 women, average age 63 years, who are participating in an ongoing, randomized study. Eight of the nine treatment groups received double-blind, subcutaneous injections of AMG 162 (six, 14 or 30 milligrams every three months, or 14, 60, 100 or 210 milligrams every six months) or a placebo. The last group received open-label 70-milligrams of oral alendronate once weekly. Urine and blood tests as well as X-rays were used to evaluate results.

An anti-resorptive response, as measured by bone turnover markers (urine and blood tests), was almost immediately evident in all patients taking the antibody, and continued to improve through month four. Depending on AMG 162 dose levels, increases in bone mineral density also were observed as early as month one. The most common adverse effect, indigestion, occurred in only a small portion of all groups. Overall, AMG 162 administered once every six months was well tolerated and caused a rapid, dose-dependent increase in bone formation and bone density.

“If ongoing clinical trials demonstrate fracture risk reduction, this therapy should lead to a dramatic improvement in patient compliance due to the ease of administration compared to presently available osteoporosis treatment,” said S.B. Cohen, MD, Radiant Research, Dallas, Texas, and an investigator in the study.

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR's annual meeting, see www.rheumatology.org/annual.

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AMG 162 Administered Every 6 Months Causes Rapid and Sustained Decreases in Bone Turnover in Postmenopausal Women With Low Bone Mineral Density (BMD)

S. B. Cohen¹, M. R. McClung², E. M. Lewiecki³, M. A. Bolognese⁴, G. Woodson⁵, A. Moffett⁶, M. Peacock⁷, P. D. Miller⁸, S. Lederman⁹, D. L. Holloway¹⁰, T. Liu¹⁰, P. J. Bekker¹⁰. ¹Radiant Research, Dallas, TX; ²OR Osteoporosis Ctr, Portland, OR; ³NM Clin Research & Osteoporosis Ctr, Albuquerque, NM; ⁴Bethesda Health Research Ctr, Bethesda, MD; ⁵Atlanta Research Ctr, Decatur, GA; ⁶OB/GYN Assoc Mid-FL, Lessburg, FL; ⁷Indiana Univ School Medicine, Indianapolis, IN; ⁸CO Ctr Bone Research, Lakewood, CO; ⁹Radiant Research, Lake Worth, FL; ¹⁰Amgen Inc., Thousand Oaks, CA.

Receptor activator of NF kappa B ligand (RANKL) is a novel therapeutic target for osteoporosis and rheumatoid arthritis.

AMG 162 is a fully human monoclonal antibody with high affinity and specificity for RANKL that inhibits osteoclastic bone resorption. The objectives of this ongoing, randomized, double-blind study were to evaluate AMG 162 in postmenopausal women (lumbar spine BMD T-score -1.8 to -4.0). Of the 9 treatment groups, 8 were randomized to receive double-blind, subcutaneous injections of AMG 162 (6, 14, or 30 mg 3-monthly or 14, 60, 100, or 210 mg 6-monthly [q6mo]) or placebo; 1 group received open-label, 70-mg oral alendronate once weekly. Bone turnover markers (serum C-telopeptide [CTX] and urine N-telopeptide [NTX]/creatinine), BMD by dual energy x-ray absorptiometry, and safety measurements have been followed for 12 months.

411 women were enrolled (40–53 per group). Baseline mean (SD) age was 63 (8) years and lumbar spine T-score -2.2 (0.8). AMG 162 treatment (q6mo) decreased serum CTX with an antiresorptive effect evident at the first time point after dosing (72 hrs). Decreases in serum CTX in all AMG 162 groups were significantly greater than alendronate ($p < 0.0001$) through month 2, and in the 3 highest AMG 162 dose groups through month 4. The response in urine NTX/creatinine confirmed the serum CTX response.

AMG 162 3-monthly dosing also showed a sustained antiresorptive response. Dose-dependent increases in BMD (4% to 7% lumbar spine and 2% to 4% total hip at 12 months in all AMG 162 groups; 5% and 2%, respectively, for alendronate) were observed as early as 1 month after dosing. AMG 162 was well tolerated. Dyspepsia, the most common adverse event in any group, occurred in 4%, 5%, and 20% of subjects in the placebo, AMG 162, and alendronate groups, respectively. One (0.3%) subject (14 mg AMG 162) had a transient, asymptomatic decrease in albumin-adjusted serum calcium below 8 mg/dL (7.8 mg/dL at 2 months). No other clinically meaningful laboratory changes occurred. Non-neutralizing anti-AMG 162 antibodies were detected at month 1 for 1 (0.3%) subject, but did not persist.

In summary, AMG 162 administered once every 6 months was well tolerated and caused a rapid, dose-dependent, decrease in bone turnover markers and a corresponding increase in BMD.

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