

Management Strategies for Osteoporosis

Jena L. Ivey, PharmD, BCPS

Clinical Assistant Professor, UNC School of Pharmacy

Clinical Pharmacist, Medication Management

Program for Older Adults

ivey@unc.edu

Objectives

- Discuss the clinical features, pathophysiology, and risk factors for osteoporosis
- Review nonpharmacological and pharmacological options for management
- Select an appropriate agent for the prevention/treatment of osteoporosis
- Discuss limitations of current treatment options

Osteoporosis

- “Silent disease” until complicated by fractures
- Most common bone disease in humans
- Characterized by:
 - Low bone mass
 - Microarchitectural deterioration
 - Compromised bone strength
 - Increased risk for fracture

Impact of Osteoporosis

- Affects enormous number of people and prevalence will increase as population ages
- In 2002, National Osteoporosis Foundation (NOF) estimated that 8 million women and 2 million men have the disease
- Additional 34 million have low bone mass
- In US, approx. half of women and one-fourth of men over 50 years of age will experience osteoporotic fracture within their lifetime
 - Important disease in men as well, although increased risk occurs about 5-10 years later

Impact of Osteoporosis

- Fractures and associated complications are relevant clinical sequelae of osteoporosis
- Most common fractures occur at the femur (hip), vertebrae (spine), and distal forearm (wrist)
- Hip fractures result in 10-20% excess mortality within 1 year
- One-third of patients who experience a hip fracture will fracture the opposite hip
- Up to 25% of hip fracture patients may require long-term nursing home care, only 40% fully regain their previous level of functioning

Impact of Osteoporosis

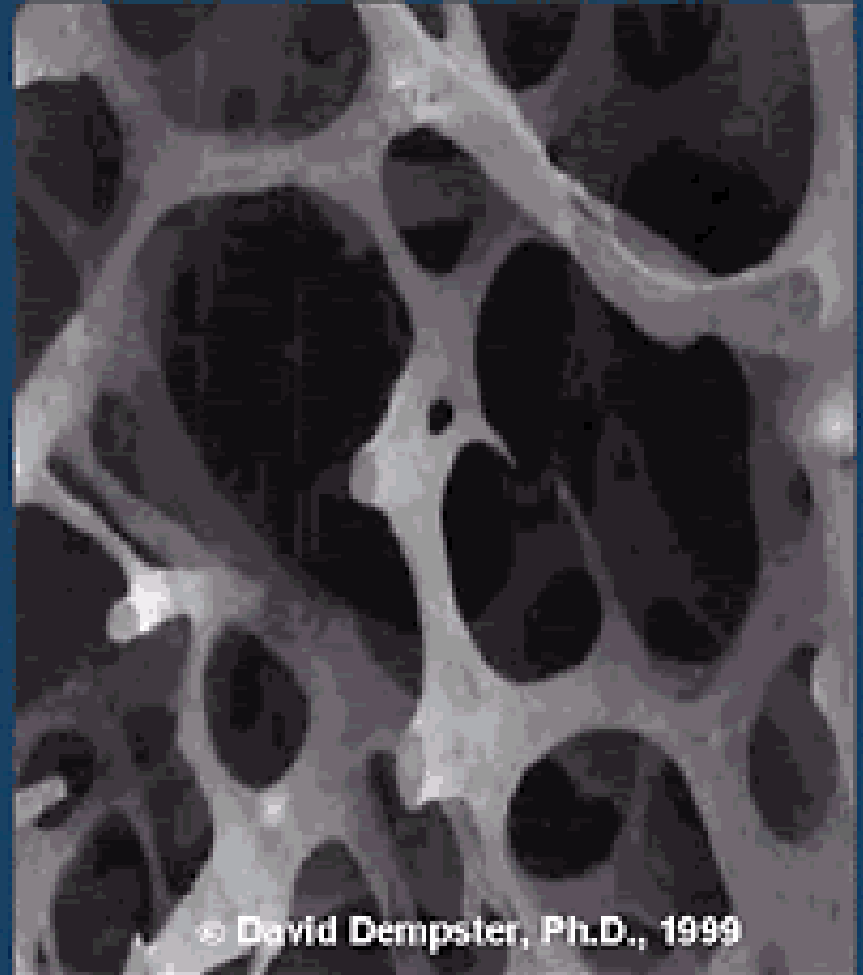
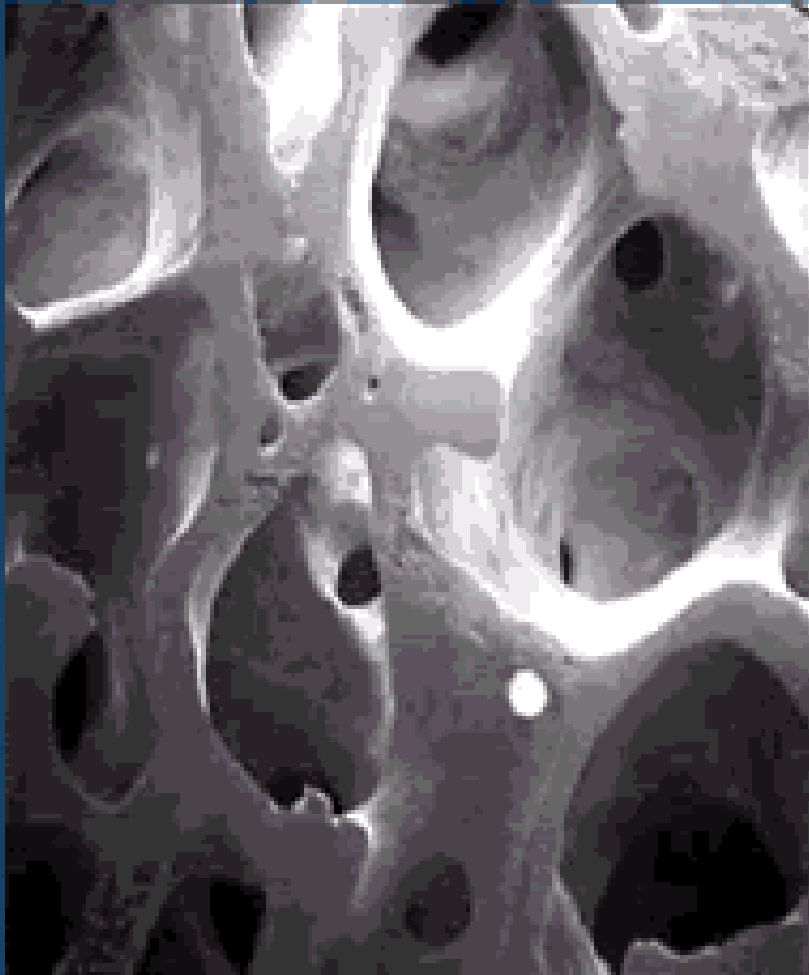
- Fractures can occur in absence of trauma or with minimal trauma
- Vertebral fracture complications include back pain, height loss, kyphosis, death
- Fractures can lead to decreased quality of life, depression, loss of self-esteem
- Projected annual direct costs of osteoporosis: \$25.3 billion by 2025, ~ \$50 billion by 2040

Pathophysiology

- Process of bone remodeling normal to maintain a healthy skeletal architecture
- Bone loss occurs when balance between bone removal and replacement is altered, resulting in greater bone removal
- Imbalance occurs with menopause and advancing age

Normal Bone vs Osteoporotic Bone

Bone strength = Bone density + Bone quality



Risk Factors

Major

- History of fracture as an adult
- Fragility fracture in first degree relative
- Caucasian/Asian postmenopausal woman
- Low body weight (< 127 lb)
- Current smoking
- Use of oral corticosteroids > 3 mo.

Additional

- Impaired vision
- Estrogen deficiency at early age (< 45 YO)
- Dementia
- Poor health/frailty
- Recent falls
- Low calcium intake (lifelong)
- Low physical activity
- > 2 alcoholic drinks per day

Medical Conditions Associated with Increased Risk of Osteoporosis

- COPD
- Cushing's syndrome
- Eating disorders
- Hyperparathyroidism
- Hypophosphatasia
- IBS
- RA, other autoimmune connective tissue disorders
- Insulin dependent diabetes
- Multiple sclerosis
- Multiple myeloma
- Stroke (CVA)
- Thyrotoxicosis
- Vitamin D deficiency
- Liver diseases

Not an inclusive list

Drugs Associated with Reduced Bone Mass

- Aluminum
- Anticonvulsants
- Cytotoxic drugs
- Glucocorticosteroids (oral/high dose inhaled)
- Immunosuppressants
- Gonadotropin-releasing hormone (e.g. Lupron)
- Lithium
- Heparin (chronic use)
- Supraphysiologic thyroxine doses
- Aromatase inhibitors
- Depo-Provera

Not an inclusive list

Glucocorticoids and Osteoporosis

- Glucocorticoids reduce bone formation, increase bone resorption
- Most common form of secondary osteoporosis
- Possible mechanisms:
 - Inhibitory effect on osteoblasts
 - Increase in osteoclast activity
 - Decrease in sex steroid production
- Also decrease intestinal calcium absorption, increase renal calcium excretion

Glucocorticoids and Osteoporosis

- Substantial increase in fracture risk in patients receiving glucocorticoid therapy
 - Appears within 3-6 months of initiating therapy
- Risk appears to be related to dose (oral and inhaled) and duration of therapy, but independent of BMD
- Evaluate BMD at hip, spine
- Use of FDA-approved medications
 - Bisphosphonates

Risk Factors: Men

- Genetics
- Smoking/alcohol
- Calcium intake
- Use of glucocorticoid therapy ≥ 7.5 mg of prednisone for > 3 mo
- Physical activity/strength
- Testosterone production
- Estrogen production

Risk Assessment/Diagnosis

- After menopause, all women should be evaluated clinically for osteoporosis risk to determine need for BMD testing
- 50-60% of men with osteoporosis have disorders known to reduce bone loss, such as hyperparathyroidism, intestinal disorders, malignancies, conditions resulting in immobilization
- BMD recommended in men with known risk factors and who have lost > 1.5 inches in height
- Diagnosis can be established in patients who have never had a fragility fracture by BMD measurement

World Health Organization Diagnostic Criteria

DIAGNOSIS	BMD CRITERIA*
• <i>Normal</i>	within 1 SD of a “young normal” adult (T-score at -1.0 and above)
• <i>Osteopenia</i>	between 1 and 2.5 SD below that of a “young normal” adult (T-score between -1 and -2.5)
• <i>Osteoporosis</i>	2.5 SD or more below that of a “young normal” adult (T-score at or below -2.5)
• <i>Severe Osteoporosis</i>	2.5 SD or more below that of a “young normal” adult and fracture(s)
• T-score is the number of SDs above or below the average BMD value for young, normal adults of the same sex	

BMD = Bone mineral density

SD = Standard deviation

*Measured at the hip, spine, or wrist

BMD Measurement

- Can be used to establish or confirm diagnosis, predict future fracture risk
- Measurement of BMD at any skeletal site predicts fracture risk
- Hip BMD best predictor of hip fractures and predicts fractures at other skeletal sites

Who Should be Tested?

- Decision to test based on individual risk profile, never indicated unless *results* influence *treatment* decision
- BMD testing should be performed on:
 1. All women 65 YOA and older regardless of risk factors*
 2. Younger postmenopausal women with one or more risk factors (other than being white, postmenopausal and female)
 3. Postmenopausal women who present with fractures (confirm diagnosis, determine disease severity)

*Medicare permits repeat BMD testing every 2 years.

BMD Testing Techniques

- Central machines (DXA) – Dual x-ray absorptiometry
 - Spine, hip, wrist
 - Used for diagnosis, predict future risk
- pDXA – Peripheral dual x-ray absorptiometry and single-energy x-ray absorptiometry (SXA)
 - Forearm, finger, heel
 - Used to identify patients at risk, predict risk for future fractures
- QCT – Quantitative computed tomography
 - Trabecular bone density in spine
- Ultrasound densitometry
 - Heel, tibia, patella, other peripheral sites where bones superficial

Biochemical Markers of Bone Turnover

- Markers of bone formation and bone resorption
- Can indicate whether or not therapeutic intervention has slowed bone loss
- Cannot diagnosis osteoporosis
 - NTX, CTX, DPD, TRAP markers for bone resorption
 - BAP, OC, PINP, PICP markers for bone formation
- May be useful in predicting rates of future bone loss independent of BMD, monitoring therapy

Guidelines for Treatment

- American Association of Clinical Endocrinologists
- Scientific Advisory Council of the Osteoporosis Society of Canada
- National Osteoporosis Foundation
- National Institutes of Health Consensus Development Panel
- North American Menopause Society
- American College of Rheumatology*
- American Gastroenterological Association*

*For special populations

Universal Recommendations

- Adequate intake of calcium, vitamin D
- Weight-bearing and muscle-strengthening exercises to reduce risk of falls/fracture
- Provide strategies for fall prevention
- Avoidance of tobacco use
- Identification and treatment of alcoholism
- Treatment of other modifiable risk factors for fracture

NOF – *Clinician's Guide to Prevention and Treatment of Osteoporosis*

www.nof.org

- Released 2/21/08 (last update 2003)
- Guidelines include African-American, Asian, Latina and other postmenopausal women, also addresses men 50 years and older
- Will help identify people at high risk for developing osteoporosis/fractures and assure appropriate treatment
- Uses new algorithm FRAX[®] by the WHO, estimates 10-year fracture probability
 - <http://www.shef.ac.uk/FRAX/>

Adequate Intake of Calcium/Vitamin D

- Adequate intakes of dietary calcium and vitamin D, including supplements if necessary
 - Elemental calcium per day (> 50 YOA) = at least 1200 - 1500 mg
 - Vitamin D₃ per day (> 50 YOA) = 800 -1000 international units (IU)
- Vitamin D plays major role in Ca absorption
- Controlled clinical trials have demonstrated the combination reduces fracture risk
- Inexpensive, well-tolerated

Calcium and Vitamin D Supplementation

- Numerous OTC products with each calcium salt delivering a different proportion of elemental calcium
- Discourage herbal calcium supplements that may contain combination of Ca salts and other additional constituents (e.g. Coral calcium)
- Doses should be limited to 500 mg elemental calcium at a time for adequate absorption
- Food enhances absorption

Calcium/D Product Selection

Product (% elemental Ca)	Elemental Calcium (mg)	Vitamin D (units)	Comments
Calcium carbonate (40) -Tums Ultra -Caltrate 600 Plus -Oscal Plus D -Viactiv Chews	400 600 500 500	200 125 100	Requires acidic environment for dissolution and disintegration. Best to take with meals. Greater risk for constipation with carbonate form.
Calcium citrate (24) -Citracal Plus D - Citracal D Creamy Bites	315	200	Take without regard to meals. Serving size usually equals 2 capsules so label can be misleading to patients.
Vitamin D -Multivitamin (D ₃) -Vitamin D	120-450	400 100-400	

Vitamin D and Fall Risk

- In addition to its effect on BMD, may contribute to reduction in fracture risk
 - Improved muscle function
 - Reduction in risk for falls
- Meta-analyses of 5 clinical trials (≥ 60 YOA) showed significant reduction in risk for falling in those taking vitamin D plus calcium versus those taking placebo
- Vitamin D deficiency prevalent in older adult population
 - Inadequate sun exposure, use of sunscreen
 - Homebound, institutionalized
 - Northern latitudes
 - Maintain 25-hydroxyvitamin D₃ at least > 30 ng/mL
 - Treatment: 50,000 IU vitD weekly x 6-8 weeks, then assess need for chronic monthly therapy

Regular Weight-Bearing Exercise

- Defined as those in which bones and muscles work against gravity as feet and legs bear the body's weight
- Include walking, jogging, Tai-Chi, stair climbing, dancing, tennis, yoga
- Improve agility, strength, balance
- May increase bone density modestly, reduce fall risk, enhance muscle strength, improve balance

Avoidance of Tobacco and Alcohol

- Tobacco products detrimental to skeleton, overall health
- NOF strongly encourages tobacco cessation programs as osteoporosis intervention
- Excessive alcohol intake also detrimental to bone health and requires treatment

Who Should Be Treated?

NOF Recommendations – 2008

- Initiate therapy to reduce fractures in postmenopausal women/men > 50 with:
 1. BMD T-scores ≤ -2.5 at hip or spine
 2. Prior vertebral or hip fracture
 3. Low bone mass (T-scores -1.0 to -2.5 at hip or spine) when:
 - 10-year probability of hip fracture is $\geq 3\%$
 - 10-year probability of major osteoporosis-related fracture is $\geq 20\%$
 - Based on US-adapted WHO algorithm

FDA-Approved Drugs for Osteoporosis

- **Bisphosphonates**
 - Alendronate, Alendronate plus D (Fosamax[®], Fosamax Plus D[®])
 - Risedronate, Risedronate with Calcium (Actonel[®])
 - Ibandronate (Boniva[®])
- **Calcitonin** (Miacalcin[®], Fortical[®], Calcimar[®])
- **Parathyroid Hormone** [PTH (1-34), teriparatide]
 - Forteo[®]
- **Selective Estrogen Receptor Modulators (SERMs)**
 - Raloxifene (Evista[®])
- **Estrogen/Hormone Therapy (ET/HT)**
 - Premarin[®], Estrace[®], Prempro[®]

Bisphosphonates – Antiresorptive Agents

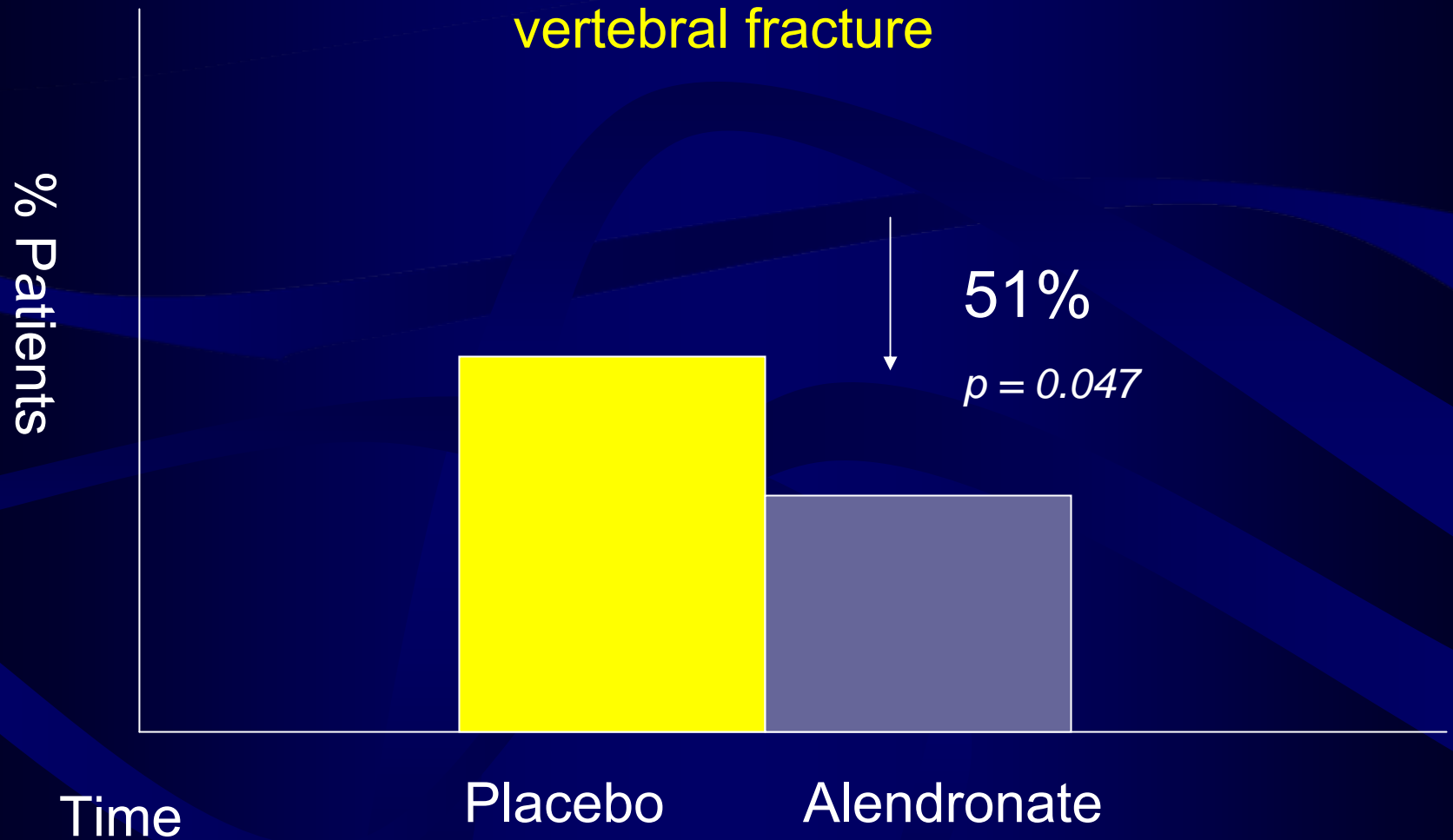
- Agents FDA-approved for:
 - Prevention and treatment of osteoporosis in postmenopausal women
 - Treatment to increase bone mass in men with osteoporosis
 - Treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids
 - Treatment of Paget's disease of bone in men and women
- Mechanism: inhibits bone resorption by attaching to bony surfaces undergoing active resorption and inhibiting action of osteoclasts
 - Leads to increases in bone density and reduced fracture risk

Bisphosphonates – Clinical Efficacy

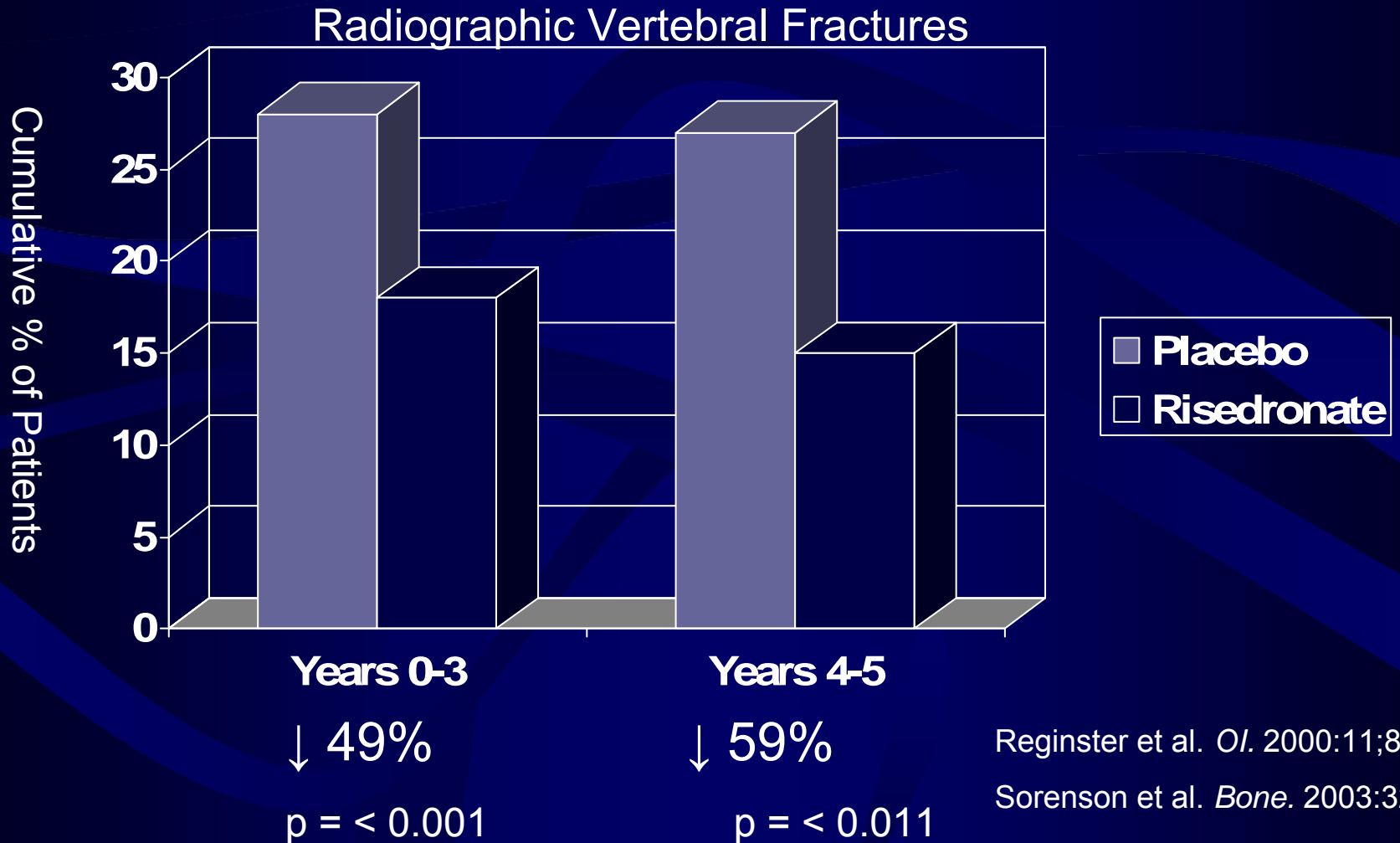
- Controlled clinical trials indicate over 3-4 year period, alendronate ↑ bone mass and ↓ incidence of vertebral, hip, and all non-vertebral fractures by 50%
- Controlled clinical trials indicate risedronate ↑ bone mass and ↓ risk of vertebral fractures by 40% and non-vertebral fractures by 30% over 3-year period
- Ibandronate has been shown in controlled clinical trials to ↑ BMD and reduce the risk of *vertebral* fracture by 50% over 3-year period
- Alendronate appears to be well tolerated and effective for at least ten years

Risk Reduction in Hip Fracture at 3 Years in FIT I Trial

In patients with low FN bone density and prevalent vertebral fracture



Reduction in Relative Risk of New Vertebral Fracture in Years 0-3 & 4-5 with Risedronate



Bisphosphonates – Dosing

- Alendronate*
 - Prevention
 - 5 mg PO daily
 - 35 mg PO weekly
 - Treatment
 - 10 mg PO daily
 - 70 mg PO weekly
 - 70 mg/2,800 IU vitamin D PO weekly
- Risedronate
 - Prevention/Treatment
 - 5 mg PO daily
 - 35 mg PO weekly
- Ibandronate
 - Prevention/Treatment
 - 2.5 mg PO daily
 - 150 mg PO monthly
 - Treatment
 - 3 mg IV every 3 months

*Alendronate also available in oral solution.

Bisphosphonates – Administration

- Must be taken *at least* one-half hour before the first food, beverage, or medication of the day with plain water only (1 hour prior for monthly ibandronate)
- Should only be taken upon arising for the day
- Tablet should be swallowed with a full glass of water (8 oz) and patients should remain upright, walking, standing, or sitting for at least 30 minutes (60 minutes for monthly ibandronate)
- Should supplement with calcium/vitamin D if dietary intake inadequate

Bisphosphonates – Adverse Effects

- Hypocalcemia (18%)
- Hypophosphatemia (10%)
- Musculoskeletal pain, cramps – recent FDA warning
- Gastrointestinal
 - Abdominal pain
 - Acid reflux
 - Dypepsia
 - Esophageal ulcer
 - Gastritis
- Osteonecrosis of the jaw (IV bisphosphonates)
- Visual disturbances (rare)

Bisphosphonates – Missed Dose

- Once weekly alendronate, risedronate
 - Take on morning after remembering, then resume once weekly on regularly chosen day
- Once monthly ibandronate
 - If next dose > 7 days away, take dose the morning following the date remembered
 - Then return to original schedule
 - If next dose < 7 days away, wait until next scheduled dose
 - Must not take two 150 mg tablets within the same week

Intravenous Bisphosphonates

- Pamidronate, Zoledronic acid, Ibandronate
- Pamidronate (Aredia®)
 - Treatment of osteolytic bone metastases associated with multiple myeloma or metastatic breast cancer, hypercalcemia
 - Frequency of dosing variable (weekly to monthly)
- Zoledronic acid (Zometa®)
 - Approved for treatment of malignancy-associated hypercalcemia, documented bone metastases from solid tumors along with standard antineoplastic therapy, Paget's disease
 - Frequency of dosing variable (weekly to monthly)

Zoledronic Acid (Reclast[®])

- Approved for treatment of osteoporosis in postmenopausal women in August 2007
- Single 5 mg infusion given IV over \geq 15 minutes
- Should still supplement with calcium/vitamin D
- May be ideal for those with GI contraindications to the oral formulations

Price Comparison

Drug	Price
Alendronate (Fosamax [®]) 10 mg once daily 70 mg once weekly 70 mg/2800 IU weekly	30 day supply: \$72.99 30 day supply: \$65.99 30 day supply: \$79.70
Risedronate (Actonel [®]) 5 mg once daily 35 mg once weekly	30 day supply: \$65.99 30 day supply: \$63.99
Ibandronate (Boniva [®]) 2.5 mg once daily 150 mg once monthly	30 day supply: \$65.99 30 day supply: \$75.99

Bisphosphonates

- Very well tolerated in patients who adhere to proper administration techniques
- Proper patient counseling for correct administration is KEY to reduce risk of adverse effects and increase tolerability
- Place in Therapy: should be considered first-line for prevention/treatment of osteoporosis in patients with no contraindications

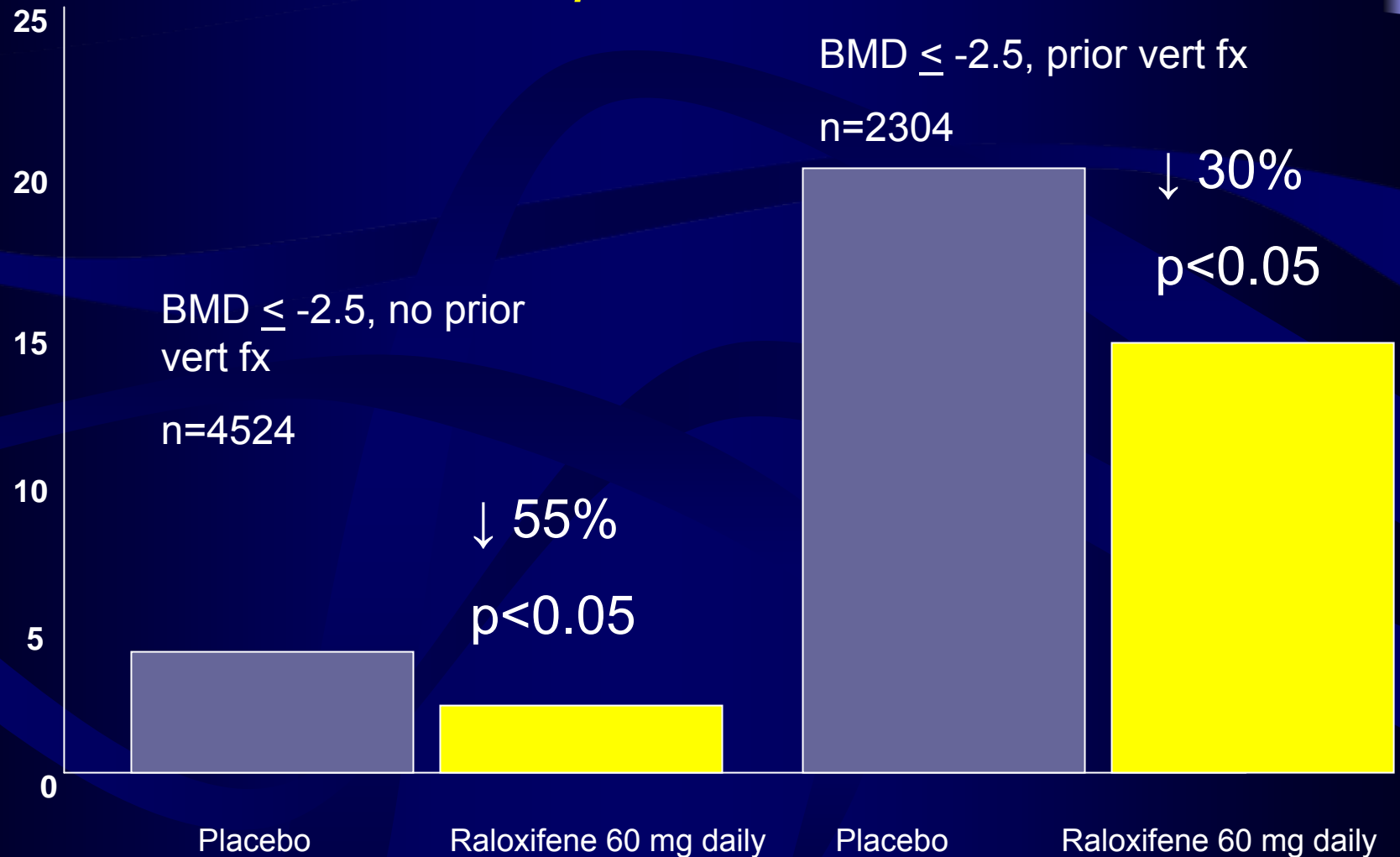
SERMs – Raloxifene

- FDA-approved for:
 - Prevention and treatment of osteoporosis in postmenopausal women
- Mechanism: tissue-selective activity, acts as an estrogen agonist on bone
 - Estrogen antagonist on breast, uterus

Raloxifene – Clinical Efficacy

- Reduces risk of vertebral fracture by 30% in patients with previous spinal fracture, 55% in patients without prior spinal fracture over 3 years
- Increases BMD at all skeletal sites and reduces total and LDL cholesterol
- Less potent antiresorptive agent than bisphosphonates, although direct comparison studies lacking

Raloxifene: Effect on Radiographic Vertebral Fractures (MORE) *Postmenopausal Women*



Raloxifene

- For prevention and treatment
 - 60 mg PO once daily
- Should supplement with calcium/vitamin D if dietary intake inadequate
- Adverse effects
 - Hot flashes
 - DVT
 - Leg cramps
 - Small increase in risk of fatal stroke
- Price
 - 30-day supply = \$86.99
 - No generic available

Raloxifene

- Place in Therapy: considered first-line in women who cannot tolerate bisphosphonates and have no contraindications to therapy
- Combination therapy (usually a bisphosphonate with a non-bisphosphonate) can provide additional small increases in BMD when compared to monotherapy
- Impact of combination therapy on fracture rate unknown

Estrogen/Hormone Therapy (ET/HT)

- FDA approved for:
 - Prevent osteoporosis
 - Treatment of moderate/severe vasomotor symptoms of menopause
 - Treatment of moderate/severe symptoms of vulvar and vaginal atrophy associated with menopause
 - Consider topical preparations to treat vaginal symptoms rather than oral ET/HT

FDA Recommendations – ET/HT

- When prescribing medications for osteoporosis, physicians should consider all non-estrogen therapies first
- When prescribing ET/HT, use smallest dose for shortest amount of time to achieve treatment goals
- Prescribe ET/HT products only when benefits believed to outweigh risks for a specific patient

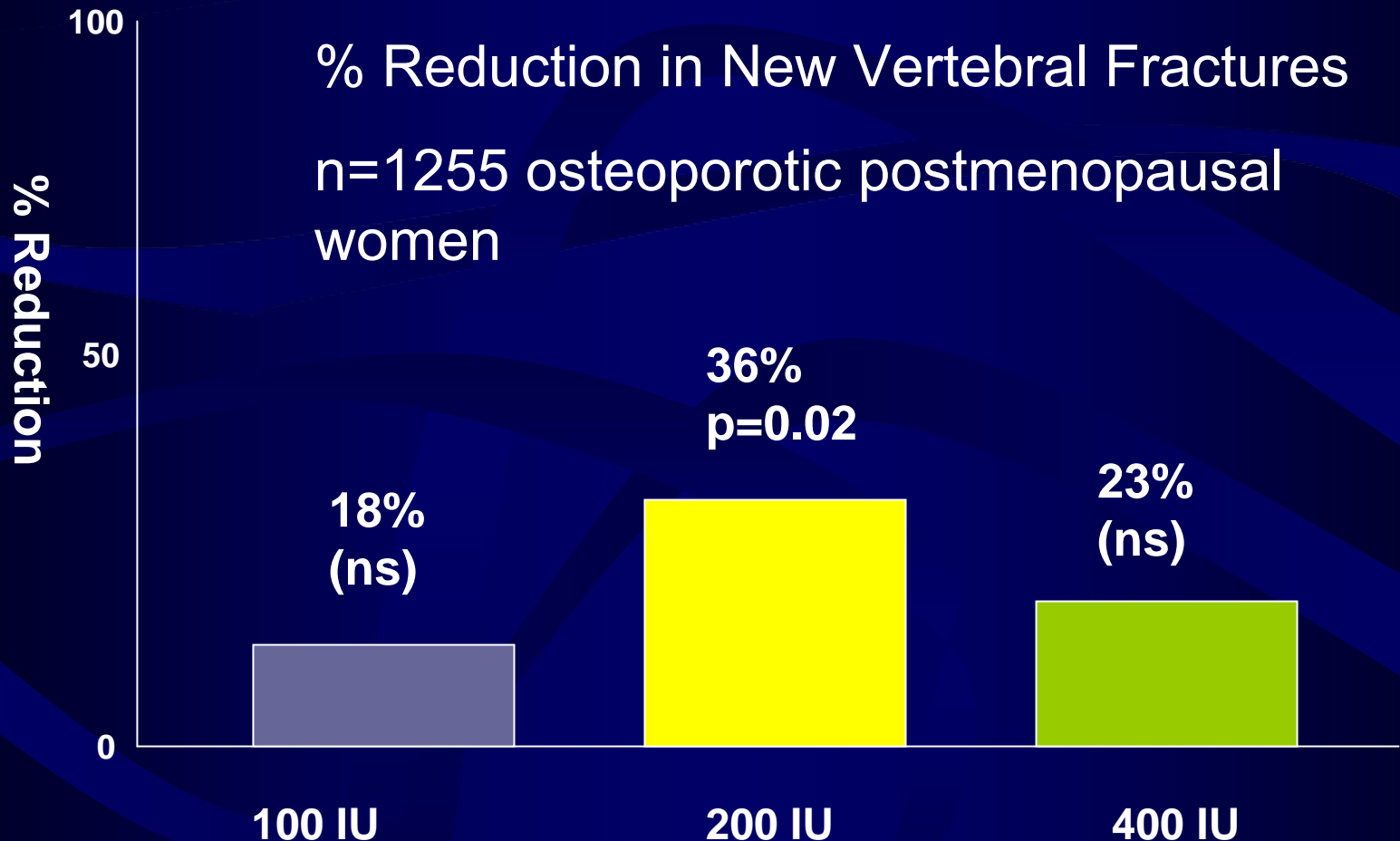
Calcitonin

- FDA-approved for:
 - Treatment of osteoporosis in women who are ≥ 5 years postmenopausal
 - Treatment of Paget's disease of bone
 - Adjunctive therapy for hypercalcemia
- Mechanism:
 - Peptide composed of 32 amino acids which binds to osteoclasts and inhibits bone resorption
 - Promotes the renal excretion of calcium, phosphate, sodium, magnesium and potassium by decreasing tubular reabsorption

Calcitonin – Clinical Efficacy

- Has been shown to increase spinal bone mass and may decrease risk of vertebral fracture
- Conflicting data on efficacy of calcitonin at sites other than the spine
- Less effective than bisphosphonates in treatment of osteoporosis
- Beneficial, short-term effect on acute bone pain after osteoporotic fracture (vertebral)

Nasal Calcitonin: Efficacy at the Spine (PROOF: 5 year analysis)



Calcitonin – Dosing/Administration

- Intranasal
 - 200 units (1 spray) alternating nares daily
 - Store unopened bottles in refrigerator, protect from freezing
 - Can store open bottles at room temperature for up to 35 days
 - Activate pump of *new* bottles until full spray produced (allow to reach room temperature before priming)
 - Each bottle contains at least 30 doses
- IM/SQ
 - 100 units/every other day (minimum effective dose not well-defined)
 - Should perform skin test prior to initiating therapy
- Should supplement with calcium/vitamin D if dietary intake inadequate

Calcitonin

- Adverse effects:
 - Nasal spray: rhinitis (12%), irritation of nasal mucosa (9%), epistaxis (3.5%), sinusitis (2.3%), back pain, arthralgia, headache
 - Injection: nausea (10%), flushing (2-5%), headache
- Temporarily withdraw use of nasal spray if ulceration of nasal mucosa occurs
- Price per month
 - 200 units/mL (2): \$42.08
 - 200 units/ACT (3.7): \$81.59

Calcitonin

- Valid option for treatment of established osteoporosis, especially when accompanied by fracture pain
- Place in therapy: because of cost, adverse effects, inconvenience of nasal administration, recommend using calcitonin until pain is no longer a problem and then switching to a bisphosphonate for long-term therapy

Parathyroid Hormone [PTH (1-34)]

Anabolic agent

- FDA-approved for:
 - Treatment of osteoporosis in postmenopausal women at high risk for fracture
 - previous osteoporotic fracture, multiple risk factors for fracture, extremely low BMD (< -2.5), or failed/intolerant to previous treatment
 - Treatment of primary or hypogonadal osteoporosis in men at high risk of fracture
- Mechanism: recombinant formulation of endogenous parathyroid hormone (PTH)
 - stimulates osteoblast function, increases gastrointestinal calcium absorption, increases renal tubular reabsorption of calcium
 - Enhances bone turnover by initiating greater bone formation

PTH (1-34) – Clinical Efficacy

- Shown to decrease the risk of new vertebral fractures by 65% and nonvertebral fractures by 53% versus placebo after median exposure of 19 months
- Increases lumbar spine BMD as well as at the femoral neck, total hip, and total body
- Safety, efficacy of PTH (1-34) has not been demonstrated beyond 2 years of treatment

PTH (1-34) – Dosing/Administration

- 20 µg SQ once daily for treatment of osteoporosis
 - Thigh or abdominal wall
- Forteo® prefilled pen contains 28 daily doses
- Important to read Medication Guide and User Manual before starting and each time medication refilled
- Should be administered initially under circumstances where the patient can immediately sit or lie down, in the event of orthostasis (dizziness, palpitations are transient)
- Should supplement with calcium/vitamin D if dietary intake inadequate

PTH (1-34) – Adverse Effects

- Most common
 - Dizziness, rash, nausea, headache, leg cramps, arthralgia, rhinitis, transient hypercalcemia
- S/s of hypercalcemia: nausea, vomiting, constipation, low energy, or muscle weakness
- Most adverse effects in the clinical trials were mild and generally did not lead to the discontinuation of the drug
- Osteosarcoma risk in animals
 - Lead to black box warning by FDA

PTH (1-34) – Warnings/Precautions

- Increased risk of osteosarcoma (rats) – clinical relevance unknown (no excess reports in humans)
- Avoid in:
 - Paget's disease of bone
 - Prior radiation therapy to skeleton
 - Bone metastases
 - Hypercalcemia
 - History of skeletal malignancy
 - Pregnant/nursing

PTH (1-34) – Price

- One-month supply \$539.99
- Lilly offers Forteo® Patient Assistance Program for Medicare-eligible (LillyMedicareAnswers) and non-Medicare eligible patients
- LillyMedicareAnswers intended for patients who are enrolled in any Medicare Part D prescription drug plan and who meet certain eligibility requirements
 - Expected to start early 2007
- For non-Medicare patients, application process includes paper application and income restrictions
- Call 1-877-795-4559 or visit www.lilly.com for more details

PTH (1-34)

- Due to safety concerns, PTH treatment should be limited to those most severely affected and for a maximum of two years
- Combination therapy with a bisphosphonate not recommended as effects do not appear additive
- Cost, daily SQ injection may be prohibitive for some patients

PTH (1-34)

Place in Therapy:

- Recommend PTH for women or men with severe osteoporosis (low bone mineral density [T-score < -2.5] and at least one fragility fracture) who are refractory to or unable to tolerate bisphosphonate therapy
- In patients considered to be bisphosphonate "failures," PTH may be started approximately 3 months after bisphosphonates are discontinued
- Antiresorptive therapy may be considered after discontinuation of PTH to maintain gains in BMD acquired with PTH alone in those at high risk for subsequent fracture

Approaches to Monitoring Therapy

- Always important to ask patients about adherence, encourage continuation of therapies to reduce fracture risk
- Monitoring of therapy should be considered, as up to 1/6 of women taking effective therapies continue to lose bone, especially if they smoke
- May measure bone mineral density at a single site after one year of therapy, but results may be misleading
- Drugs may decrease a patient's risk for fracture even when there is no apparent increase in BMD

Monitoring Therapy

Option 1 — Bone density measurement can be repeated after one year of therapy

- If BMD stable or improving, evidence for treatment response
- If BMD declines at one year, adherence with drug, calcium and vitamin D should be verified, and evaluation for secondary causes should be performed
- If patient healthy and well, and taking the drug and supplements correctly, correct action is controversial

Monitoring Therapy

Option 2 — Repeat measurement of bone mineral density after two years of therapy

- Problem with this approach is it may delay detection of poor response

Option 3 — Combines measurement of biochemical markers of bone turnover with measurement of bone mineral density

- Bone mineral density and marker of bone turnover measured at baseline, followed by repeat measurement of the marker in six months
- If the marker falls significantly (>50% for urine NTX and >30% for serum CTX), evidence that the drug having desired effect, and BMD can be repeated after two years

Monitoring Therapy

Option 4 — Monitoring for effectiveness of antiresorptive therapy is unnecessary

- No evidence that we can improve outcomes in those who do not respond well to therapy
- Questions?
 - Do not know if they are best served by increasing the dose of the antiresorptive agent
 - Switching therapy altogether
 - Adding a second antiresorptive agent
 - Continuing therapy, assuming they would lose more bone mass if therapy was stopped

Questions Left Unanswered

- How can we better identify and assess patients at high risk for fracture?
- What strategies should be implemented to identify and modify risk factors for falling?
- How effective are pharmacotherapeutic agents in preventing fractures in patients with moderately low bone mass?

Questions Left Unanswered

- How long should antiresorptive therapies be continued?
- Are combination therapies useful and if so, which are the useful combos and when should they be used?
- Can we identify agents to significantly increase bone mass and return bone structure to normal?

References

- Actonel[®] Prescribing Information (www.actonel.com)
- Ann Intern Med 1990;112:352
- Ann Intern Med 2006;144:753
- Boniva[®] Prescribing Information (www.boniva.com)
- Clinical Reviews in Bone and Mineral Metabolism 2004;2(4):291
- Evista[®] Prescribing Information (www.evista.com)
- Forteo[®] Prescribing Information (www.forteo.com)
- Fortical[®] Prescribing Information (www.fortical.com)
- Fosamax[®] Prescribing Information (www.fosamax.com)

References

- JAMA 2004;291(16):1999
- J Clin Densitom 2004;7(1):1-6
- J Am Acad Orthop Surg 2006;14:347
- Miacalcin[®] Prescribing Information (www.miacalcin.com)
- Reclast[®] Prescribing Information (www.reclast.com)
- National Osteoporosis Foundation (<http://www.nof.org>)
- NEJM 2003;348:1187
- NEJM 2004;350(12):1189-99
- Osteoporosis Int 1998;8:1