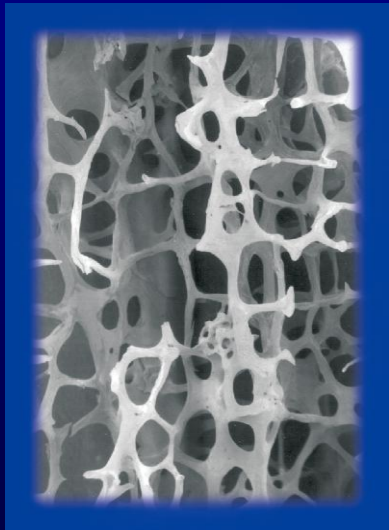


Long Term Efficacy and Safety of Osteoporosis Therapies

OSTEOS-2011

Beirut

December 3, 2011



Michael R. McClung, MD, FACP
Oregon Osteoporosis Center
Portland, Oregon, USA
mmclung@orst.com

OOC



Long Term Efficacy and Safety of Osteoporosis Therapies

- **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

- **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)**

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Bisphosphonates

- **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 ¹
 - 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 ²



Denosumab

A Human Antibody RANK Ligand Inhibitor

- **Effects¹**
 - **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 ²**