STUDY SUPPORTS BISPHOSPHONATE USE PRIOR TO DENOSUMAB TO PREVENT LOSS OF BONE MINERAL DENSITY IN POST-MENOPAUSAL WOMEN

Significantly more patients with stable bone mineral density after discontinuation of denosumab received zoledronate prior to initiation of denosumab.

Madrid, Spain, 13 June 2019: The results of a study presented today at the Annual European Congress of Rheumatology (EULAR 2019) finds the risk of bone mineral density (BMD) loss after denosumab discontinuation is associated with younger age, high bone turnover markers, and not receiving the bisphosphonate, zoledronate, prior to initiation of denosumab.

The study followed 71 post-menopausal women who were classified into ‘loser’ or ‘stable’ groups based on their BMD loss one year after discontinuation of denosumab. Between group analysis revealed that, at initiation of denosumab, the ‘loser’ group was significantly younger (61.4 ±7.3 vs. 65.5±8.2, p=0.034), with higher level of the bone turnover marker sCTX (644.7 vs. 474.1ng/ml, p=0.005). The use of bisphosphonates after denosumab discontinuation was comparable between groups; however, interestingly none of the ‘loser’ group had received zoledronate prior to initiation of denosumab vs. 12% of the ‘stable’ group (p=0.047). Other pre-denosumab characteristics were not different.

“Our study suggests that being younger, having higher bone turnover markers and not having received zoledronate before denosumab introduction increase the risk of bone mineral density loss following discontinuation of denosumab,” said Dr Bérengère Aubry-Rozier, Rheumatology Unit, Lausanne University Hospital, Lausanne, Switzerland. “Our results support the use of denosumab after a bisphosphonate to reduce the bone mineral density loss at its discontinuation, and close monitoring of sCTX to maintain levels below the upper limit of the normal range for premenopausal women.”

Denosumab is a human monoclonal antibody that prevents the maturation of osteoclasts by binding to and inhibiting NF-κB ligand (RANKL), a central regulator of bone metabolism. Bisphosphonates, such as zoledronate, act mainly by inhibiting osteoclast-mediated bone resorption and are characterised by their high affinity with bone and a long half-life within the skeleton. This long-lasting retention on bone provides a residual treatment effect on bone resorption even after treatment discontinuation. In contrast, the effect of denosumab is limited to the period of drug exposure. In addition, the discontinuation of denosumab is associated with significant bone turnover rebound, rapid loss of bone mass, and a risk of multiple vertebral fractures. One to ten per cent of patients are at risk of multiple vertebral fractures, with a median of five vertebral fractures in the seven to 20 months following denosumab discontinuation.
“There has previously been a lack of evidence related to the risk of fracture following discontinuation of denosumab and measures to prevent it,” said Professor Hans Bijlsma, President, EULAR. “Therefore, we welcome these data that will contribute to our understanding in this area.”

The study included 71 post-menopausal women from the ReoLaus (Rebound Effect Observatory in Lausanne) Bone Project who had BMD follow up for more than one year after discontinuation of denosumab. Patients who had a lumbar spine BMD loss of over 3.96% at one year after denosumab discontinuation were defined as ‘losers’ (n=30) with the rest termed ‘stable’ (n=41).¹

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NOTES TO EDITORS
For further information on this study, or to request an interview with the study lead, please do not hesitate to contact the EULAR Press Office:

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About Rheumatic and Musculoskeletal Diseases
Rheumatic and musculoskeletal diseases (RMDs) are a diverse group of diseases that commonly affect the joints, but can also affect the muscles, other tissues and internal organs. There are more than 200 different RMDs, affecting both children and adults. They are usually caused by problems of the immune system, inflammation, infections or gradual deterioration of joints, muscle and bones. Many of these diseases are long term and worsen over time. They are typically painful and limit function. In severe cases, RMDs can result in significant disability, having a major impact on both quality of life and life expectancy.³

About EULAR
The European League against Rheumatism (EULAR) is the European umbrella organisation representing scientific societies, health professional associations and organisations for people with RMDs. EULAR aims to reduce the burden of RMDs on individuals and society and to improve the treatment, prevention and rehabilitation of RMDs. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes the translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the EU institutions through advocacy action.

To find out more about the activities of EULAR, visit: www.eular.org
References


