Bone metastases

- Spread of cancer cells to the bones
- Can occur in up to 75% of patients within 2 years of metastatic disease
- Approximately 5% will present with bone involvement
- Fractures are our biggest concern
- Baseline bone integrity plays a major role in risk of developing fractures
  - Calcium/Vitamin D3
  - Body habitus/activity level
  - Family history
  - Prior treatment (chemo/hormonal therapy)
Skeletal Related Events (SREs)

- Represent bony complications due to cancer
  - May occur in up to 50% of patients

- May result in several changes affecting QOL
  - Interruption of treatment
  - Initiation of pain medications to include narcotics
  - Need for surgery or radiation
  - Need for hospitalization

- 4 types of presentations
  - Hypercalcemia (elevated calcium): 19%
  - Pathologic fracture (fracture due to cancer): 19%
  - Spinal cord compression: 10%
  - Bone pain: 80%
SRE: Risk Factors

- Possible risk factors
  - Chemotherapy
  - Aromatase inhibitors (Letrozole, Anastrozole, Exemestane)
  - Tamoxifen
- Baseline bone density (DEXA)
  - Normal (T-score < -1.0)
  - Osteopenia (T-score -1.0 to -2.5)
  - Osteoporosis (T-score > -2.5)
- Additional Factors
  - Young age
  - Tumor size > 5 cm
  - More aggressive tumor (Grade 3)
  - > 4 lymph nodes
  - Infiltrating lobular carcinoma > ductal
  - ER/PR/Her2 and menopausal status did not seem to play a role
SRE: Prevention & Treatment

- Calcium and Vitamin D3 supplementation
  - Premenopausal: Calcium 1000 mg, Vitamin D3 600 IU
  - Postmenopausal: Calcium 1200 mg, Vitamin D3 600 IU
  - Vitamin D level (25-OH D): Goal 20-60 ng/ml

- Osteopenia and Osteoporosis (Bone density/DEXA scan)
  - Oral agents (Fosamax, Boniva, Evista)
  - Early breast cancer:
    - Denosumab (Prolia) and Zoledronate (Zometa)
  - Metastatic breast cancer:
    - Denosumab (Xgeva, subq), Zoledronate (Zometa, IV) and Pamidronate (Aredia, IV)
  - Dental visit at baseline & follow-up with good oral health
  - Side effects: Hypocalcemia, Osteonecrosis of the Jaw (ONJ), Pain/Fatigue

- Bone metastases
  - Osteoblastic (bone formation) versus Osteolytic (bone breakdown)
  - Breast cancer tends to be osteolytic or mixed
  - Bisphosphonates (Zometa) versus RANKL inhibitors (Xgeva)
Pathogenesis of Osteolytic Lesions

Fig. 1. Schematic representation of osteolytic bone metastases secondary to breast cancer. The molecules are derived from the BC cells and the bone extracellular matrix (ECM); together these factors promote metastasis, BC cell homing to bone, colonisation, osteoclastogenesis and osteolysis.
ASCO/CCO Guidelines 2018

- American Society of Clinical Oncology and Cancer Care Ontario
- Reviewed 273 articles with 6 articles meeting criteria for review
- 2 Major Questions:
  - 1. Best interval for Zometa dosing
  - 2. Role of BMAs to control pain from bone metastases
- Q#1: Best dosing interval
  - 4 mg every 3-4 weeks versus 12 weeks
ASCOC/CCO Guidelines 2018

Q#2: Control of pain
- Effects are modest thus should not be used alone
- Analgesia, XRT, surgery and systemic therapy
- Referral to Palliative Care and/or Pain Clinic
- Xgeva slightly better than Zometa

Cost differences
Other important benefits of BMAs
- Need for pain medications
- ER visits/hospitalizations
- Need for surgery, radiation and kypho/vertebroplasty
- Impact on survival?

Unanswered questions?
- Optimal duration of therapy? (indefinite)
- Is there a population of patients who benefit from shorter intervals?
- Is there a population of patients who benefit from a specific drug?
- Once an SRE occurs, what is the next step?
Thank you!!!