Postmenopausal Osteoporosis: Latest Guidelines

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KEYWORDS

• Postmenopausal osteoporosis • Osteopenia • Fragility fracture • DXA • FRAX
• Treatment guidelines • AACE • ACE

KEY POINTS

- Significant development has occurred in the treatment of Postmenopausal Osteoporosis. We review the most recent guidelines from American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE), Endocrine Society (ES), and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis/International Osteoporosis Foundation (ESCEO/IOF).
- The new anabolic agent, Romosozumab, is now approved for use in treatment of postmenopausal osteoporosis and is now included in the treatment algorithm in major endocrinology/osteoporosis society guidelines.
- AACE/ACE, ES, and ESCEO/IOF Clinical guidelines highlights the importance of fracture risk assessment to help stratify patients and guide decision-making in pharmacologic therapy.

OSTEOPOROSIS

Osteoporosis is a disease characterized by increased bone turnover and decreased bone mass with associated skeletal fragility, resulting in an increased risk of fracture.[1] It is a well-defined and growing public health problem. The National Osteoporosis Foundation estimates that 10.2 million Americans have osteoporosis and that an additional 43.4 million have low bone mass. It is estimated that by 2030, the number of adults with osteoporosis and low bone mass will increase to 71 million.[2]

More than 2 million osteoporosis-related fractures occur annually in the United States. Approximately 1 in 2 White women and 1 in 5 men will experience an osteoporotic-related fracture in their lifetime. By 2025, the burden in the country is projected to increase by almost 50% to more than 3 million fractures and US$253 billion per year.[3]

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In 1994, a Working Group of the World Health Organization established an operational definition of osteoporosis based on bone mineral density (BMD). Osteoporosis is defined as a BMD 2.5 SD or more below the average value for premenopausal women.[4] Normal BMD is defined as T-score of −1.0 or higher and a T-score between −1.0 and −2.5 is defined as osteopenia or low bone mass.

Although osteoporosis has traditionally been diagnosed based on low bone density in the absence of fracture, the 2016 and 2020 American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) Clinical Practice Guidelines for Diagnosis and Treatment of Postmenopausal Osteoporosis[5] agree that osteoporosis may also be diagnosed in patients with osteopenia and increased fracture risk using FRAX country-specific thresholds (**Table 1**).

DIAGNOSIS

History and physical examination should include assessment of risk factors for fractures as well as secondary causes of osteoporosis (**Box 1**).

The fracture risk assessment tool known as FRAX, introduced in 2008, is a computer-based algorithm (http://www.shef.ac.uk/FRAX) that calculates the 10-year probability of a major osteoporotic fracture (hip, clinical spine, humerus, or wrist fracture) and the 10-year probability of hip fracture.[6] Fracture risk is calculated from age, body mass index, and well-validated dichotomized risk factors (**Table 2**).

The risk factors included in FRAX are listed in **Table 2**. When using the FRAX tool, pharmacologic intervention is recommended for patients with greater than or equal to 20% probability of major osteoporotic fracture or greater than or equal to 3% probability of hip fracture in the next 10 years in the United States, and this may be slightly different in other countries.

TREATMENT

Nonpharmacologic Management

Screening for causes of secondary osteoporosis should be completed and corrected. Preventive therapy, with calcium and vitamin D supplements, and medication compliance and fall prevention need to be stressed to the patients at every visit.

Table 1
Diagnostic criteria

WHO Criteria for Classification of Osteopenia and Osteoporosis		2016 and 2020 AACE Diagnosis of Osteoporosis in Postmenopausal Women
Category	T-score	1. T-score −2.5 or below in the lumbar spine, femoral neck, total proximal femur, or 1/3 radius
Normal	−1.0 or above	
Low bone mass (osteopenia)	Between −1.0 and −2.5	2. Low-trauma spine or hip fracture (regardless of BMD)
Osteoporosis	−2.5 or below	3. T-score between −1.0 and −2.5 and a fragility fracture of proximal humerus, pelvis, or distal forearm
Severe or established osteoporosis	−2.5 or below with fragility fracture	4. T-score between −1.0 and −2.5 and high FRAX (or if available, TBS-adjusted FRAX) fracture probability based on country-specific thresholds

Abbreviations: AACE, American Association of Clinical Endocrinologists; BMD, bone mineral density; TBS, trabecular bone score; WHO, World Health Organization.

Box 1
Causes of secondary osteoporosis

Endocrine or Metabolic Causes
- Hyperparathyroidism
- Hypophosphatasia
- Hypercortisolism
- Diabetes
- Adrenal insufficiency
- Hypogonadism
- Hyperthyroidism
- Growth hormone deficiency
- Acromegaly
- Pregnancy

Nutritional and gastrointestinal conditions
- Vitamin D deficiency
- Calcium deficiency
- High caffeine intake
- Anorexia nervosa
- Alcoholism
- Chronic liver disease
- Malabsorption (inflammatory bowel diseases, celiac sprue, pancreatic disease, gastric resection or bypass)

Medications
- Glucocorticoids
- Aromatase inhibitors
- Gonadotropin-releasing hormone agonists
- Lithium
- Medroxyprogesterone acetate
- Chemotherapy and immunosuppressant
- Antiepileptics (phenobarbital, phenytoin, carbamazepine, valproate)
- Anticoagulants (heparin and coumadin)
- Thiazolidinediones
- Proton pump inhibitors
- Thyroid hormone (in supraphysiologic doses)
- Antiretrovirals (tenofovir, adefovir)
- Sodium-glucose co-transporter-2 inhibitors

Connective tissue disorders
- Osteogenesis imperfecta
- Marfan syndrome
- Ehlers-Danlos syndrome
- Homocystinuria

Hematologic disorders
- Multiple myeloma
- Leukemia and lymphoma
- Hemophilia
- Sickle cell disease
- Thalassemia
- Systemic mastocytosis

Miscellaneous
- Idiopathic hypercalciuria
- Immobilization
- Low physical activity
- Rheumatoid arthritis
- Chronic obstructive pulmonary disease
- Chronic kidney disease
- Congestive heart failure
- Human immunodeficiency virus and acquired immunodeficiency syndrome

Table 2
FRAX tool

Country of Origin	
Ethnicity	(US models only—white, black, Hispanic, and Asian)
Age	The model accepts ages between 40 and 90 y. If ages younger than or older than are entered, FRAX tool will compute probabilities at 40 and 90 y, respectively.
Sex	
Weight	(in kg)
Height	(in cm)
Previous fracture	(defined as fracture in adult life occurring spontaneously or fragility/low-trauma fracture)
Parental history of hip fracture	
Current smoking	
Glucocorticoid use	(defined as oral glucocorticoid use for more than 3 mo at a dosage of prednisolone $\geq$ 5 mg/d, or equivalent dose of other glucocorticoids)
Rheumatoid arthritis	
Secondary osteoporosis	(including type 1 diabetes mellitus, osteogenesis imperfecta, untreated longstanding hyperthyroidism, hypogonadism or premature menopause, chronic malnutrition or malabsorption, and chronic liver disease)
Alcohol use	($\geq$3 units of alcohol per day, the definition of a unit of alcohol depends on the country ranging from 8–10 g of alcohol)
Femoral neck bone mineral density (BMD) (or *T*-score)	In patients without a BMD test, the field should be left blank

The AACE 2020 guidelines recommend the following measures to prevent bone loss: adequate calcium intake of 1200 mg/d for women age $\geq$50 years (total intake including diet plus supplement, if needed), vitamin D3 supplementation if needed, with a daily dosage of 1000 to 2000 international units to maintain 25 OHD levels between 30 and 50 ng/mL, less than 2 servings of alcohol per day, limiting caffeine intake, smoking cessation, and maintaining an active lifestyle with recommended 30 minutes of weight-bearing exercise a day. Use of bone turnover markers in the initial evaluation and follow-up of osteoporosis patients can also be considered as elevated levels can predict more rapid rates of bone loss and higher fracture risk.[5]

Decision-Making on Pharmacologic Therapy

The goal of using pharmacologic therapies to treat low BMD or osteoporosis in postmenopausal women is to decrease the burden of major osteoporotic fractures. Pharmacologic therapy is indicated in patients with *T*-scores in the osteoporotic range and those with history of fragility fracture. However it is important to note that most fractures occur in patients with osteopenia or low bone mass (*T*-score between -1.0 and -2.5), as these individuals outnumber those with osteoporosis. Therefore, major osteoporosis guidelines[5,7] also recommend the treatment of patients with history of hip or vertebral fracture; or patients with osteopenia and a history of fragility fractures or with greater than or equal to 20% probability of major osteoporotic fracture or

greater than or equal to 3% probability of a hip fracture in the next 10 years (or based on country-specific threshold) based on FRAX tool. In an update to the European Guidelines, patients are stratified into patients into low risk, high risk, and very high risk based on clinical factors such as age, sex, body mass index, prior fractures, with or without BMD.[8]

When starting treatment, it is appropriate to stratify patients by level of fracture risk (**Table 3**) because this may influence selection of initial treatment as well as the duration of therapy. Most patients are started on treatment because of high fracture risk. Some who are at very high fracture risk may require more aggressive treatment to achieve an acceptable level of fracture risk (**Tables 4** and **5**).

Several agents are approved by the Food and Drug Administration (FDA) for prevention and/or treatment of postmenopausal osteoporosis (**Table 6**). Head-to-head trial data are limited. Approved agents with efficacy to reduce hip, nonvertebral, and spine fractures including alendronate, denosumab, risedronate, and zoledronate are appropriate as initial therapy for most osteoporotic patients with high fracture risk. Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for patients unable to use oral therapy and as initial therapy for patients at very high fracture risk (see **Tables 4** and **5**). These drugs also should be considered for those who have gastrointestinal problems and might not tolerate or absorb oral medication, and for patients who have trouble remembering to take oral medications or coordinating an oral bisphosphonate with other oral medications or daily routine. Ibandronate or raloxifene may be appropriate initial therapy in some cases for patients requiring drugs with spine-specific efficacy.

ANTIRESORPTIVE AGENTS

Bisphosphonates

Bisphosphonates are the most widely used class of medication for treatment of osteoporosis. These pyrophosphate analogues bind to hydroxyapatite crystals in the bone, inhibit function and recruitment of osteoclasts, and increase osteoclast apoptosis. Oral bioavailability is only 1% to 3%, but they have prolonged skeletal retention. In the United States, 4 bisphosphonates are available (alendronate, ibandronate, risedronate, and zoledronate), all available as generic preparations. Three of the 4 (alendronate, risedronate, and zoledronate) have evidence for broad-spectrum antifracture efficacy. A systematic review of trials published between 2005 and 2019 confirmed the vertebral fracture prevention efficacy of alendronate, risedronate, zoledronic acid, and ibandronate, compared with placebo.[10] Alendronate, risedronate, and zoledronic acid also reduce the risk of hip and other nonvertebral fractures.[11]

Oral bisphosphonates should be taken in the morning on an empty stomach (for maximal absorption) and with a full glass of water. Patients should be advised to remain upright for at least 30 minutes after ingestion. Bisphosphonates should be used with caution, if at all, in patients with reduced kidney function (glomerular filtration rate <30 mL/min for risedronate and ibandronate or <35 mL/min for alendronate). Before the administration of intravenous bisphosphonate, zoledronate, a creatinine clearance should be calculated based on the serum creatinine and actual body weight using the Cockcroft-Gault formula before each dose, and is not recommended for patients with creatinine clearance less than 35 mL/min.

Raloxifene

Raloxifene is a selective estrogen receptor modulator, with agonistic effects on bone. It is approved by the FDA for prevention and treatment of postmenopausal

Table 3
Risk stratification

Risk for Fractures	AACE/ACE 2020	Endocrine Society 2020	ESCEO/IOF 2019
Very high risk	Recent fracture (eg, within the past 12 mo) Fractures while on approved osteoporosis therapy History of multiple fractures Fractures while on drugs causing bone loss (eg, long-term glucocorticoids) Very low T-score (eg, <−3.0) High risk for falls History of very high fracture probability by FRAX	Multiple spine fractures BMD T-score at the hip or spine of −2.5 or below	Low, high, and very high risk based on FRAX/with or without BMD, refer to intervention thresholds[a] Examples: Prior fracture (of uncertain recency) Prior clinical vertebral fracture within the past 2 years Family history of hip fracture, exposure to glucocorticoids, exposure to higher than average doses of glucocorticoids B Bone mineral density (BMD) T-score at the femoral neck[b]
High risk	Patients who have been diagnosed with osteoporosis but are not at very high fracture risk as above	Prior spine or hip fracture BMD T-score at the hip or spine of −2.5 or below 10-y hip fracture risk ≥ 3%, or risk ofmajor osteoporoticfracture risk ≥ 20%	
Moderate risk		No prior hip or spine fractures BMD T-score at the hip and spine both above −2.5 10-y hip fracture risk < 3% or risk ofmajor osteoporotic fractures < 20%	
Low risk		No prior hip or spine fractures BMD T-score at the hip and spine both above −1.0 10-y hip fracture risk < 3%, and 10-yrisk ofmajor osteoporotic fractures < 20%	

Abbreviations: AACE/ACE, American Association of Clinical Endocrinologists/American College of Endocrinology; BMD, bone mineral density; ESCEO/IOF, European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis/International Osteoporosis Foundation.

[a] https://link.springer.com/article/10.1007/s00198-019-05176-3/figures/2.

[b] https://link.springer.com/article/10.1007/s00198-019-05176-3/tables/1.

Data from Refs.[5,7–9]

Table 4
Initial choice of agents

AACE/ACE 2020	Endocrine Society 2020	ESCEO/IOF 2019/2020
High risk: alendronate, risedronate, denosumab, zoledronate Very high risk: abaloparatide, denosumab, romosozumab, teriparatide, zoledronate	High risk: alendronate, risedronate, zoledronic acid, and ibandronate. Denosumab as alternative Very high risk: teriparatide, abaloparatide, romosozumab	High risk: oral bisphosphonates and other inhibitors of bone resorption Very high risk: anabolic agent followed by inhibitor of bone resorption

Abbreviations: AACE/ACE, American Association of Clinical Endocrinologists/American College of Endocrinology; ESCEO/IOF, European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis/International Osteoporosis Foundation.
Data from Refs.[5,7,8]

osteoporosis as well as for the reduction of risk of breast cancer in women with postmenopausal osteoporosis or at high risk of breast cancer. The major efficacy trial for raloxifene was the Multiple Outcomes of Raloxifene Evaluation (MORE) trial.[12] Raloxifene has been shown to reduce the risk of vertebral fracture. No significant difference in nonvertebral and hip fracture reduction was observed.

Calcitonin

Calcitonin is most useful as an alternative agent after an acute vertebral fracture given its systemic analgesic effects. It has modest effect on BMD and fracture reduction, and is recommended to be used with a stronger antiresorptive when possible.[13]

Estrogen

Although once considered the treatment of choice for postmenopausal osteoporosis, estrogen was never specifically approved for this use. Estrogen is approved by the FDA for prevention of postmenopausal osteoporosis with the added caveat, "when prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom nonestrogen medications are not considered to be appropriate." Current recommendations are to use estrogen for the relief of menopausal symptoms in the lowest dose necessary and for the shortest time possible.[5]

Table 5
Duration of therapy

AACE/ACE 2020	Endocrine Society 2020	ESCEO/IOF 2019/2020
Oral bisphosphonates for 5 y for high risk/up to 10 y for very high risk Zoledronate 3 y for high risk/up to 6 y for very high risk Assess fracture risk annually	Reassess fracture risk at 3–5 y	Reassess bisphosphonate use after 3–5 y Reassess after a new fracture

Abbreviations: AACE/ACE, American Association of Clinical Endocrinologists/American College of Endocrinology; ESCEO/IOF, European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis/International Osteoporosis Foundation.
Data from Refs.[5,7,9]

Table 6
Pharmacologic therapies: drugs approved by the U.S. Food and Drug Administration for treatment of postmenopausal osteoporosis

Antiresorptive Agents		Parathyroid Hormone Analogues		Romosozumab	
Bisphosphonates	10 mg PO daily	Teriparatide (Forteo)	20 μg SQ daily	Humanized monoclonal antibody against osteocyte-derived sclerostin (Evenity)	210 mg SQ monthly
Alendronate (Fosamax)	70 mg PO weekly	Abaloparatide (Tymlos)	80 μg SQ daily		
Risedronate(Actonel, Atelvia)	5 mg PO daily 35 mg PO weekly				
Ibandronate (Boniva)	150 mg PO monthly				
Zoledronate (Reclast)	2.5 mg PO daily				
Denosumab (Prolia)	150 mg PO monthly				
Selective estrogen agonists/antagonists	3 mg IV every 3 mo 5 mg IV once yearly				
Raloxifene (Evista)	60 mg SQ every 6 mo				
Estrogens	60 mg PO daily				
Multiple formulations	200 IU intranasally once daily or 100 IU SQ qod				
Calcitonin (Miacalcin, Fortical)					

Abbreviations: IV, intravenous; PO, by mouth; qod, every other day; SQ, subcutaneous.

Denosumab

Denosumab is a human monoclonal antibody to Receptor activator of nuclear factor κB ligand (RANKL) that reversibly inhibits osteoclast-mediated bone resorption. RANKL binds to its receptor RANK on osteoclasts and osteoclast precursors acting as a key mediator of osteoclast differentiation, action, and survival. This process is regulated by a decoy receptor called osteoprotegrin that binds RANKL and prevents activation of osteoclasts. It is FDA approved for the treatment of osteoporosis in postmenopausal women, male osteoporosis, glucocorticoid-induced osteoporosis, and cancer treatment–induced bone loss.

Denosumab is administered as a 60-mg subcutaneous injection every 6 months. The effects of denosumab on bone remodeling, reflected in bone turnover markers, reverse after 6 months if the drug is not taken on schedule.[7] Case reports of multiple vertebral fractures on stopping denosumab therapy have been reported.[14] Drug holidays from denosumab are therefore not recommended because of this potential increased fracture risk. Although more data are needed to further elucidate the clinical impact of this phenomenon, patients should be informed about the importance of not missing a dose of denosumab and discontinuation of denosumab should be avoided without a proper treatment transition plan. The AACE/ACE Postmenopausal Osteoporosis Guidelines recommended that patients be transitioned with intravenous zoledronic acid or alternatively alendronate for 1 year. During this transition period, bone turnover markers and DXA can be followed and the patients closely monitored for evidence of rebound increase in bone resorption or multiple vertebral fractures[5] The ESCEO/IOF Guidelines also recommended the use of bisphosphonate after denosumab therapy to prevent an increase in vertebral fracture rate.[8]

ANABOLIC AGENTS

Teriparatide and Abaloparatide

Synthetic human parathyroid hormone (PTH) 1 to 34, or teriparatide (Forteo), is an anabolic agent that has been approved for the treatment of postmenopausal and male osteoporosis. The landmark trial in postmenopausal women was the Fracture Prevention Trial (FPT). In this randomized placebo-controlled trial (n = 1637) by Neer and colleagues,[15] postmenopausal women with at least 1 prior vertebral fracture, 20 μg teriparatide administered daily decreased the risk for new vertebral fractures by 65% and nonvertebral fragility fractures by 53%, with an increased BMD at lumbar spine by 9% and at femoral neck by 3% over a median follow-up period of 21 months.[15]

Abaloparatide (modified PTH-related peptide [PTHrP] 1–34) is approved by the FDA for the treatment of women with postmenopausal osteoporosis who are at high risk of fracture or have failed or been intolerant of previous osteoporosis therapy. It is also injected subcutaneously but it does not require refrigeration after use, compared with teriparatide.

The dose of abaloparatide is 80 μg daily, whereas teriparatide is given at 20 μg daily. It is recommended to measure serum calcium, PTH, and 25(OH)D levels, and alkaline phosphatase (to rule out Paget disease) before treatment with either medication.

Teriparatide was approved by the FDA in December of 2002 with a “black box” warning for potential increased risk of osteosarcoma, which was observed in a high percentage of rodents treated with high doses of teriparatide for most of their lifespan. A postmarketing surveillance program for evaluation of an association between osteosarcoma and treatment with teriparatide did not show any patients with

osteosarcoma with prior teriparatide treatment.[16] Side effects of abaloparatide and teriparatide are similar and mild and transient and include nausea, orthostatic hypotension, and leg cramps. Elevated calcium level was also reported, but is usually mild, and transient. If serum calcium is measured, the blood should be drawn at least 16 hours after drug administration.

Teriparatide and abaloparatide are approved for treatment for up to 2 years for the reduction of vertebral and nonvertebral fractures. Once treatment course is completed, treatment with antiresorptive osteoporosis therapies to maintain bone density gain is recommended.

ROMOSOZUMAB

Romosozumab is a monoclonal antibody directed against sclerostin. Sclerostin is a product of the SOST gene that binds LRP5/6 and inhibits the Wnt signaling pathway and the differentiation of precursor cells into mature bone-forming osteoblasts. Blocking sclerostin binding to osteoblasts allows osteoblast activity to increase. Thus, inactivation or inhibition of sclerostin can lead to increased bone mass. The drug appears to have both an antiresorptive and anabolic effect.

Approval of romosozumab for postmenopausal women at high risk of fracture was based on 2 large trials. In the larger of the 2 trials (n = 7180),[17] patients were randomly assigned to receive subcutaneous injections of romosozumab (at a dosage of 210 mg) or placebo monthly for 12 months; thereafter, patients in each group received denosumab for 12 months, at a dosage of 60 mg, administered subcutaneously every 6 months. At 12 months, new vertebral fractures had occurred in 16 (0.5%) of 3321 patients in the romosozumab group, as compared with 59 (1.8%) of 3322 in the placebo group (representing a 73% lower risk with romosozumab; $P < .001$). Clinical fractures had occurred in 58 (1.6%) of 3589 patients in the romosozumab group, as compared with 90 (2.5%) of 3591 in the placebo group (a 36% lower risk with romosozumab; $P = .008$). Nonvertebral fractures had occurred in 56 (1.6%) of 3589 patients in the romosozumab group and in 75 (2.1%) of 3591 in the placebo group ($P = .10$). At 24 months, the rates of vertebral fractures were significantly lower in the romosozumab group than in the placebo group after each group made the transition to denosumab (0.6% [21 of 3325 patients] in the romosozumab group vs 2.5% [84 of 3327] in the placebo group, a 75% lower risk with romosozumab; $P < .001$).

In the other trial,[18] 4093 postmenopausal women with osteoporosis and a fragility fracture were assigned to receive monthly subcutaneous romosozumab (210 mg) or weekly oral alendronate (70 mg) in a blinded fashion for 12 months, followed by open-label alendronate in both groups. Over a period of 24 months, a 48% lower risk of new vertebral fractures was observed in the romosozumab-to-alendronate group (6.2% [127 of 2046 patients]) than in the alendronate-to-alendronate group (11.9% [243 of 2047 patients]) ($P < .001$). Clinical fractures occurred in 198 (9.7%) of 2046 patients in the romosozumab-to-alendronate group versus 266 (13.0%) of 2047 patients in the alendronate-to-alendronate group, representing a 27% lower risk with romosozumab ($P < .001$).

The recommended dosage is 210 mg monthly by subcutaneous injection for 12 months (**Table 7**). Women at high risk or with prior history of cardiovascular disease and stroke should not be considered for romosozumab pending further studies on cardiovascular risk associated with this treatment.

Romosozumab has also been studied in men but is not currently approved for male osteoporosis.

Table 7
Romosozumab use

AACE/ACE 2020	Endocrine Society 2020	ESCEO/IOF 2019
For very high risk patients, with prior fractures Follow with antiresorptive agent	Very high risk of fracture, such as those with severe osteoporosis (ie, low T-score < −2.5 and fractures) or multiple vertebral fractures Follow with antiresorptive agent	Not available at the time of publication

Abbreviations: AACE/ACE, American Association of Clinical Endocrinologists/American College of Endocrinology; ESCEO/IOF, European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis/International Osteoporosis Foundation.
Data from Refs.[5,7,9]

SUMMARY

Significant advances have been made in the treatment of postmenopausal osteoporosis in the past decade. The latest guidelines from AACE, Endocrine Society, and the ESCEO/IOF have been updated and are mostly concordant in their recommendations as to risk stratification, initial therapy, and duration of treatment, as well as long-term follow-up patients.

CLINICS CARE POINTS

- When starting treatment, it is appropriate to stratify patients by level of fracture risk (low, high, and very high risk) to guide decision making in pharmacologic therapy such as selection of initial treatment and duration of therapy.
- Drug holidays from denosumab are not recommended due to potential increased fracture risk.
- Discontinuation of denosumab should be avoided without a proper treatment transition plan.
- Romosozumab, a monoclonal antibody directed against sclerostin, is now approved for use in treatment of postmenopausal osteoporosis.

DISCLOSURE

The author has nothing to disclose. Principal Investigator – Romosozumab ARCH Trial.

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