Question 4 – Endocrinology

An 84-year-old female nursing home resident is ambulant but rarely goes outside. She is thin, eats little and has reflux oesophagitis. Medical history includes mastectomy and radiation therapy for breast cancer at age 60 years. There is a past history of deep venous thrombosis (DVT). Dual-energy X-ray absorptiometry (DEXA) scan reveals a T score of -2.2 at the spine and -3.0 at the femoral neck. Serum calcium is normal. In addition to calcium supplementation, which of the following is the most appropriate initial therapy for her osteoporosis?
A. Alendronate.
B. Calcitonin.
C. Vitamin D.
D. Oestrogen.
E. Raloxifene.

Definition of Osteoporosis
- Bone mineral density [BMD] 2.5 SD below the mean of young women

Risk factors for Osteoporosis
- Female
- Lack of estrogen
- Long term steroid use
- Hyperthyroidism
- Hyperparathyroidism
- Low 1,25-OH Vitamin D
- Drugs - heparin, cyclosporine, vitamin A
- Smoking
- Menopause- related bone loss
- Age related bone loss

Non-pharmacological
- Calcium/Vitamin D
- Weight training
- Cessation of smoking

Pharmacological
1. Raloxifene
   - Selective Estrogen receptor Modulator (SERM)
   - MORE trial
     a. 4 yrs of raloxifene treatment (60mg/day), Lumbar spine and femoral neck BMD increased from 2.0 to 2.7% in raloxifene groups compared with placebo
     b. reduced risk of vertebral # (ARR 1.3 per 1000)
     c. Benefit of raloxifene on BMD and on nonvertebral # risk still measurable after 7 years of treatment
   - Side effects
     i. No increase risk of endometrial Ca
     ii. Increased risk of incidence of thromboembolic disease (RR 3.1 compared with placebo)
     iii. No difference in overall stroke risk but ass with increased risk of fatal stroke
     iv. CHD
     v. Hot flushes
     vi. Influenza- like symptoms
     vii. Peripheral edema
     viii. Leg cramps

2. Bisphosphonate
   - Inhibit osteoclastic bone resopotion
   - Poorly absorbed orally (1-5% of oral dose) and absorption is best on empty stomach
   - Plasma half life is approximate 1 hr
   - Persists in bone for lifetime
Year 2005 Paper two: Questions supplied by Ilynn

- Relative risk of vertebral # 0.52
- Relative risk of non vertebral # was 0.51
- Side effects
  i. Gastrointestinal symptoms
  ii. Slightly reduce serum Ca concentration
  iii. IV administration of bisphosphonates
     - transient flu-like febrile illness
     - Associated with transient lymphopenia
     - bone pain - rapid infusion
  iv. Osteonecrosis of jaw

3. Calcitonin

- Binds to osteoclasts and inhibit bone resorption
- shown to increase the BMD of vertebral spine by 1.5%
- reduce risk of vertebral #.
- Alendronate results in greater increases in spine and hip bone density compared with nasal calcitonin
- Expensive
- Used 1st line in patients with substantial pain from acute osteoporotic # because of analgesis actions

4. Strontium ranelate

- 2 atoms of stable strontium with an organic moiety (ranelic acid)
- Oral agent
- Decreases osteoclast differentiation and activity
- Promotes bone formation by stimulating the replication of preosteoblasts

2 large clinical phase III trials
1. Spinal Osteoporosis Therapeutic Invervention (SOTI)
2. Treatment of Peripheral Osteoporosis (TROPOS)

41% risk reduction for vertebral # over 3 years (NNT = 9)
16% risk reduction fo all non-vertebral # over 3 years

Tolerability & safety
nausea  (6.6% vs 4.3% placebo)
Diarrhoea (6.5% vs 4.6% placebo) --> resolved after 1st 3 months of therapy
Anti-fracture efficacy of strontium ranelate is in line with any conventional therapy in osteoporosis
Effective & well tolerated
Not commercially available yet

Answer: Vit D