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Editorial

An Editorial: Osteoporosis and Romosozumab

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A bone disorder with low bone density, impaired bone architecture and low bone strength leading to predisposed fractures is termed as Osteoporosis [1]. Since the bone loss occurs without symptoms this is often called as the silent disease [2]. Due to reduced bone formation loss of bone mass occurs in either third or fourth decade in both men and women [1]. Deficiency of hormone, calcium and vitamin D results in accelerated bone turnover and decreased osteoblast formation causing Osteoporosis. Drug induced osteoporosis may be caused by systemic corticosteroids, anti-epileptics like Phenytoin and Phenobarbital, Depot medroxyprogesterone acetate etc [1].

Incidence of Osteoporosis increases with age and it is more common in females (9 - 38%) than males (2 - 8%). There are over 200 million people with Osteoporosis and approximately 9 million fractures per year are related to osteoporosis across the world [3]. Fracture of vertebrae, proximal femur and distal radius are quite common. Drugs used for treating Osteoporosis generally focus on either decreased resorption or increased bone formation. (i) Antiresorptive agents like Calcium and Vitamin D supplements, Bisphosphonates inhibits resorption and improves bone mineral density. (ii) RANK (Receptor Activator of Nuclear factor Kappa) ligand inhibitor like Denosumab inhibits osteoclast formation thereby reduces bone breakdown. (iii) Mixed Estrogen agonists and antagonists act by decreasing bone loss. (iv) Anabolic agents like Teriparatide, a recombinant product increases osteoblast formation thereby facilitating new bone formation [1].

Unlike all these drugs, Romosozumab (EVENITY) developed by Amgen and UCB was approved by U. S FDA in April 2019 which can facilitate bone formation and decreases bone resorption. It is a monoclonal humanized antibody (IgG2) produced by recombinant DNA technology that inhibits sclerostin [4]. Sclerostin is secreted by osteocytes and is considered as a negative regulator for bone formation [5].

Development of romosozumab

Sclerosteosis and Van Buchmen disease are the two autosomal recessive disorders characterized by high bone mineral density due to deficiency of Sclerostin. Recognition of sclerostin effects led to the development of sclerostin inhibitors which can act as the potential treatment option for Osteoporosis. Canonical Wnt pathway activation leads to a series of intracellular events which translocates β-catenin to the nucleus of osteoblasts and also gene transcription that facilitates bone formation by stimulating osteoblast differentiation, proliferation and survival. SOST, Sclerostin binding gene is expressed in osteocytes. Osteoblasts contain Low density lipoprotein Receptor Protein 5 and 6 (LRP 5/6) and Frizzled co-receptors. When Sclerostin binds to these receptors, the canonical Wnt pathway is inhibited resulting in decreased bone formation. Sclerostin also increases production of Receptor Activator of Nuclear factor Kappa (RANK) ligand by osteocytes facilitating bone resorption. Hence, sclerostin inhibitor Romosozumab promotes bone formation and decreases bone resorption [6].

In a phase 2 trail, after one year of administration of Romosozumab in post-menopausal women with osteoporosis lower risk of vertebral and clinical fractures are found compared to placebo. Increase in bone mineral density is noticed at hip and spine. The foundation for ongoing reduction in risk of fracture is laid with Sequential therapy involving Denosumab. Adverse events are balanced in both groups [5].

In a randomized study involving one year of Romosozumab vs placebo which is followed by Denosumab for 2 years the incidence of cardiovascular event, deaths are low and similar in both the groups. This study concluded that the regimen Romosozumab followed by Denosumab increased bone mineral density and is the potential regimen for treating post-menopausal women having osteoporosis and is at high risk for fracture [7].

In a phase 3 multicentre, randomized study rapid increase in bone mineral density and decreased risk of fracture is seen with Romosozumab compared to Alendronate for one year [8].

Recommended dosage

Inject two prefilled syringes 105 mg/1.17 ml each one after another. Total dose of 210 mg administered subcutaneously once every month in the abdomen, thigh or upper arm.

Duration of therapy: 12 months.

Warnings and precautions

Adequate precautions should be taken before administration and the following conditions are to be considered: Major adverse cardiac events, hypersensitivity reactions, hypocalcaemia, osteonecrosis of the jaw, atypical sub trochanteric and diaphyseal fractures [4].

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