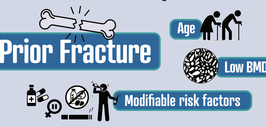
CLINICAL PEARLS FOR INJECTABLE OSTEOPOROSIS TREATMENTS

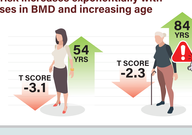
DIAGNOSING OSTEOPOROSIS AND RISK ASSESSMENT

Several factors contribute to long-term fracture risk:



Fracture risk increases exponentially with decreases in BMD and increasing age

The relationship is also age dependent, so older women (in the absence of other risk factors) may have a greater fracture risk with a lower T score than a younger woman with a higher T score.



Risk assessment includes:

1. Number of fractures
2. Bone quantity and quality
3. Fall risk

FRAX can be used with or without BMD or TBS

Combine BMD with clinical risk factors

This enables better assessment of fracture risk than BMD or risk factors alone

The FRAX tool without BMD is also reasonable

Fragility fracture confirms presence of osteoporosis

It also increases the risk of hip fracture

High fracture risk includes

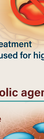
1. Hip or vertebral fracture, or >1 fracture
2. Steroid use and prior fragility fracture

Or, use the very high fracture list from the AACE guidelines

AN OVERVIEW OF OSTEOPOROSIS TREATMENT OPTIONS

Anti-remodeling agents

MOA
Inhibit bone turnover



WHEN TO USE
- Long-term treatment
- Denosumab used for high-risk patients

LIST OF AGENTS
- Calcitonin
- Estrogen agonists/antagonist (raloxifene)
- Bisphosphonates (oral and IV)
- RANK ligand inhibitor (denosumab)*

Osteoanabolic agents

MOA
Activate bone formation

WHEN TO USE
- Used for high and very high risk patients

LIST OF AGENTS
- Remodeling stimulators *(increase formation and resorption)*
  - —Parathyroid hormone receptor activators, teriparatide and abaloparatide*
- Modeling stimulators *(increase formation, decrease resorption)*
  - —Sclerostin inhibitor, romosozumab*

*SC/injectable agents

INJECTABLE OSTEOPOROSIS TREATMENTS — A COMPARISON GUIDE

	Denosumab[a]	Teriparatide[b]	Abaloparatide	Romosozumab
Primary indication	*Treatment of postmenopausal women with osteoporosis at high risk of fracture*			
Safety concerns	Skin rash and eczema vs placebo Serious adverse effects related to infection Rapid loss of BMD and vertebral fracture protection upon stopping therapy **In 10 years of follow-up:** • no duration-dependent adverse effects • osteonecrosis of the jaw (5.2/10,000 person-years) • atypical femoral fracture – 2 cases (0.8/10,000 person-years)	Hypercalcemia: in ACTIVE study, 6.4% with teriparatide, 3.4% with abaloparatide **Serious Safety Concerns** • High dose, lifelong therapy in rats was associated with osteosarcoma • Boxed warnings about risk of osteosarcoma for abaloparatide • Neither drug is recommended for use in patients at risk for osteosarcoma		Injection site reactions in 4.4-5.2% vs 2.6-2.9% with placebo Rare hypersensitivity reactions **Serious Safety Concerns** Increased risk of major adverse cardiovascular events vs alendronate but not vs placebo
Route of administration	SC Q6 months	SC daily	SC daily	2 injections SC monthly
Duration of therapy	No limit (safety and efficacy data to 10 years) If therapy discontinued, follow with a bisphosphonate	24 months unless patient remains at or has returned to having a high risk for fracture	Cumulative use of any parathyroid hormone analogs for more than 2 years during a patient's lifetime is not recommended (under regulatory review; pivotal study evaluated 18 months therapy	12 months maximum
Key points	Adherence and patient satisfaction with therapy better than with oral bisphosphonates Progressive increase in BMD and reduction in non-vertebral fracture risk with longer therapy Increases BMD when given after bisphosphonate therapy	May cause kidney stones in patients with hypercalciuria Hypercalciuria is rare. If this develops, repeat the blood test 24 hours after last injection		The decision to use romosozumab in a patient with CV risk factors must be individualized Use only in patients at very high risk of fracture Avoid its use in patients at very high risk for myocardial infarction and stroke

a. Denosumab is also indicated as treatment, in patients at high risk for fracture, to increase bone mass in men with osteoporosis, of glucocorticoid-induced osteoporosis in men and women, and to increase bone mass in men and women receiving androgen deprivation therapy or adjuvant aromatase inhibitor for nonmetastatic prostate and breast cancer.

b. Teriparatide is also indicated as treatment to increase bone mass in men with primary or hypogonadal osteoporosis and for the treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone) at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy.

TREATMENT SELECTION AND SEQUENCING

Both AACE and IOF recommend choosing therapy based on fracture risk

BMD — especially in the spine — increases more and faster with anabolic therapies vs anti-remodeling drugs

The fracture protection afforded by 12-18 months of anabolic therapy persists for at least 2 years after transitioning to an anti-remodeling agent

Teriparatide and romosozumab reduce fracture risk better than oral bisphosphonates

HIGH RISK/ NO PRIOR FRACTURES[a,b]

- Alendronate, denosumab, risedronate, zoledronate[c]
- ALTERNATIVE THERAPY: ibandronate, raloxifene

REASSESS YEARLY FOR RESPONSE TO THERAPY AND FRACTURE RISK

Increasing or stable BMD and no fractures	Progression of bone loss or recurrent fractures
Consider a drug holiday after 5 years of oral and 3 years of IV bisphosphonate therapy	• Assess compliance • Re-evaluate for causes of secondary osteoporosis and factors leading to suboptimal response to therapy
Resume therapy when a fracture occurs, BMD declines beyond LSC, BTMs rise to pretreatment values or patient meets initial treatment criteria	• Switch to injectable antiresorptive if on oral agent • Switch to abaloparatide, romosozumab, or teriparatide if on injectable antiresorptive or at very high risk of fracture • Factors leading to suboptimal response

From the AACE/ACE 2020 Postmenopausal Osteoporosis Treatment Algorithm, for educational purposes only.

VERY HIGH RISK/ PRIOR FRACTURES[a,b]

- Abaloparatide, denosumab, romosozumab, teriparatide, zoledronate[c]
- ALTERNATIVE THERAPY: Alendronate, risedronate

REASSESS YEARLY FOR RESPONSE TO THERAPY AND FRACTURE RISK

Denosumab	Romosozumab for 1 year	Abaloparatide or teriparatide for up to 2 years	Zoledronate
Continue therapy until the patient is no longer high risk and ensure transition with another antiresorptive agent	Sequential therapy with oral or injectable antiresorptive agent	Sequential therapy with oral or injectable antiresorptive agent	• If stable, continue therapy for 6 years* • If progression of bone loss or recurrent fractures, consider switching to abalo-paratide, teriparatide, or romosozumab

a. Indicators of very high fracture risk in patients with low bone density would include advanced age, frailty, glucocorticoids, very low T scores, or increased fall risk.

b. From the AACE/ACE 2020 Postmenopausal Osteoporosis Treatment Algorithm, for educational purposes only.

c. Medications are listed alphabetically.

d. Consider a drug holiday after 6 years of IV zoledronate. During the holiday, an anabolic agent or a weaker antiresorptive such as raloxifene could be used.

SUMMARY OF OSTEOPOROSIS MANAGEMENT

- Osteoporosis is a chronic problem that requires life-long management
- Therapy should be individualized, considering current fracture risk among other things
- On-treatment increases in BMD correlate with reductions in current fracture risk

OSTEOANABOLIC THERAPIES:

- Larger increases in BMD and faster reduction in fracture risk than with oral bisphosphonates
- Must be followed by an anti-remodeling drug to maintain the benefit