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Plenary Panel Members

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Disclosures

Nelson B. Watts, MD – Consultant: Amgen Speaker: Amgen, Radius

Clifford J. Rosen, MD – No conflicts of interest


Dolores Shoback, MD – No conflicts of interest
Access Guideline and Other Resources

**Guideline**
J Clin Endocrinol Metab 2019; 104(5): 1595–1622

**Guideline Resource Page**
[endocrine.org/2019Osteoporosis](endocrine.org/2019Osteoporosis)

Includes access to:
- Full published guideline and systematic review papers
- Patient resources
- Pocket Card
- Interview with the Guideline Writing Committee Chair
Overview of Guideline

Clifford J. Rosen, MD
Senior Scientist, Director, Maine Medical Center
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Introduction: Guideline Development

- Guideline Writing Committee and the Chair consisted of five content experts and a methodologist.
- Recommendations were evidence-based; classified using the GRADE approach.
- 2 systematic reviews and 1 meta-analysis:
  1. Synthesized the evidence derived from RCTs in postmenopausal women with primary osteoporosis.
  2. Evaluated values and preferences relevant to the management of osteoporosis.
Risk of Fracture in Response to Treatment

**Relative Risk and 95% CI**
Effect of treatment compared to placebo
Direct calculation

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*Eastell R, Rosen CJ, Black DM, Cheung AM, Murad H, Shoback D. JCEM, 2019; 104(5)*
Women’s Values & Preferences of Treatment

**Equally Ranked**
- Efficacy/effectiveness
- Adverse effects

**Convenient Administration**
- Oral preferred over injectable
- Less frequent dosing preferred over more frequent
  - Injectable acceptable if less frequent doses

**Other Decisional Factors**
- Cost (out of pocket)
- Duration of treatment
  - Natural drug, doesn’t cause hormonal effects
- Drug time on the market
- Less drug-drug interactions
Algorithm for the Management of Postmenopausal Osteoporosis

All Postmenopausal Women
1) Lifestyle and Nutritional Optimization of Bone Health Especially Calcium and Vitamin D
2) Determine the 10-year Fracture Risk According to Country-Specific Guidelines

Low-Moderate Risk
- Low Risk
  - Reassess fracture risk in 2-4 yrs
  - (2.1) Bisphosphonates
    - (2.1.1) Reassess fracture risk in 3-5 yrs
    - (2.1.2) 5 yrs for oral, 3 yrs for IV

Moderate Risk
- (3.1) Denosumab
  - (3.1.1) Reassess fracture risk in 5-10 yrs

High-Very High Risk
- (4.1) Teriparatide or Abaloparatide
  - For 2 yrs

Low-Moderate Risk
- (2.2) Consider a drug holiday
  - (2.2.1) Reassess fracture risk every 2-4 yrs

High Risk
- (2.3) Continue therapy or switch to another therapy

Intolerant to or Inappropriate for above therapies

Age <60 or <10 yrs past menopause
  - No Vascular Symptoms
    - High Breast Cancer Risk
      - (5.1) SERM (raloxifene, bazedoxifene)
  - With Vascular Symptoms
    - (6.1-6.2) HT (no uterus, Estrogen; with uterus, Estrogen + Progestin) or Tibolone

Age >60
- Low-Moderate Risk
  - Consider giving bisphosphonates and then stopping for a drug holiday
    - (11.1) Reassess fracture risk every 1-3 yrs

High Risk
- (12.1) Continue therapy or switch to another therapy

(6.3) Calcium + Vitamin D as adjunct therapy

Key Points

- Treat high risk individuals - particularly those with previous fracture.
- For risk-assessment follow country-specific risk assessment and intervention thresholds.
- Bisphosphonates and denosumab should be the first therapeutic choices for postmenopausal women at high risk of fracture.
- Reassess fracture risk after being on bisphosphonates for 3 – 5 years.
Key Points (cont.)

- Women who are on bisphosphonates and low-to-moderate risk of fractures should be considered for a bisphosphonate holiday after being reassessed.
- Prescribe anabolic therapy for women at very high risk of fractures, including those with multiple fractures.
- Supplement calcium and vitamin D in the diet or via supplements in all women undergoing treatment with other osteoporosis therapies.
- Monitor the BMD of high risk individuals with a low BMD every 1 to 3 years.
Cases, Panel Discussion & Audience Questions

Nelson B. Watts, MD
Director, Mercy Health Osteoporosis and Bone Health Services, Cincinnati, OH
Case discussions to focus on:

1. Selecting Initial Treatment
2. Bisphosphonate Holidays
3. Denosumab: Why would you stop? What would you do?
4. Anabolic Agent for Initial Treatment
5. Combination Therapy
6. If you consider teriparatide for a denosumab user, would you add or switch?
Case 1: Selecting Initial Treatment

Presentation:
Helen is a 74-year old woman who has been well all her life. Her weight is 105 pounds (47.6 Kgs) and is 5’8” (1.7 m) tall. BMI is 16 kg/m². Menopause was age 53. Her mother had a hip fracture at age 82.

T-scores:
- Spine -3.2; Femoral neck -2.7

Z-scores:
- Spine -1.0; Femoral neck -0.9

Other Labs:
- Calcium and creatinine - normal;
- 25-OH D -satisfactory

Follow country-specific risk assessment, and intervention thresholds, in countries that do not include T-score.

Question: What pharmacologic treatment would you recommend?

A. An oral bisphosphonate
B. An IV bisphosphonate
C. Raloxifene
D. Denosumab
Guideline:
• She is at high risk as she has BMD T-score of -2.5 or less.
• Thus, the guidelines would recommend bisphosphonate (oral or iv) or denosumab, taking into account patient preference.
• We would have recommended raloxifene (or menopausal hormone therapy) had the patient been intolerant of the above treatments.
Case 2: Bisphosphonate Holidays

Presentation:
Teresa is a 60-year old woman with a history of facial neuralgia and acid reflux. She is known to have osteoporosis and had fractures at spine (T6 in 2013 - fell down the stairs), clavicle, and humerus.

Treatment:
Received 3 annual infusions of zoledronic acid, last in March 2017. Now on vitamin D and calcium.

T- scores:
- Spine -2.4 (-4.4% since 2016)
- Total hip -1.0 (-3.5% since 2016)

Other Labs:
- P1NP - 39 μg/L (previous 13 in 2015)

Question: What is the next best step?
A. Nothing; follow up
B. Give another 3 infusions of zoledronic acid
C. Give 1 infusion of zoledronic acid
D. Switch to another treatment
E. Discharge; she no longer has osteoporosis according to BMD criteria
Bisphosphonate Holidays

Panel Discussion

Audience Questions

Guideline

- A bisphosphonate drug holiday is considered after 3 years of treatment with zoledronic acid if the BMD T-scores is above -2.5.
- Bisphosphonate (or other treatment) should be resumed within 5 years of stopping it or when there is evidence that the treatment is no longer working.
- Here, the PINP level has increased significantly (by more than 10 mcg/L) and the BMD decreased significantly, the treatment is no longer working.
Case 3: Denosumab

Presentation:
Denise is a 71-year old woman who has been receiving denosumab every 6 months without side effects, started 5 years ago. Cost is not an issue.

T-scores:
- Spine -3.2 → -1.1
- Total hip -2.7 → -0.9

Question: What is the next best step?
A. Stop treatment
B. Carry on with denosumab
C. Change to zoledronic acid
D. Change to an oral bisphosphonate
Panel Discussion
Audience Questions

**Denosumab**
Why would you stop? What would you do?

Guideline:
- Denosumab should not be stopped without subsequent anti-resorptive therapy (bisphosphonate, HT or SERM).
- Follow-on treatment prevents the rebound in bone turnover, rapid bone loss and increased risk of vertebral fracture that may occur after stopping denosumab.
Presentation:
Joan is 70 year-old woman, menopausal for 25 years, referred for osteoporosis management. No prior therapy. No prior radiation therapy. Recent painful T12 compression fracture.

T-scores:
Spine -3.5; Femoral neck -2.9

Z-scores:
Spine -1.3; Femoral neck -1.1

Other Labs:
Calcium, creatinine, PTH, ALP, SPEP, UPEP normal
25-OH D satisfactory

Question: What therapy would you initiate?
A. An oral bisphosphonate
B. An IV bisphosphonate
C. Denosumab
D. Teriparatide or abaloparatide
Anabolic Agent for Initial Rx

Panel Discussion

Audience Questions

Guideline:
- She is at very high risk of fracture as she has a recent vertebral fracture as well as BMD T-score of -2.5 or less.
- She could be considered for an anabolic treatment (teriparatide or abaloparatide) or for an anti-resorptive treatment.
- If she receives an anabolic treatment this should be followed by an anti-resorptive treatment to maintain bone density gains.
Case 5: Combination Therapy

Presentation:
Rebecca is a 58-year old woman. Natural menopause was age 52. Wrist fracture age 57 (fell while fly fishing) – “worst the orthopedist had ever seen”. Calcium intake and exercise are OK. Father - hip fracture age 79. Mother - may have had osteoporosis (stroke age 62).

T-scores:
- Spine -3.2 Femoral neck -3.0

Z-scores:
- Spine -1.8 Femoral neck -1.9

Other Labs:
- Calcium, creatinine, SPEP, kappa and lambda light chains, PTH, 24-h urine calcium normal.
- 25-OH D satisfactory.

She says cost is no problem and wants whatever will increase her bone density fastest and greatest.

Question: What do you tell her that would be?
A. Teriparatide
B. Abaloparatide
C. Denosumab
D. Combination teriparatide + denosumab
Guideline:
• She is at high risk as she has BMD T-score of -2.5 or less. Thus, the guidelines would recommend bisphosphonate (oral or iv) or denosumab, taking into account patient preference.
• We would have recommended teriparatide or abaloparatide had the fracture risk been very high.
Case 6: Teriparatide for Denosumab User - Add or Switch?

Presentation:
Jane is a 67-year old white woman. She had a remote vertebral fracture discovered one year ago. She has been otherwise healthy; no history of radiation therapy. Treatment with denosumab was started (2 doses so far). She fell last week and sustained a fracture of her proximal humerus.

T-scores:
Spine -3.5; Femoral neck -2.7

Other Labs:
Calcium and creatinine are normal, 25-OH D is satisfactory.

You are considering teriparatide.

Question: What would you do?
A. Continue denosumab and not add teriparatide
B. Continue denosumab and add teriparatide
C. Stop denosumab and begin teriparatide
Guideline:

- In clinical practice, the occurrence of one fracture while on effective therapy and in a compliant patient will raise the consideration of changing therapy.
- We would recommend consideration for teriparatide of abaloparatide treatment.