

 Pharmacologic Therapy

 Level of risk and the choice of agents

 Out of risk and the choice of agents

 Some may benefit from sequential antiresorptive monotherapy especially those with BMD close to -2.5

 Bisphosphonates mid/late 60's

Osteoporotic Patients: Level of Risk and Choice of Pharmacologic Agent

High Risk (not meeting previous criteria but diagnosed with osteoporosis): >Postmenopausal women or men over age 50 with a prior hip or spine fracture

- >Postmenopausal women or men over 50 with a BMD T-score of -2.5 or lower at the hip or spine
- Postmenopausal women or men over 50 with T-score between -1 and -2.5 at the femoral neck, total hip, or spine if:
- 10 year probability (from FRAX) of hip fracture is ≥ 3%
 10 year probability of a major osteoporosis-related fracture is ≥ 20%

Camacho PM, Petak SM, et al, American Association of Clinical Endocrinologistal/American College of Endocrinology Clinical Practice Guidelines For The Diagnosis and Treatment of Post Menopausal Oxideopossis- 3020 Update, endocrine Practice, 2020;26:5-6.

Risk Stratification and Treatment Decisions

High risk

- > Older single prior fracture (> 2 years earlier) or T-score -2.5 or T-score -1 to -2.5 with FRAX ≥20% MOF or ≥3% Hip Goal: Improve BMD to T-score >-2.5 and reduce
- fracture risk
- Younger women may benefit from estrogen/raloxifene especially if spine T-score is low and hip is > -2.5
 Usually bisphosphonates or denosumab
- Anabolic agents are appropriate for some

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Camacho PM, Petak SM, et al, American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines For The Disgnosis and Treatment of Post Meropausal Osteoporals - 2020 Update, endocrine Practice, 2020-26:5-6.

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Osteoporotic Patients: Level of Risk and Choice of Pharmacologic Agent

Very High Risk:

- > Recent fracture (within the last 12 months)
- Fractures while on approved drug therapy, multiple fractures, fractures while on drugs causing skeletal harm (i.e. glucocorticoids)
- > Very low T-score (e.g. less than -3.0)
- > High risk for falls or history of injurious falls
- Very high fracture probability by FRAX
 Major osteoporotic fracture >30%
 Hip fracture >4.5%

Camacho PM, Petak SM, et al, American Association of Clinical Endocrinologists/American College of Endocrinology Clinis The Diagnosis and Treatment of Post Menopausal Osteoporosis-2020 Update, endocrine Practice, 2020:26:5-6.

7

Choosing a Pharmacologic Agent

Approved agents with efficacy to reduce hip, nonvertebral and spine fractures as initial therapy:

- > High fracture risk:
- Alendronate, risedronate, zolendronate, denosumab appropriate

> Very high fracture risk:

- Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronic acid
- And consider for patients who are unable to tolerate oral therapy

Camacho PM, Petak SM, et al. American Association of Clinical Endocrinologista/American College of Endocrinology Clinical Practice Guidelines For The Diagnosis and Treatment of Post Menopausal Osteoporosis-2020 Update, endocrine Practice, 2020;26:5-4.

8

Anabolic Agents and Treatment Sequence in Appropriate Patients

- > Recent trials have changed the thinking on when to use anabolic agents:
 - Not a drug of "last resort"
 - After multiple fractures
 - Failure of other medications
- The three anabolic agents (teriparatide, abaloparatide and romosozumab) reduce non-vertebral and vertebral fractures faster and to a greater extent than potent antiresorptive agents

Cossman F, Anabolic Therapy and Optimal Treatment Sequences for Patients With Osteoporosis at High Risk for Fracture, Endo Practice. Accessed for Publication. 2020

9

Anabolic Agents and Treatment Sequence in Appropriate Patients

- Sequence of drug therapy matters
 Bone density accrual is maximized when the
- anabolic agent is given first and followed with antiresorptive therapy
- Total hip score is considered the best measurement for future fracture risk
- Obtaining a greater hip BMD is a treatment goal for high risk osteoporosis patients

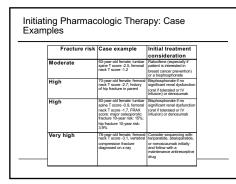
Cossman F, Anabolic Therapy and Optimal Treatment Sequences for Patients With Osteoporosis at High Risk for Fracture, Endocrine Practice, Accepted for Publication. 2020

10

Anabolic Agents and Treatment Sequence in Appropriate Patients

- Identifying appropriate patients for anabolic therapy: > Patients with prior fractures
- Patients who present with very low BMD (T-score below -3.0) even in the absence of prior fracture
 Especially with other risk factors such as advanced age, high fall risk, physical or cognitive disability

Cossman F, Anabolic Therapy and Optimal Treatment Sequences for Patients With Osteoporosis at High Risk for Fracture, Endecrine Practice, Accepted for Publication. 2020



Monitoring Pharmacologic Treatment

- > Repeat DXA every 1 to 2 years until findings are stable
- > The 1/3 radius may be considered as an alternate site when the lumbar spine/hip are not evaluable
- > Continue to follow every 1 to 2 years depending on the clinical circumstances
- > Bone turnover markers may be used to assess patient compliance and efficacy of therapy.

Carnacho PM, Pelak SM, et al. American Association of Clinical Endocrinologiata/American College of Endocrinology Clinical Practice Guidelines For The Diagnosis and Treatment of Post Manopassal Dateoporasis-2020 Update, endocrine Practice, 2020 26:5-6.

How to Determine if Treatment is Successful

- > Stable or increasing bone mineral density
- > No evidence of new fractures or vertebral fracture progression
- > One new fracture may not necessarily be evidence of treatment failure
- > Consider two or more fragility fractures as evidence of treatment failure

Camacho PM, Pelak SM, et al, American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines For The Disgnosis and Treatment of Post Menopausal Osteoporosis-2020 Update, endocrine Practice, 2020;26:5-6.

13

Length of Treatment > Abaloparatide and teriparatide treatment is 2 years - Follow with a bisphosphonate or denosumab > Romosozumab is 1 year and follow with a drug intended for long term use > Oral bisphosphonate - Consider drug holiday after 5 years if fracture risk is no longer high - Such as T- score is greater than -2.5 • No fractures - Continue up to 10 years if fracture risk remains high



Length of Treatment

 Consider a drug holiday after 3 years in high-risk patients or until fracture risk is no longer high
 Continue up to 6 years in very-high risk patients

Camacho PM, Petak SM, et al, American Association of Clinical Endocrinologiata/American College of Endocrinology Clinical Practice Guidelines For The Diagnosis and Treatment of Post Menopausal Osteoporosis-2020 Update, endocrine Practice, 2020;26:5-6.

16

14

Drug Holiday

- > End is based on individual patient circumstances such:
 - An increase in fracture risk
 - Decrease in bone mineral density
 - Increase in bone turnover markers
- > NEVER START A DRUG HOLIDAY WITH NON-BISPHOSPHONATE ANTIRESORPTIVE DRUGS
 > If denosumab is discontinued, patient should be
- transitioned to another antiresorptive

Camacho PM, Petak SM, et al, American Association of Clinical Endocrinologista/American College of Endocrinology Clinical Practice Guidelines Exe The Dispersion and Treatment of Peat Managaural Ostroporosis: 2020 Update, endocrine Practice, 2020;26:5-6.

Addressing Recent Controversies in the Treatment of Osteoporosis

Addressing

Recent Controversies

- > Long term use of bisphosphonate therapy
- > Bisphosphonate therapy and the occurrence of fractures of the subtrochanteric or diaphyseal femur
- > Osteonecrosis of the jaw (ONJ)

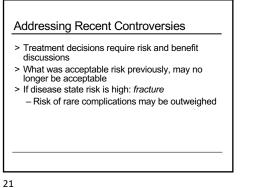
Bisphosphonates

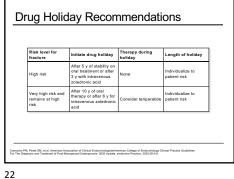
Clung M, et al. Am J Med. 2013;126(1):13-20.

20

- > Concerning adverse effects:
- · Osteonecrosis of the jaw • Risk 1:1.000 to 1:263.000
- · Not associated with treatment duration
- Potential risk factors include poor oral hygiene, glucocorticoid therapy, and chemotherapy
- Atypical femur fractures
- Risk increases with longer therapy duration
- Subtrochanteric and diaphyseal femoral fractures
- > Bisphosphonates accumulate in the bone, so drug holidays are recommended to reduce long-term risk

19





Effective Patient Management in the Primary Care Setting

Effective Patient Management in the Primary Care Setting

Patients may need in depth counseling on why treatment is recommended:

- > Patients may not be compliant to treatment regimens if they do not understand the risk of something (low bone mass) and increased fracture risk, when they don't feel symptoms
- > Based on a patient's level of education, they may require more detail on their BMD, FRAX or treatment recommendations

THIS REQUIRES TIME!

Osteoporosis and Fracture Prevention in the Primary Care Setting

- Patients need to participate in shared decision making regarding starting pharmacologic therapy as treatment or for preventative care for significant 10 year fracture risk
- Patients need to understand the idea of risk and benefit when they decide whether they will take medication

Educational Gaps and Opportunities

- > Current guidelines for who to screen
- Decreased reimbursement by Medicare for bone
- densitometry – Underscreening of women and men and low rate of Medicare coverage
- > Current guidelines for who to treat:
- Identification of patients who are untreated after a hip or spine fracture
- Identification of patients who have not had appropriate BMD testing
- Utilization of FRAX to identify osteoporotic patients who are not yet osteoporotic by T- score

25

26

Educational Gaps and Opportunities

- Keeping up with controversies and options for changing medication, drug holiday and continuation of rank ligand inhibitor
- > Consideration of anabolic agents in appropriate patients and setting up a referral source if the clinician is not comfortable initiating the treatment
- > Having dialogue with specialists when indicated for consultation on appropriate therapy with chronic kidney disease and other conditions
- > The need for individualization of treatment plan includes the need to avoid overtreatment

Potential Missed Opportunities!

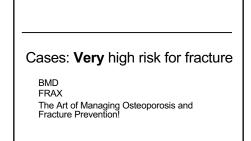
- > BMD testing in women 65 and older
- > BMD testing in men 70 and older
- > Treatment of men and women at high 10 year fracture risk by FRAX who are not yet osteoporotic
- > Vertebral or hip fracture history
- > Women on aromatase inhibitor therapy
 > Men on androgen-deprivation therapy for prostate cancer
- > Men and women on glucocorticoid therapy

27

28

Summary

- > Osteoporosis is under diagnosed and preventative care is under utilized
- Current practice requires dialogue between patient and practitioner in regards to individual risk and risk and benefits of therapeutic options
- > Treatment strategies must be individualized to obtain greater compliance to therapy
- Practitioners will need to stay current while treatment recommendations continue to be reviewed and possibly changed



76 yo Caucasian female: menopause at age 55. 64 inches tall, 170 lbs. hypertensive, hyperlipidemia, type 2 DM. 10/7/21 BMD: right and left hip: -2.0 and -3.2

right and left femoral neck: -3.0 and -4.0 Change from BMD: 10/14/15 LS 2.9%, left femoral neck -20.3%, right femoral

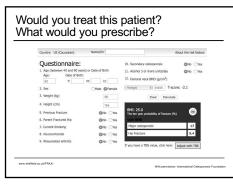
neck -10.4%

FRAX: Major osteoporotic fracture: 35.8% Hip: 19.9%

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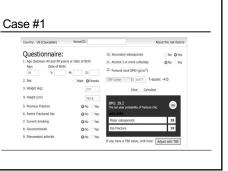
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- > What is her fracture risk?
- > What is the patient's desire for treatment
- > What is the patient's insurance coverage?
- > What are the important medical history questions?
- > What labs would you draw?
- > How would you treat this patient?
- > Would you refer this patient?

32



Case #2

82 yo woman LS: normal with -0.9 Hip: Moderate low bone mass (Osteopenia) -2.0

Patient has never been treated with pharmacologic therapy. She denies problem with swallowing, GERD or known esophagus problem. She has mild CKD and is being followed by a nephrologist.

34

Case #3

76 yo Caucasian female, menopause at 51. Hypertension, type 2 DM, hyperlipidemia. GERD. Normal kidney function. 12/6/22 T-score right and left hip: 0.5 and 0.2. Right and left femoral neck -0.6 and -0.3. Forearm: -3.7. Has completed 2 infusions of zoledronic acid and last one was one year ago.

Change from previous BMD: 9/17/20 Forearm: -3.0

What will you recommend that the patient does at this time?

- 80 yr old Caucasian patient presents for a 1st visit. History of hypertension and hyperlipidemia
- She states that she took a pill for osteoporosis for a few years and then was switched to denosumab. After 7 years on the drug, she developed a severe bilstering skin rash, Saw 2 dermatologists and had 2 skin biopsies that were reported as non-specific inflammatory change.
- > She was advised to stop the denosumab and has not taken any osteoporosis therapy for the last 2 years.
- > She never smoked. No history of hip fracture in parent. No history of adult fracture. Not diabetic. Walks regularly for exercise
- > Reports adult height loss of 2 inches

Height: 4'8

Weight: 100 pounds

37

Case #4

BMD: T-scores: LS -3.6 Left femoral neck: -3.4 Total hip: -2.1 Change from previous: LS -14.6% Total hip: -2.4% FRAX: Major Osteoporotic Fracture: 27% Hip: 12%

38

Case #4

How would you manage this patient? Questions:

- > What pharmacologic therapy would you recommend?
- > What about patient counseling regarding choices?
- > Will you consider denosumab and would the patient take it?
- > What are the risks and benefits of options?
- > What did the patient prefer and why?

39

Case #5

67 yr old has her 1st bone density test. She reports menopause at age 48. On medication for hypertension and hyperlipidemia. No history of adult fracture, no hip fracture in parent, never smoked, occasional glass of wine. Exercises regularly

BMD:

Right and left total hip: -2.9 and -2.8 Femoral neck: -3.1 and -3.5 LS -1.2

FRAX: Major Osteoporotic Fracture: 23.1% Hip Fracture: 9.3%

40

Case #5

How would you manage this patient?

- Questions:
- > Does she require a work-up regarding secondary causes of osteoporosis?
- > What pharmacologic therapy would you recommend?
- > What about patient counseling regarding choices?
- > What are the risks and benefits of options?
- > What did the patient prefer and why?
- > Is she a candidate for anabolic therapy?

Case #6

78 yr old black woman with dementia who lives with her husband. Has been taking oral bisphosphonate for 2 years. According to her husband, she takes it once a week and waits 30 minutes before eating, drinking, or laying down.
> Normal kidney function. No history of adult fracture. No hip fracture in parent. No diabetes.

Right and left total hip: -2.9 and -3.1

Right and left femoral neck: -2.8 and -3.1

LS: -1.2 FRAX: Major Osteoporotic Fracture: 11.6%

Hip: 4.7%

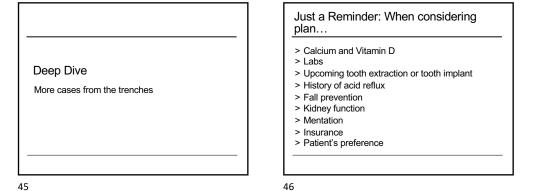
- BMD Change from previous BMD 2 years ago:
- > LS -5.4%
- > Left Total hip: -10.2%
- > Right Total hip: -11.4%

Case #6

- How would you manage this patient? Questions: > What pharmacologic therapy would you recommend? > What about patient counseling regarding choices? > Will you consider denosumab and would the patient take it?
- > What are the risks and benefits of options? > What did the patient prefer and why?

43

44



45

Case #1

59 yo Black female with history of surgical menopause at age 34. Took estrogen for only a few years after surgery. Healthy. No kidney disease. No diabetes or hypertension. BMD: right and left total hip: -2.4 -3.1 right and left femoral neck: -2.6 -2.9 Lumbar spine: -2.5 Is she osteoporotic? Is she at high or very high risk of fracture? What would you suggest for treatment? What labs would you draw?

Case #1

- > Pt is interested in anabolic therapy after discussion of the option due to her low bone density.
- > What are her options?
- What are the logistics in trying to start her on an anabolic agent?

74 yo black female: History per diagnostic center -hysterectomy at age 30. Relates steroid use of unspecified duration. History of RA. BMD: right and left hip: -0.7 and -0.5 right and left femoral neck: -2.4 -1.9 Loss at all levels from previous: 7% and 8.7%

Information Provided by Testing Center Country: US (Black) Questionnaire: 1. Age (between 40 and 90 years) or Date of Birth Age: Date of Birth: 74 Y: M: D: 11. Alcohol 3 or more units/day O No Ve 12. Femoral neck BMD (g/cm²) Male O Female (0E-Lunar 0) 0.701 T-score: -2.4 2. Sex 3. Weight (kg) 78.9 Clear Calcu 4. Height (cm) 167.6 No OYes

O No Yes

No OYes

Recalculation After Taking History From

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cocorticoids ONo Yes hip Hacture 2.0	sight (cm) evious Fracture nent Fractured Hip irrent Smoking ucocorticoids	O No Yes O No Yes	The ten year probability of fracture (%) with BMD		

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49

Case #3

6. Parent Fractured His

7. Current Smoking

9. Rheumatoid arth

86 yo black female with hysterectomy at age 57.

BMD: right and left hip: -2.4 -2.3 right and left femoral neck: -2.7 -2.1 What questions would you ask the patient? Does she need labs? What would you prescribe?

52

50

Case #4

71 yo white male: Pt has been on oral alendronate for 2 years.

BMD: right and left hip: -2.4 -2.5 right and left femoral neck: -2.9 -2.6 Lumbar spine: -0.6 Values represent a loss of bone mineral density at the right and left hips: 2.7% and 2.4%

Case #4

- > What is his fracture risk?
- > What is the patient's desire for treatment
- > What is the patient's insurance coverage?
- > What are the important medical history questions?
- > What labs would you draw?
- > How would you treat this patient?
- > Would you refer this patient?

- > Serum calcium, PTH, testosterone free and total, TSH, protein electrophoresis: WNL
- > 24 hour urine:
- Calcium, creatinine, sodium: WNL
- N-Teleopeptide: elevated to 784 (Normal range male: 21 83)
- > What does this mean? Pt has been on an antiresorptive agent for 2 years

Case #5

72 yo white male with current smoking history and diabetes. BMD: right and left total hip: -2.1 -3.4 right and left femoral neck: -1.5 -2.2 FRAX: MOF: 13.8 Hip: 6.4

What labs would you order? What are your options for pharmacologic therapy?

55

56

Case #6

79 yo female with menopause at age 53. Pt has never taken any medication for fracture prevention. BMD: right and left total hip: -3.5 -3.4 right and left femoral neck: -3.5 -3.1 FRAX: MOF: 34% Hip: 16.6

What are your options for treating this patient? What labs would you obtain?

Case #6

- > What is her fracture risk?
- > What is the patient's desire for treatment
- > What is the patient's insurance coverage?
- > What are the important medical history questions?
- > What labs would you draw?
- > How would you treat this patient?
- > Would you refer this patient?

57

58

Case #6

- > What would you discuss regarding sequencing with anabolic therapy?
- > What are the risks and benefits?
- > If pt agrees and she did, what are the logistics?

Case #7

74 yo black female with surgical menopause at age 49 BMD: Total hip: -2.4 -2.5 Femoral neck: -2.4 -2.3 LS: -0.6

FRAX: MOF: 7.1% Hip: 2.1%

- > What is her fracture risk?
- > What is the patient's desire for treatment
- > What is the patient's insurance coverage?
- > What are the important medical history questions?
- > What labs would you draw?
- > How would you treat this patient?
- > Would you refer this patient?

Case #8

78 yo white female with history of surgical menopause at age 37.

BMD: Right and left total hip: -0.2 -0.4 Right and left femoral neck: -1.7 -1.3 LS: 1.4 FRAX: MOF: 20% Hip: 4.6%

61

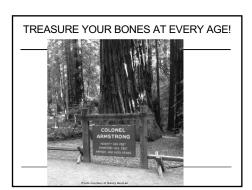
62

Case #8

- > What is her fracture risk?
- > What is the patient's desire for treatment
- > What is the patient's insurance coverage?
- > What are the important medical history questions?
- > What labs would you draw?
- > How would you treat this patient?
- > Would you refer this patient?

Resources Bone Health and Osteoporosis Foundation www.bonehealthandosteoporosis.org North American Menopause Society (NAMS) www.menopause.org 64

63



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67