RESUMENES DE OSTEOPOROSIS

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Switching to Denosumab or Bisphosphonates after completion of teriparatide treatment in women with severe postmenopausal osteoporosis.

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Objective: We compared bone mineral density (BMD) changes after 12 months' treatment with denosumab or bisphosphonates in postmenopausal women with severe osteoporosis after stopping teriparatide therapy. Methods: We retrospectively analyzed 140 postmenopausal women (mean age 74.2 years) with severe osteoporosis who had been treated with teriparatide for 18–24 months at our outpatient clinic in a tertiary endocrine center between 2006 and 2015. After stopping teriparatide, they continued treatment with a bisphosphonate (alendronate, risedronate, ibandronate, or zoledronic acid) or denosumab, while receiving daily vitamin D and calcium. BMD at the lumbar spine (LS), total hip (TH), and femoral neck (FN) was measured by dual-energy X-ray absorptiometry when teriparatide was discontinued (baseline) and after 12 months of further treatment. Multivariate linear regression models were used to identify predictors of BMD gain. Results: After stopping teriparatide, 70 women continued treatment with bisphosphonates and 70 received denosumab. LS, but not TH or FN, BMD gain was significantly greater in the denosumab than the bisphosphonates group at 12 months. Multivariate analysis showed that BMD gain at the LS was negatively associated with bisphosphonate versus denosumab treatment, and positively associated with baseline serum total procollagen type 1 N-terminal propeptide (PINP). BMD gains at the FN were predicted by higher baseline serum urate levels. BMD gains at the TH and FN were negatively associated with pretreatment BMD gains at the same site. Conclusions: Twelve months after stopping teriparatide, sequential denosumab treatment appears to yield higher additional LS BMD gain on average compared to bisphosphonates.

Should denosumab treatment for osteoporosis be continued indefinitely?

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Denosumab was approved for the treatment of postmenopausal osteoporosis in 2010, based on the FREEDOM study, which indicated a benefit in terms of increased bone mineral density and reduced risk of major osteoporotic fracture. In the initial clinical studies it was noted that discontinuation of denosumab can lead to a rebound of bone turnover markers and loss of accrued bone mineral density. An increased risk of fractures (multiple vertebral fractures in particular) associated with discontinuation was noted after approval and marketing of denosumab. For many patients experiencing gain in bone mineral density and fracture prevention while taking denosumab, there is no reason to stop therapy. However, discontinuation of denosumab may happen due to non-adherence; potential lack of efficacy in an individual; where reimbursement for therapy is limited to those with bone mineral density in the osteoporosis range, when assessment reveals this has been exceeded; or patient or physician concern regarding side effects. This review paper aims to discuss these concerns and to summarize the data available to date regarding sequential osteoporosis therapy following denosumab cessation to reduce the risk of multiple vertebral fracture.

Management of osteoporosis in older men .
Jean-Marc Kaufman
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As many as one out of three fragility fractures occur in older men and the outcome of major osteoporotic fractures, in particular hip fractures, is worse in men than in women. Osteoporosis in older men is thus an important threat to the quality of life of individual patients and a considerable burden for society. However, only a small minority of older men with high or very high fracture risk are receiving therapy. This does not need to be so as tools for fracture risk assessment are available, and several drugs have been approved for treatment. Nevertheless, the evidence base for the management of osteoporosis in older men remains limited. This narrative review summarizes the evidence for older men on the burden of osteoporosis, the pathophysiology of fragility fractures, the clinical presentation, diagnosis and risk assessment, the patient evaluation, and the non-pharmacological and pharmacological management.

Romosozumab: A Review in Postmenopausal Osteoporosis.
Paik, J., Scott, L.J.
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Romosozumab (Evenity®), a humanized monoclonal antibody, promotes bone formation and inhibits bone resorption by inhibiting sclerostin, a protein involved in the regulation of bone formation. Subcutaneous romosozumab is approved in several countries, including those of the EU for treating severe osteoporosis as well as in the USA for osteoporosis in postmenopausal women at high risk of fracture. In pivotal phase III trials (FRAME and ARCH), 12 months' once monthly romosozumab 210 mg significantly reduced vertebral and clinical fracture risk versus placebo and oral alendronate in postmenopausal women with osteoporosis. After patients transitioned from romosozumab to 12–24 months of subcutaneous denosumab or oral alendronate, fracture risks were significantly improved versus placebo-to-denosumab and alendronate-only treatment. In these trials and a phase IIIb trial, romosozumab significantly increased bone mineral density (BMD) relative to placebo, alendronate and subcutaneous teriparatide at 12 months, with these benefits maintained 12–24 months after patients transitioned from romosozumab to alendronate or denosumab in pivotal trials. Romosozumab had a generally manageable tolerability profile. While further clinical experience is needed to more definitively establish its efficacy and safety, including its CV safety, romosozumab extends the treatment options in postmenopausal women with osteoporosis who have a high risk of fracture and in those who have failed or are intolerant to other available osteoporosis therapy.

How to manage osteoporosis before the age of 50.
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Maturitas 2020, 138:14.25

This narrative review discusses several aspects of the management of osteoporosis in patients under 50 years of age. Peak bone mass is genetically determined but can also be affected by lifestyle factors. Puberty constitutes a vulnerable period. Idiopathic osteoporosis is a rare, heterogeneous condition in young adults due in part to decreased osteoblast function and deficient bone acquisition. There are no evidence-based treatment recommendations. Drugs use can be proposed to elderly patients at very high risk. Diagnosis and management of osteoporosis in the young can be challenging, in particular in the absence of a manifest secondary cause. Young adults with low bone mineral density (BMD) do not necessarily have osteoporosis and it is important to avoid unnecessary treatment. A determination of BMD is recommended for premenopausal women who have had a fragility fracture or who have secondary causes of osteoporosis: secondary causes of excessive bone loss need to be excluded and treatment should be targeted. Adequate calcium, vitamin D, and a healthy lifestyle should be recommended. In the absence of fractures, conservative management is generally sufficient, but in rare cases, such as chemotherapy-induced osteoporosis, antiresorptive medication can be used. Osteoporosis in young men

is most often of secondary origin and hypogonadism is a major cause; testosterone replacement therapy will improve BMD in these patients. Diabetes is characterized by major alterations in bone quality, implying that medical therapy should be started sooner than for other causes of osteoporosis. Primary hyperparathyroidism, hyperthyroidism, Cushing's syndrome and growth hormone deficiency or excess affect cortical bone more often than trabecular bone.

Molecular Mechanisms and Emerging Therapeutics for Osteoporosis
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Int. J. Mol. Sci. 2020, 21, 7623; doi:10.3390/ijms21207623

Osteoporosis is the most common chronic metabolic bone disease. It has been estimated that more than 10 million people in the United States and 200 million men and women worldwide have osteoporosis. Given that the aging population is rapidly increasing in many countries, osteoporosis could become a global challenge with an impact on the quality of life of the affected individuals. Osteoporosis can be defined as a condition characterized by low bone density and increased risk of fractures due to the deterioration of the bone architecture. Thus, the major goal of treatment is to reduce the risk for fractures. There are several treatment options, mostly medications that can control disease progression in risk groups, such as postmenopausal women and elderly men. Recent studies on the basic molecular mechanisms and clinical implications of osteoporosis have identified novel therapeutic targets. Emerging therapies targeting novel disease mechanisms could provide powerful approaches for osteoporosis management in the future. Here, we review the etiology of osteoporosis and the molecular mechanism of bone remodeling, present current pharmacological options, and discuss emerging therapies targeting novel mechanisms, investigational treatments, and new promising therapeutic approaches.

Pathogenesis of glucocorticoid-induced osteoporosis and options for treatment
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Nature Reviews Endocrinology 2020;16:437-447

Glucocorticoids are widely used to suppress inflammation or the immune system. High doses and long-term use of glucocorticoids lead to an important and common iatrogenic complication, glucocorticoid-induced osteoporosis, in a substantial proportion of patients. Glucocorticoids mainly increase bone resorption during the initial phase (the first year of treatment) by enhancing the differentiation and maturation of osteoclasts. Glucocorticoids also inhibit osteoblastogenesis and promote apoptosis of osteoblasts and osteocytes, resulting in decreased bone formation during long-term use. Several indirect effects of glucocorticoids on bone metabolism, such as suppression of production of insulin-like growth factor 1 or growth hormone, are involved in the pathogenesis of glucocorticoid-induced osteoporosis. Fracture risk assessment for all patients with long-term use of oral glucocorticoids is required. Nonpharmacological interventions to manage the risk of fracture should be prescribed to all patients, while pharmacological management is reserved for patients who have increased fracture risk. Various treatment options can be used, ranging from bisphosphonates to denosumab, as well as teriparatide. Finally, appropriate monitoring during treatment is also important

Advances in mesenchymal stem cell transplantation for the treatment of osteoporosis
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Osteoporosis is a systemic metabolic bone disease with characteristics of bone loss and microstructural degeneration. The personal and societal costs of osteoporosis are increasing year by year as the ageing of population, posing challenges to public health care. Homing disorders, impaired capability of osteogenic differentiation, senescence of mesenchymal stem cells (MSCs), an imbalanced microenvironment, and disordered immunoregulation play important roles during the pathogenesis of osteoporosis. The MSC transplantation promises to increase osteoblast differentiation and block osteoclast activation, and to rebalance bone formation and resorption. Preclinical investigations on MSC transplantation in the osteoporosis treatment provide evidences of enhancing osteogenic differentiation, increasing bone mineral density, and halting the deterioration of

osteoporosis. Meanwhile, the latest techniques, such as gene modification, targeted modification and co-transplantation, are promising approaches to enhance the therapeutic effect and efficacy of MSCs. In addition, clinical trials of MSC therapy to treat osteoporosis are underway, which will fill the gap of clinical data. Although MSCs tend to be effective to treat osteoporosis, the urgent issues of safety, transplant efficiency and standardization of the manufacturing process have to be settled. Moreover, a comprehensive evaluation of clinical trials, including safety and efficacy, is still needed as an important basis for clinical translation.

Is there a role for menopausal hormone therapy in the management of postmenopausal osteoporosis? .

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We provide an evidence base and guidance for the use of menopausal hormone therapy (MHT) for the maintenance of skeletal health and prevention of future fractures in recently menopausal women. Despite controversy over associated side effects, which has limited its use in recent decades, the potential role for MHT soon after menopause in the management of postmenopausal osteoporosis is increasingly recognized. We present a narrative review of the benefits versus risks of using MHT in the management of postmenopausal osteoporosis. Current literature suggests robust anti-fracture efficacy of MHT in patients unselected for low BMD, regardless of concomitant use with progestogens, but with limited evidence of persisting skeletal benefits following cessation of therapy. Side effects include cardiovascular events, thromboembolic disease, stroke and breast cancer, but the benefit-risk profile differs according to the use of opposed versus unopposed oestrogens, type of oestrogen/progestogen, dose and route of delivery and, for cardiovascular events, timing of MHT use. Overall, the benefit-risk profile supports MHT treatment in women who have recently (< 10 years) become menopausal, who have menopausal symptoms and who are less than 60 years old, with a low baseline risk for adverse events. MHT should be considered as an option for the maintenance of skeletal health in women, specifically as an additional benefit in the context of treatment of menopausal symptoms, when commenced at the menopause, or shortly thereafter, in the context of a personalized benefit-risk evaluation.

European Consensus Statement on the diagnosis and management of osteoporosis in chronic kidney disease stages G4–G5D

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Controlling the excessive fracture burden in patients with chronic kidney disease (CKD) Stages G4–G5D remains an impressive challenge. The reasons are 2-fold. First, the pathophysiology of bone fragility in patients with CKD G4–G5D is complex and multifaceted, comprising a mixture of age-related (primary male/postmenopausal), drug-induced and CKD related bone abnormalities. Second, our current armamentarium of osteoporosis medications has not been developed for, or adequately studied in patients with CKD G4–G5D, partly related to difficulties in diagnosing osteoporosis in this specific setting and fear of complications. Doubts about the optimal diagnostic and therapeutic approach fuel inertia in daily clinical practice. The scope of the present consensus paper is to review and update the assessment and diagnosis of osteoporosis in patients with CKD G4-G5D and to discuss the therapeutic interventions available and the manner in which these can be used to develop management strategies for the prevention of fragility fracture. As such, it aims to stimulate a cohesive approach to the management of osteoporosis in patients with CKD G4–G5D to replace current variations in care and treatment nihilism.