

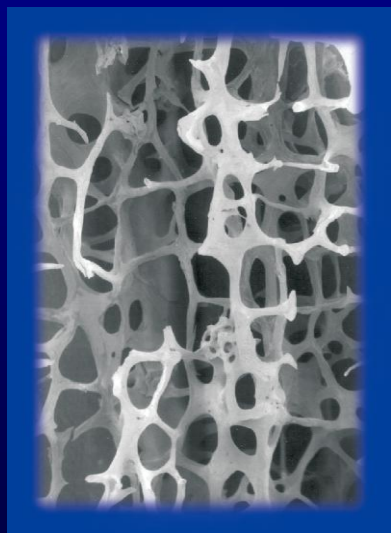
# ***Long Term Efficacy and Safety of Osteoporosis Therapies***

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**OOC**



# Long Term Efficacy and Safety of Osteoporosis Therapies

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- **Effects**

- Fracture risk reduction has been observed in pivotal placebo-controlled trials lasting no more than 3 years
- Little controlled data exists beyond the 3 year studies
- It appears that fracture risk reduction persists but does not improve with longer-term therapy
- With most drugs, the benefits of therapy on BMD and fracture risk disappear quickly upon stopping treatment

- **Safety**

- With the exception of bisphosphonates (and perhaps denosumab), no new complications have been observed with long-term therapy

# Bisphosphonates

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- **Effects**

- **Increased bone density in the spine by 5-8% and at the hip by 3-6% after 3 years**
- **Reduced incidence of vertebral fractures by 40-70%**
- **Alendronate, risedronate and zoledronic acid reduced non-vertebral fractures (25-40%), including hip fractures (40-60%), in women with osteoporosis**
- **Ibandronate: overall, no effect observed on non-vertebral or hip fractures. In post-hoc analysis, non-vertebral fracture reduction was seen in high-risk subgroup (baseline femoral neck T-score less than -3.0)**

Black DM et al. *Lancet*. 1996;341:1535-41

Harris ST et al. *JAMA* 1999;282:1344-52

McClung MR et al. *N Engl J Med*. 2001;344:333-40

Chesnut III CH et al. *J Bone Miner Res*. 2004;19:1241-9

Black DM *N Engl J Med*. 2007;356:1809-22

Cummings SR, et al. *N Engl J Med* 2009;361:756-65

# Bisphosphonates

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- **Side Effects**
  - **UGI symptoms with oral agents: not demonstrated in trials**
  - **Acute phase reaction with IV and high-dose oral regimens**
  - **Musculoskeletal symptoms - uncertain**
- **Safety concerns**
  - **Rare inflammatory eye problems**
  - **Hypocalcemia with vitamin D deficiency or low serum calcium**
  - **Atrial fibrillation with IV zoledronic acid (unproven)**
  - **Esophageal cancer with oral agents (unproven)**
  - **Skeletal safety: ONJ (very rare) and atypical femoral fractures**

# Bisphosphonates: Atypical Femur Fractures

- Atypical (tranverse) fractures of femoral shaft have been reported in patients taking oral bisphosphonates for osteoporosis <sup>1</sup>
  - Minimal trauma
  - Often bilateral
  - Prodromal pain in 70%
  - Cortical thickening
  - Slow fracture healing
  - Often on other drugs (steroids, estrogen)
  - Incidence related to duration of therapy  
2/100,000 after 2 yrs; 78/100,000 at 8 yrs <sup>2</sup>



# Denosumab

## A Human Antibody RANK Ligand Inhibitor

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- **Effects<sup>1</sup>**
  - **Increase in BMD of 9% at spine and 6% at the hip after 3 years**
  - **Decreased incidence of vertebral (68%), hip (40%) and non-vertebral fractures (20%) in women with osteoporosis**
  - **Persistent effects to at least 6 years**
- **Adverse Events: skin rash and infection; serious adverse events related to infection and inflammation**
- **Risk of ONJ and atypical fractures not yet known**
- **No dose adjustment required with impaired renal function; ONJ has been observed**
- **Loss of effect when therapy is stopped <sup>2</sup>**