Medication-Related Osteonecrosis of the Jaws (MRONJ)

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Objectives

1/OMFS at CCHS

2/Practical Review of MRONJ
Oral and Maxillofacial Surgery
Evolution of the Specialty

This is not your father's Oldsmobile.
OMFS Scope of Practice

- Treatments may be performed on the craniomaxillofacial complex: mouth, jaws, neck, face, skull, and include:

- **Facial Fractures**
- **Cosmetic Surgery**
- **Obstructive Sleep Apnea via Maxillomandibular Advancement**
- **Orthognathic Surgery**
- **Temporomandibular joint disorders (TMJ)**
- **Congenital/Craniofacial Surgery**
- **Cutaneous Malignancy**
- **Pathology, Benign and Malignant**
- **Dental Implants**
- **Dentoalveolar**
- **Anesthesia**
2013 General Motors
Oral and Maxillofacial Surgery
Dentoalveolar Surgery
Odontogenic Infections
Ludwig’s
Osteomyelitis
Trauma
Naso-orbital-ethmoid fracture
Dogbite—pre-op
Paramedial Forehead Flap
Auricular Cartilage Graft
Septo-mucosal flap
6 months after 1\textsuperscript{st} surgery
Midface Soft Tissue Injuries

- Facial Nerve
- Parotid Duct
- Parotid Gland
GSW
S/P ORIF, Wound Vac, HWR, & Advancement Flap
Multiple Facial Fractures including atrophic mandible fracture
Pathology
Jaw Tumor
1 Scan the patient
2 Plan during interactive planning session
3 Approve the surgical plan
4 Receive guides and anatomical models
5 Perform the surgery
Pathology
Oral Cancer
Orthognathic Surgery

http://youtu.be/9RH9qAB_gA0
Obstructive Sleep Apnea
MMA – Maxillomandibular Advancement

Pre advance

Post advance

Prediction advance

Actual advance—how much to advance?
Posterior Airway Space Changes

Preop

Postop
TMJ Disorders
TMJ-Joint Replacement
Palatal Defect & Palatoplasty vs Tongue Flap
Nasal Nevus
Esthetic Surgery
Cheek Implant
Right Malar Implant
Septorhinoplasty
Temporal Implant
• Treatments may be performed on the craniomaxillofacial complex: mouth, jaws, neck, face, skull, and include:
  • Facial Fractures
  • Cosmetic Surgery
  • Obstructive Sleep Apnea via Maxillomandibular Advancement
  • Orthognathic Surgery
  • Temporomandibular joint disorders (TMJ)
  • Congenital/Craniofacial Surgery
  • Cutaneous Malignancy
  • Pathology, Benign and Malignant
  • Dental Implants
  • Dentoalveolar
  • Anesthesia
MRONJ
Outline

- Antiresorptive Medications
- BRONJ—BIONJ—ARONJ—MRONJ
- Pathophysiology
- Risk Factors
- Management Strategies
- Staging
- Discussion
- Conclusions
Osteonecrosis of the Jaws Associated With Cancer Chemotherapy

J. Wang, DMD, MD, MPH, *N.M. Goodger, FRCS, FDS, DLORCS, †
and M.A. Pogrel, DDS, MD‡

Osteonecrosis of the jaws can result from a number of causes, including radiation therapy1-4 and chronic osteomyelitis.5 Herpes zoster has been described as a rare cause of osteonecrosis.6,7 Neuralgia inducing cavitary osteonecrosis (NICO) is a recently described and controversial cause of osteonecrosis of the jaws.8,9 We describe 3 cases of osteonecrosis of the jaws associated with cancer chemotherapy for metastatic breast cancer.

Report of Cases

CASE 1

A 53-year-old white woman presented with a 3-year history of metastatic breast cancer treated with intermittent chemotherapy with docetaxel (Taxotere; Rhone-Poulenc-Rorer, Collegeville, PA) 30 mg, dolasetron 50 mg, pamidronate 90 mg, and dexamethasone 4 mg in weekly cycles. She had a 2-year history of a nonhealing socket after extraction of the lower left third molar. The socket had been unresponsive to antibiotics and local curettage. Examination showed a 1.5 cm × 8 mm region of exposed and
LETTERS TO THE EDITOR

PAMIDRONATE (AREDIA) AND ZOLEDRONATE (ZOMETA) INDUCED AVASCULAR NECROSIS OF THE JAWS: A GROWING EPIDEMIC

To the Editor—Preliminary to a manuscript submitted to a refereed scientific journal, this preliminary communication is being issued by the Division of Oral and Maxillofacial Surgery at the University of Miami School of Medicine. It identifies 36 cases of painful bone exposure in the mandible, maxilla, or both, that were unresponsive to surgical or medical treatments. All patients were receiving pamidronate (Aredia; Novartis Pharmaceuticals, East Hanover, NJ) or zoledronate (Zometa; Novartis Pharmaceuticals) therapy. It represents a heretofore unrecognized and unreported serious adverse affect; caution should be used when prescribing these drugs.

down regulation of matrix metalloproteinases. Their resultant reduction in osteoclastic activity reduces bone resorption and thus supports their published indications, which includes reducing the hypercalcemia in some malignancies and reducing osteolysis in bone metastases and in some cases of Paget’s disease. However, normal osteoclasts is vital to bone turnover and bone viability. Osteocytes develop from osteoblasts, which have secreted hydroxyapatite crystals into a collagen matrix known as mineralized bone, which then encases the osteocyte. The osteocyte is a terminal cell with a life span of about 150 days.6 As the osteocyte lives out its normal life span it no longer can maintain its mineral matrix which surrounds it and microfractures develop. Normal osteoclasts resorbs nonvital bone and releases cytokines such as bone morphogenetic protein (BMP) and insulin-like growth factors 1 and 2 (ILG, and
AVASCULAR NECROSIS OF THE JAWS: RISK FACTORS IN METASTATIC CANCER PATIENTS

To the Editor.—In his letter in the September issue of the Journal of Oral and Maxillofacial Surgery (J Oral Maxillofac Surg 61:1115-1117, 2003), Dr Marx suggested a possible association between the use of bisphosphonates such as pamidronate and zoledronic acid to the development of avascular necrosis of the jaws. The case reports cited in the letter are not adequate to suggest a causal association, much less a “growing epidemic.” A thorough review of the medical literature and our ongoing review of the reported cases reveal multiple risk factors for avascular necrosis of the jaws in cancer patients.

Prior to those cases reported by Marx and others, no cases of this condition had been previously reported in multiple, well-controlled clinical trials of more than 3,000 cancer patients that had been conducted as far back as the early 1990s. Since their introduction, it is estimated that pamidronate and zoledronic acid have been used in approximately 2.5 million patients worldwide and reports of this condition during this extensive postmarketing experience have been rare.

The treatment needs of people with cancer are generally complex, and may involve a variety of therapies such as radiation, chemotherapy, and other concomitant medications such as steroids, that are well-known and documented causes of osteonecrosis. Importantly, recognized risk factors for osteonecrosis of the jaws are common in cancer patients and include infections of dental and sinus origin,
BISPHOSPHONATES AND BONE NECROSIS

To the Editor.—I am writing this letter in clarification and expansion of our article published in the September edition of the Journal (J Oral Maxillofac Surg 61:1104-1107, 2003). This article involves 3 patients who had developed bone necrosis in the maxillofacial region after cancer chemotherapy. In each case, part of the chemotherapy consisted of a bisphosphonate, but in our discussion we tended to dismiss the concept that bisphosphonates could be the cause of this necrosis since it had not been previously reported and did not seem to correspond with the metabolic action of bisphosphonates. However, since this article was published

LETTERS TO THE EDITOR

Ruggerio, DMD, MD, from New York (in an article submitted to the New England Journal of Medicine) and Robert Marx, DDS (J Oral Maxillofac Surg 61:115-118, 2003), amongst others, have documented a considerable number of cases of maxillofacial bone necrosis, which does appear to be secondary to bisphosphonates. In the light of this more recent information, it does seem in retrospect that the cases we reported were probably largely bisphosphonate induced as well and not necessarily due to the other chemotherapeutic agents given. We offer this letter in clarification.

M. ANTHONY POGREL, DDS, MD, FRCS
San Francisco, CA

doi:10.1016/j.joms.2003.11.003
IMPORTANT DRUG PRECAUTION FOR
DENTAL HEALTH PROFESSIONALS
WITH PATIENTS BEING TREATED FOR CANCER

May 05, 2005

Dear Doctor:

We are writing to inform you of an adverse event Osteonecrosis of the Jaw (ONJ) observed in cancer patients receiving treatment with intravenous bisphosphonates, Aredia and Zometa, which may have an impact on the dental care of patients within your practice. **While on treatment, invasive dental procedures should be avoided, if possible.**

The prescribing information recommends that cancer patients:

- **receive a dental examination** prior to **initiating therapy with intravenous bisphosphonates** (Aredia and Zometa); and

- **avoid invasive dental procedures while receiving bisphosphonate treatment.** For patients who develop ONJ while on bisphosphonate therapy, **dental surgery may exacerbate the condition.** Clinical judgment by the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

Aredia is used in the treatment of hypercalcemia of malignancy, Paget’s disease, osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma. Zometa is used in the
nates. In September 2004, Novartis, the manufacturer of the IV bisphosphonates pamidronate (Aredia®) and zoledronic acid (Zometa®), notified healthcare professionals of additions to the labeling of these products, which provided cautionary language related to the development of osteonecrosis of the jaws. This was followed in 2005 by a broader drug class warning of this complication for all bisphosphonates including the oral preparations. More recently, other antiresorptive agents and novel anti-cancer drugs have been linked to the development of jaw necrosis
Cases of osteonecrosis / osteomyelitis over 28 month period

- 56 (89%): Oncologic Diagnosis
  - All received IV Bisphosphonate for at least 1 year (Aredia or Zometa)
- 7 (11%): Osteoporosis
  - All received oral Bisphosphonate (Fosamax or Actonel)
63 Cases: Ruggiero et al.

- **Region of exposed bone:**
  - 63% mandible
  - 38% maxilla
  - 1% all four quadrants

- **Etiology:**
  - 86% recent extraction
  - 14% no history of trauma
Courtesy of Ruggiero et al.
Courtesy of Ruggiero et al.
Courtesy of Ruggiero et al.
63 Cases: Ruggiero et al.

- Cultures: Normal flora
  Biopsies: Necrotic bone

- Treatment ranged from minor debridement to resection

- Five patients continue to develop new regions of exposed bone following cessation of bisphosphonate therapy

- No definitive treatment recommendations given
119 Cases: Marx et al.

- 26% pamidronate (Aredia)
- 40% zoledronate (Zometa)
- 30% pamidronate then zoledronate
- 3% alendronate (Fosamax)
119 Cases: Marx et al.

- Indication for bisphosphonate therapy
  - 52% multiple myeloma
  - 42% metastatic breast cancer
  - 3% metastatic prostate cancer
  - 3% osteoporosis
119 Cases: Marx et al.

- Presenting findings (in addition to exposed bone)
  - 69% pain
  - 31% asymptomatic
  - 24% tooth mobility
  - 18% nonhealing fistulas
119 Cases: Marx et al.

- Location
  - 68% mandible
  - 28% maxilla
  - 4% mandible and maxilla
119 Cases: Marx et al.

- Medical comorbidities
  - 98% metastatic disease
  - 98% previous and/or maintenance chemotherapy
  - 60% dexamethasone
119 Cases: Marx et al.

- Dental comorbidities
  - 84% periodontitis
  - 29% dental caries
  - 13% abscessed teeth
  - 11% root canal treatments
  - 9% mandibular tori
119 Cases: Marx et al.

- Precipitating factor
  - 38% extraction
  - 29% advanced periodontitis
  - 25% spontaneous
  - 11% periodontal surgery
  - 3% implant surgery
  - <1% endodontics
119 Cases: Marx et al.

- Treatment outcomes
  - 90% functioning free of pain
  - 10% experienced intermittent episodes of pain requiring adjustment to antibiotics and chairside daily wound irrigations
  - 3% required brief hospitalization for cellulitis and pain
## Appendix I: Antiresorptive Preparations Commonly Used in the U.S.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Primary Indication</th>
<th>Nitrogen Containing</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate (Fosamax®)</td>
<td>Osteoporosis</td>
<td>Yes</td>
<td>10 mg/day 70 mg/week</td>
<td>Oral</td>
</tr>
<tr>
<td>Risedronate (Actonel®)</td>
<td>Osteoporosis</td>
<td>Yes</td>
<td>5 mg/day 35 mg/week</td>
<td>Oral</td>
</tr>
<tr>
<td>Ibandronate (Boniva®)</td>
<td>Osteoporosis</td>
<td>Yes</td>
<td>2.5 mg/day 150 mg/month</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 mg every 3 months</td>
<td>IV</td>
</tr>
<tr>
<td>Pamidronate (Aredia®)</td>
<td>Bone Metastases</td>
<td>Yes</td>
<td>90 mg/3 weeks</td>
<td>IV</td>
</tr>
<tr>
<td>Zolendronate (Zometa®)</td>
<td>Bone Metastases</td>
<td>Yes</td>
<td>4 mg/3 weeks</td>
<td>IV</td>
</tr>
<tr>
<td>(Reclast®)</td>
<td></td>
<td></td>
<td>5 mg/year</td>
<td>IV</td>
</tr>
<tr>
<td>Denosumab (Xgeva®)</td>
<td>Bone metastases</td>
<td>No Humanized monoclonal antibody</td>
<td>120 mg/4 weeks 60 mg/6 months</td>
<td>SQ</td>
</tr>
<tr>
<td>(Prolia®)</td>
<td>Osteoporosis</td>
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Exposure

age, 5.1 million patients over the age of 55 years received a prescription for a bisphosphonate in year 2008. A recent federal study estimated that the prevalence of BP exposure was 7 for every 100 US population receiving a prescription for a bisphosphonate in the outpatient setting for the treatment
Bisphosphonates

- 250,000 + patients worldwide
  - Fosamax
    - 37th most prescribed drug in 2005
    - Over 20 million prescriptions
    - More than Viagra, Coumadin, Pen VK
  - Actonel
    - 122nd most prescribed drug in 2005
Bisphosphonate Related Osteonecrosis of the Jaws (BRONJ)

- Growing number of patients exhibiting symptoms of BRONJ

- Characterized by exposed, necrotic bone in the maxillofacial region

- Investigation revealed link between IV and oral bisphosphonate drug treatment
What are Bisphosphonates?

- Related to pyrophosphates
- 2 phosphate groups “Bis” covalently bonded to carbon
- R-group determines potency
- Inhibit bone resorption
Mechanism of Action

- Upon IV or oral delivery, bisphosphonates bind to Ca in the mineral matrix of bone.
- Repeated doses increase the amount bound to bone.
- Osteoclasts ingest bisphosphonates during bone remodeling.
- Drug stops GTPase enzymes that inhibit cell apoptosis and cell death.
  - **Mevalonate Pathway**
  - Reduce serum Calcium
  - Decrease bone induction proteins
  - Hypermineralization of bone
Pharmacokinetics

- Only 0.64% of oral form absorbed in small intestines
- If taken with meals amount absorbed decreases
- 30-40% excreted by kidneys
- Circulating half-life is between 0.5 hrs and 2 hours
  - Rapid Uptake into bone
- Can only be removed from bone matrix by osteoclasts but is toxic to cells
- Toxicity is both time and dose dependent
- Half life exceeds 11 years.
Uses for Bisphosphonates

- Osteoporosis
- Paget’s
- Multiple myeloma
- Small cell cancer of lungs
- Off Label Uses
  - Osteogenesis imperfecta
  - Steroid induced osteoporosis
  - Fibrous dysplasia
Dosing
Side Effects

- Long Term Use
  - Atypical Fractures
    - Mainly of long bones
      - Femur/Tibia
  - Esophageal Cancer?
    - Oral Use
  - Renal Failure
    - Due to elimination by the kidneys
Ingestion and Apoptosis
Once the Osteoclast dies

- No bone resorption
- No release of BMP or insulin-like growth factors
- Old bone is not removed/remodeled
- NO NEW OSTEOID is formed.
- Osteocytes die and dead bone is then left behind.
- Hypermineralization
History of BIONJ

- "Phossy Jaw"
  - Found in phosphate miners and match makers
  - Due to phosphate vapors inhaled
  - First reported in 1800's
- BIONJ (bisphosphonate induced osteonecrosis of the jaw)
  - First reported in 2002
  - Associated with Pamidronate or Zoledronate (Zometa and Novartis)
- 1100 + reports have been published
Clinical Manifestations

- Exposed Alveolar bone
  - Open mucosal wound
  - Necrotic bone
- Infection
  - Purulence, bone pain
  - Orocutaneous fistula
Severe Radiographic Evidence

- Severe osteolysis
- Pathologic Fracture
- Osteoclast retracts loses its ruffled edges
Histology

- No osteoid formation
- No osteocytes in lacunae
Not to be Confused With…

- Osteoradionecrosis (ORN)
  - Avascular necrosis secondary to radiation
- Osteomyelitis
  - Thrombosis of small blood vessels leading to infection within bone marrow
- Steroid-induced osteonecrosis
  - More common in long bones
  - Rarely is bone exposed
# Appendix I: Antiresorptive Preparations Commonly Used in the U.S.

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<tr>
<td>Zolendronate (Zometa&lt;sup&gt;®&lt;/sup&gt;) (Reclast&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>Bone Metastases</td>
<td>Yes</td>
<td>4 mg/3 weeks</td>
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<td>Denosumab (Xgeva&lt;sup&gt;®&lt;/sup&gt;) (Prolia&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>Bone metastases</td>
<td>No Humanized monoclonal antibody</td>
<td>120 mg/4 weeks 60 mg/6 months</td>
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Position Paper

American Association of Oral and Maxillofacial Surgeons

Medication-Related Osteonecrosis of the Jaw—2014 Update

Special Committee on Medication-Related Osteonecrosis of the Jaws:

Introduction
Types

Antiresorptive medications

Intravenous (IV) bisphosphonates (BPs) are antiresorptive medications used to manage cancer-related conditions including hypercalcemia of malignancy, skeletal-related events (SRE) associated with bone metastases in the context of solid tumors such as breast cancer, prostate cancer, and lung cancers, and for management of lytic lesions in the setting of multiple myeloma. While the potential for bisphosphonates to improve cancer-specific survival remains controversial, these medications have had a significant positive effect on the quality of life for patients with advanced cancer involving the skeleton.

IV BPs, ie once yearly infusion of zolendronate (Reclast®) and a parenteral formulation of ibandronate (Boniva®) administered every three months, have FDA approval for management of osteoporosis.
**Oral bisphosphonates** are approved for treatment of osteoporosis and are frequently used to treat osteopenia as well.\(^{15}\) They are also used for a variety of less common conditions such as Paget’s disease of bone, and osteogenesis imperfecta.\(^{16,17}\) The most common use, however, is for osteopenia and osteoporosis.\(^{18,19}\)

**RANK ligand inhibitor (denosumab)** is an antiresorptive agent that exists as a fully humanized antibody against RANK ligand (RANK-L) and inhibits osteoclast function and associated bone resorption. When denosumab (Prolia®) is administered subcutaneously every 6 months there is a reduction in the risk of vertebral, non-vertebral, and hip fractures in osteoporotic patients.\(^{20,21}\) Denosumab (Xgeva®) is also effective in reducing SRE related to metastatic bone disease from solid tumors when administered monthly.\(^{22,23}\) Denosumab therapy is not indicated for the treatment of multiple myeloma. Interestingly, in contrast to bisphosphonates, RANK ligand inhibitors do not bind to bone and their effects on bone remodeling are mostly diminished within 6 months of treatment cessation.

**Antiangiogenic medications**

Angiogenesis inhibitors interfere with the formation of new blood vessels by binding to various signaling mol-
Appendix II: Medications Used in the Treatment of Various Cancers that are Antiangiogenic or Targets of the Vascular Endothelial Growth Factor (VEGF) Pathway that have been Associated with Jaw Necrosis*.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Primary indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunitinib (Sutent®)</td>
<td>Tyrosine kinase inhibitor</td>
<td>GIST, RCC, pNET</td>
</tr>
<tr>
<td>Sorafenib (Nexavar®)</td>
<td>Tyrosine kinase inhibitor</td>
<td>HCC, RCC</td>
</tr>
<tr>
<td>Bevacizumab (Avastin®)</td>
<td>Humanized monoclonal antibody</td>
<td>mCRC, NSCLC, Glio, mRCC</td>
</tr>
<tr>
<td>Sirolimus (Rapamune®)</td>
<td>Mammalian target of rapamycin pathway</td>
<td>Organ rejection in renal transplant</td>
</tr>
</tbody>
</table>

Abbreviations: GIST gastrointestinal stromal tumor; RCC renal cell carcinoma; pNET pancreatic neuroendocrine tumor; HCC hepatocellular carcinoma; mCRC metastatic colorectal carcinoma; NSCLC non-squamous non-small cell lung carcinoma; Glio Glioblastoma; mRCC metastatic renal cell carcinoma
MRONJ Case Definition

In order to distinguish MRONJ from other delayed healing conditions and address evolving clinical observations and concerns about under-reporting of disease, the working definition of MRONJ has been modified from the 2009 AAOMS Position Paper:¹

Patients may be considered to have MRONJ if all of the following characteristics are present:

1. Current or previous treatment with antiresorptive or antiangiogenic agents;

2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than eight weeks; and

3. No history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
Why is necrosis only seen in the jaws?

- Alveolar bone remodels significantly more than other bones of body and locations in the maxilla and mandible.
  - 10x the rate of tibia
  - 5x the rate of inferior border
  - 3-5x the rate at IAN canal
- Due to rapid remodeling secondary to occlusal forces increase in uptake of bisphosphonates.
- Tori have thin mucosa, poor vascularity
High Concentration in Jaws

- Greater blood supply than other bones
- Faster bone turnover rate related to daily activity
- Presence of teeth and periodontal ligaments
- ? bisphosphonates directly toxic to overlying oral epithelium (Reid IR et al in Bone, 2007 Sep;41(3):318-20)
Are Nitrogen-Containing Intravenous Bisphosphonates Implicated in Osteonecrosis of Appendicular Bones and Bones Other Than the Jaws? A Survey and Literature Review

Edwin L. Granite, DMD*

**Purpose:** The purpose of this study was to determine the incidence of osteonecrosis of appendicular bones due to nitrogen-containing intravenous bisphosphonates and the incidence of adverse effects in bones other than the jaws.

**Materials and Methods:** A detailed search of the professional medical and dental literature was conducted. In addition, a questionnaire was mailed to all known orthopedic surgery training programs in the United States. Programs were queried as to clinical findings and other various scenarios.

**Results:** There was a great paucity of literature that addressed the issue. Of the 154 questionnaires mailed, 29 (19%) were returned. Identification was optional; therefore, it was impossible to determine the geographic origin of the returned questionnaires. No orthopedic surgery training program indicated positive findings of osteonecrosis in the long bones due to nitrogen-containing intravenous bisphosphonates. There were rare reports in the literature of osteonecrosis in other areas of the bony skeleton.

**Conclusion:** On the basis of literature searches and national orthopedic questionnaires, there is only a rare incidence of osteonecrosis of the appendicular bones and bones other than the jaws due to nitrogen-containing intravenous bisphosphonates. There were no reports of adverse long bone effects, based on the questionnaires. There were rare reports in the literature.

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*J Oral Maxillofac Surg 70:837-841, 2012*
Pathophysiology

A. Inhibition of osteoclastic bone resorption and remodeling

B. Inflammation/Infection

C. Inhibition of Angiogenesis
- Denosumab
- Bisphosphonates

**Cellular toxicity of bisphosphonates on bone surface**

- Impaired macrophage function
- Reduced bone turnover

**Impaired epithelial repair**

**Microbial access to bone surface**

**Chronic bone infection ± microbial biofilm formation**

- Bone necrosis
- Bone resorption
- Exposed bone in the mouth

**Trauma**
Risk factors for MRONJ

A. Medication-related risk factors

For patients receiving oral bisphosphonate therapy to manage osteoporosis, the prevalence of ONJ increases over time from near 0 at baseline to 0.21% after four or more years of BP exposure (see Figure 1). The median duration of BP exposure for patients with ONJ and ONJ-like features was 4.4 years. For patients without ONJ, the median

Among cancer patients exposed to denosumab, a RANK L inhibitor, the risk of MRONJ ranges from 0.7% - 1.9% (70-90 cases per 10,000 patients). The risk for ONJ among cancer patient exposed to denosumab is comparable to the risk of ONJ in patients exposed to zolendronate. 

In a survey study of over 13,000 Kaiser Permanente members, the prevalence of BRONJ in patients receiving long-term oral bisphosphonate therapy was reported at 0.1% (10 cases per 10,000) which increased to 0.21 (21 cases per 10,000) among patients with greater than 4 years of oral BP exposure. Felsenberg and Hoffmeister reported a
Local factors

Estimates for developing ONJ after tooth extraction among cancer patients exposed to intravenous BPs ranges from 1.6 to 14.8%. In a retrospective cohort study...

Demographic and systemic factors and other medication factors

Corticosteroids are associated with an increased risk for MRONJ. Antiangiogenic agents, when given in addition to antiresorptive medications, are associated with an increased risk of ONJ.

Tobacco use has been inconsistently reported as a risk factor for MRONJ. In a case-control study, tobacco use approached statistical significance as a risk factor for ONJ in cancer patients (OR=3.0; 95% CI= 0.8 - 11.6) of 42 pediatric patients who had received IV bisphosphonate therapy (mean duration of therapy 6.5 years) for a variety of metabolic bone diseases. No cases of ONJ were reported despite invasive dental treatment...

Anatomic factors

Limited new information regarding anatomic risk factors for MRONJ is available. MRONJ is more likely to appear in the mandible (73%) than the maxilla (22.5%) but can appear in both jaws (4.5%). Denture use was associated with...
Oral Bisphosphonate-Induced Osteonecrosis: Risk Factors, Prediction of Risk Using Serum CTX Testing, Prevention, and Treatment

Robert E. Marx, DDS,* Joseph E. Cillo, Jr, DDS,† and Juan J. Ulloa, DDS‡

FIGURE 5. Mean size of osteonecrosis versus duration of bisphosphonate exposure.


Table 2. MEAN SIZE OF OSTEO NECROSIS AND DURATION OF BISPHOSPHONATE EXPOSURE

<table>
<thead>
<tr>
<th>Duration of Oral BP Use</th>
<th>n</th>
<th>Mean Size of Exposure</th>
<th>Pain</th>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to 4 years</td>
<td>8</td>
<td>0.6cm²</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4 to 5 years</td>
<td>6</td>
<td>1.5cm²</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>5 to 6 years</td>
<td>5</td>
<td>3.8cm²</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>6 to 7 years</td>
<td>3</td>
<td>4.7cm²</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>More than 7 years</td>
<td>8</td>
<td>7.9cm²</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

Abbreviation: BP, bisphosphonate.
Bisphosphonate-Related Osteonecrosis of the Jaw: Clinical Features, Risk Factors, Management, and Treatment Outcomes of 26 Patients

Vivek Thumbigere-Math, BDS,* Ma’Ann C. Sabino, DDS, PhD,†
Rajaram Gopalakrishnan, BDS, PhD,‡
Sabrina Huckabay, DDS,§ Arkadiusz Z. Dudek, MD, PhD,¶
Saonli Basu, PhD,‖ Pamela J. Hughes, DDS,∥
Bryan S. Michalowicz, DDS, MS,** Joseph W. Leach, MD,††
Karen K. Swenson, RN, PhD,‡‡ James Q. Swift, DDS, §§
Cheryl Adkinson, MD,¶¶ and David L. Basi, DMD, PhD\\

**Conclusions:** Long-term n-BIS therapy and recent dental procedures are consistent findings in patients with BRONJ. Spontaneous BRONJ lesions respond favorably to current BRONJ treatment strategies. © 2009 American Association of Oral and Maxillofacial Surgeons

### Table 2. BRONJ CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Maxilla</td>
<td>4 (15.4)</td>
</tr>
<tr>
<td>Mandible</td>
<td>22 (84.7)</td>
</tr>
<tr>
<td>Anterior sextant</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Posterior sextant</td>
<td>23 (88.4)</td>
</tr>
<tr>
<td>BRONJ onset</td>
<td></td>
</tr>
<tr>
<td>Tooth extraction</td>
<td>13 (50.0)</td>
</tr>
<tr>
<td>Root canal treatment</td>
<td>2 (7.7)</td>
</tr>
<tr>
<td>Crown preparation</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>10 (38.4)</td>
</tr>
<tr>
<td>Clinical findings</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>21 (80.7)</td>
</tr>
<tr>
<td>Infection</td>
<td>18 (69.0)</td>
</tr>
<tr>
<td>Purulent discharge</td>
<td>14 (53.8)</td>
</tr>
<tr>
<td>Facial swelling</td>
<td>9 (34.6)</td>
</tr>
<tr>
<td>Fistula</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Fracture</td>
<td>2 (7.7)</td>
</tr>
</tbody>
</table>

Abbreviation: BRONJ, bisphosphonate-related osteonecrosis of jaw.

**FIGURE 1.** A, Nonhealing right mandibular first and second molar extraction sites with exposed alveolar bone (0.5 cm × 0.5 cm). B, Note rapid progression of lesion (1.3 cm × 0.2 cm). C, Axial postero-eremission tomography-computed tomography image showing diffuse, intense hypermetabolic activity. D, Computed tomography scan showing extensive area of involved bone that was not clinically apparent. E, Necrotic bone resected through submandibular approach. F, Immediate reconstruction using reconstruction plate. (Figure 1 continued on next page.)
Fluorodeoxyglucose Positron Emission Tomography With Computed Tomography Detects Greater Metabolic Changes That Are Not Represented by Plain Radiography for Patients With Osteonecrosis of the Jaw

Kenneth E. Fleisher, DDS, * Roy A. Raad, MD, † Rajan Rakheja, MD, ‡ Vikas Gupta, §
King Chong Chan, DMD, MS, || Kent P. Friedman, MD, ¶ Karen A. Mourtzikos, MD, #
Malvin Janal, PhD, ** and Robert S. Glickman, DMD††

**Conclusion:** The results of this study show that FDG PET/CT detects local and diffuse metabolic changes that may not be represented by plain radiography for patients with ONJ related to antiresorptive therapy. The target-to-background ratio allowed the discrimination between ONJ lesions and background changes. Future studies are necessary to determine whether FDG PET/CT can determine risk and facilitate management of ONJ.

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**FIGURE 2.** Osteonecrosis of the jaw, case 20. A, Exposed bone on the medial aspect of the right mandible adjacent to the second premolar and first molar teeth. B, Localized periodontal bone loss associated with the mandibular right first and second molar teeth. C, Fused positron-emission tomogram and computed tomogram with local fluorodeoxyglucose uptake extending from the medial to the lateral cortex of the right mandible.
Management Strategies for Patients Treated with Antiresorptives or Antiangiogenics

Prevention of MRONJ

The implementation of dental screening and appropriate dental measures before initiating antiresorptive therapy reduced the risk of ONJ.

Cessation of at-risk medication therapy prior to tooth extraction or other procedures, which involve osseous injury (eg dental implant placement, periodontal or
Prevention

- Communication
- Dental evaluation/treatment
Risk Assessment

- Medical History
  - Identify risk factors
  - Comorbidities
- Examinations
  - Radiographs
  - Intraoral exam
- CTX?
  - Assess bone turnover
Are we asking the important questions? Especially to those on Bisphosphonates.
- Which have been taken?
- How long have you taken them?
- What dose?
- How frequent?
- Are they taking steroids?
A C-Terminal Crosslinking Telopeptide Test-Based Protocol for Patients on Oral Bisphosphonates Requiring Extraction: A Prospective Single-Center Controlled Study

April Hugheson, Andrew Cheng, MBBS, BDS, FRACDS(OMS),
Ranjit Kunchar, MBBS, BDS, Brian Stein, MBBS, FRACP,
Paul Sambrook, MBBS, MDS, FRACDS(OMS),
and Alastair Goss, DDS, FRACDS(OMS)

Purpose: Patients undergoing extraction are at risk for bisphosphonate-related osteonecrosis of the jaws (BRONJ). A C-terminal crosslinking telopeptide (CTX) level lower than 150 pg/mL has been suggested as a predictor of BRONJ risk. The authors aimed to increase the precision of estimates of the risk of BRONJ in osteoporosis after extraction and to assess value of CTX testing at extraction time in cases of BRONJ in a large prospective cohort.

Patients and Methods: All patients on oral bisphosphonates for osteoporosis referred for extractions over a period of 6.5 years were included in a standard protocol. Pre-extraction fasted CTX levels were obtained. All patients were followed until healing. If the CTX level was lower than 150 pg/mL, they were offered a drug holiday. If they declined, if the CTX level was above 150 pg/mL at baseline, or after the drug holiday, they had extractions performed under local anesthesia. Age-matched controls not on bisphosphonates were identified.

Results: Nine hundred fifty patients had 2,461 extractions. One hundred eighty-one patients had a CTX level lower than 150 pg/mL. Four patients developed BRONJ; all had a CTX level lower than 150 pg/mL. All were on alendronate. The case-control comparison approached significance (<150 pg/mL; P = .073). Alendronate was associated with a low CTX level (P < .05). A CTX level lower than 150 pg/mL had a sensitivity of 100% and specificity of 81%. Bayesian analysis yielded a population expected risk of BRONJ of 0.29% (95% confidence interval, 0.12-0.52); the expected risk was 0.42% for a CTX level lower than 150 pg/mL and 0.13% for a CTX level higher than 150 pg/mL.

Conclusion: The risk of BRONJ for patients with osteoporosis on bisphosphonates having extractions is approximately 0.2%. A CTX level lower than 150 pg/mL is sensitive and is associated with an approximately 3-fold greater risk of BRONJ.

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Laboratory Test

- **CTX**
  - Assesses bone turnover and roughly correlates systemic suppression of bone renewal.
  - Measures the carboxy terminal octapeptide fragment cleaved from the cross-linking peptide of type-I collagen by osteoclasts.
Risk Stratification

- Serum C-Terminal Telopeptide (CTX):
  - predictor of risk-related to oral bisphosphonates and surgical complications
- CTX: pg=picograms
- <100 pg/mL=high risk (do no surgery)
- 101-150 pg/mL=moderate risk
- >151 pg/mL=little to no risk (surgery OK)
- CTX values increase with cessation of oral bisphosphonates (Fosamax, Actonel, Boniva)
Case Example

- 60 y/o female with osteoporosis, HTN
- Fosamax for 8 years
- Referred for second opinion regarding surgery
Prevention

- Communication
- Dental evaluation/treatment
In 2003, Robert E. Marx, DDS of Miami, FL identified 36 cases of painful bone exposure in the mandible, maxilla or both that were unresponsive to surgical or medical treatments. Dr. Marx noted that most of the patients had received either pamidronate (Aredia) or zoledronate (Zometa) at the time of presentation for hypercalcemia related to multiple myeloma, metastatic breast carcinoma or osteoporosis (1 patient). He cited several articles that explained the mechanism by which the drugs affect bone and bone healing.

Further, he noted that no other bisphosphonates used to treat osteoporosis had, at that time, been associated with avascular bone necrosis in the jaws. Two articles were cited in criticism of Dr. Marx' letter, citing that there had been no cases of osteonecrosis in Novartis' clinical trials of more than 3,000 cancer patients.

The subject was again addressed in 2004, when Dr. Salvatore Ruggiero et al published a paper in the Journal of Oral and Maxillofacial Surgery citing their experience with increasing numbers of patients presenting with necrotic lesion(s) of the jaw that shared the common clinical factor of having received chronic bisphosphonate therapy. Having noticed the cluster of patients with the disease process, Dr. Ruggiero and his group carried out a retrospective chart review of the patients who had presented to their service at Long Island Jewish Medical Center in
Exposure

age, 5.1 million patients over the age of 55 years received a prescription for a bisphosphonate in year 2008. A recent federal study estimated that the prevalence of BP exposure was 7 for every 100 US population receiving a prescription for a bisphosphonate in the outpatient setting for the treatment
What do we do when this walks in the door?

- Medical History
- Examination
  - Pain
  - Purulence
  - Bad taste
  - Numbness
- Discussion/Communication
  - Is the drug actually needed anymore?
  - Half-life
  - Reason patient is still on drug?
Antibiotic Recommendations

- 1st choice
  - Pen VK 500mg q6h
- What if penicillin allergic?
  - Clinda?
    - Probably not best choice due to resistance of Actinomyces, Eikenella, Moraxella.
    - These colonize secondarily on exposed bone.
    - Culturing is recommended to establish best susceptibility
- Chlorhexidine oral rinse
### Table 1 Staging and Treatment Strategies

<table>
<thead>
<tr>
<th>MRONJ† Staging</th>
<th>Treatment Strategies‡</th>
</tr>
</thead>
</table>
| **At risk category** No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates | • No treatment indicated  
• Patient education |
| **Stage 0** No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms | • Systemic management, including the use of pain medication and antibiotics |
| **Stage 1** Exposed and necrotic bone, or fistulae that probes to bone, in patients who are asymptomatic and have no evidence of infection | • Antibacterial mouth rinse  
• Clinical follow-up on a quarterly basis  
• Patient education and review of indications for continued bisphosphonate therapy |
| **Stage 2** Exposed and necrotic bone, or fistulae that probes to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage | • Symptomatic treatment with oral antibiotics  
• Oral antibacterial mouth rinse  
• Pain control  
• Debridement to relieve soft tissue irritation and infection control |
| **Stage 3** Exposed and necrotic bone or a fistula that probes to bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone, (i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extra-oral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible of sinus floor | • Antibacterial mouth rinse  
• Antibiotic therapy and pain control  
• Surgical debridement/resection for longer term palliation of infection and pain |

† Exposed or probable bone in the maxillofacial region without resolution for greater than 8 weeks in patients treated with an antiresorptive and/or an antiangiogenic agent who have not received radiation therapy to the jaws.

‡ Regardless of the disease stage, mobile segments of bony sequestrum should be removed without exposing uninvolved bone. The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.
Temporal Correlation Between Bisphosphonate Termination and Symptom Resolution in Osteonecrosis of the Jaw: A Pooled Case Report Analysis

Andrew M. Hinson, BS, * Eric R. Siegel, MS, † and Brendan C. Stack Jr, MD‡

Purpose: To investigate whether termination of bisphosphonates (BPs) affects resolution of bone exposure and symptomatic disease in patients with established medication-related osteonecrosis of the jaw (MRONJ).

Patients and Methods: The studied population included 84 patients with established MRONJ who discontinued BP therapy before treatment (n = 21), at treatment initiation (n = 38), or later (or never) in the treatment course (n = 25). These 3 groups were compared using Kaplan-Meier curves and log-rank tests for differences in the respective times to resolution of 1) bone exposure for any treatment modality, 2) bone exposure not requiring radical surgery, and 3) disease symptoms.

Results: Patients who continued BPs after the start of treatment exhibited significantly delayed resolution of symptoms (median 12 months; 95% confidence interval 8 to 15) compared with those who discontinued BPs before (3 months; 2 to 5) and at (6 months; 3 to 7) presentation (P < .005).

Conclusions: Independent of treatment modality and MRONJ stage at presentation, discontinuing BP before or at treatment initiation is associated with faster resolution of MRONJ symptoms compared with continuing the drug throughout jaw treatment. Patients should be counseled that continuing their BP medication after an established MRONJ diagnosis (compared to stopping the BP at diagnosis) may delay resolution of maxillofacial symptoms by approximately 6 months.

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Resolution of Bisphosphonate-Associated Osteonecrosis of the Mandible: Possible Application for Intermittent Low-Dose Parathyroid Hormone [rhPTH(1-34)]

Richard P. Harper, DDS, PhD, FRCD(C), * and Eugene Fung, MD, FRCP(C)†

Intermittent, low-dose rhPTH(1-34) is anabolic with respect to bone. This hormone has proven effective in the treatment of osteoporosis and may be a valuable therapeutic in the treatment of bisphosphonate associated osteonecrosis of the mandible or maxilla.
though we are optimistic about the favorable early response of the HBO group, we believe that the use of HBO as the sole treatment for BRONJ is not indicated and that it should only be used as an adjunct to surgery. It is too early in the ongoing

**FIGURE 11.** Patient 3 in hyperbaric chamber.
The Role of Surgical Resection in the Management of Bisphosphonate-Related Osteonecrosis of the Jaws

Eric R. Carlson, DMD, MD,* and John D. Basile, DMD†
FIGURE 2. Left facial swelling (A) and a nonhealing wound of the left face and oral mucosa (B, C) in a 65-year-old man treated with Zometa related to his diagnosis of multiple myeloma. He had undergone removal of teeth in the left mandible 20 months after the initiation of Zometa therapy. D. The panoramic radiograph shows the destructive nature of his Zometa-related osteonecrosis of the left mandible with periosteally derived bone formation. E, F, Computed tomograms confirm the presence of advanced disease. (Figure 2 continued on next page.)

FIGURE 2 (cont’d). G. The patient was treated with a disarticulation segmental resection of the left mandible for the diagnosis of stage III M. H, I. Acceptable skin and mucosal healing is appreciated at 1 year postoperatively.
FIGURE 3. A, A nonhealing wound of the right maxilla of 6 months’ duration in a patient who underwent full mouth extraction 38 months earlier. He had undergone this extraction before the initiation of Zometa therapy and subsequently underwent maxillary denture fabrication. A diagnosis of stage II B RONJ was made, presumably resulting from trauma from the denture. B, Preoperative computed tomograms identified the extent of his osteonecrosis. C, D, The patient underwent partial maxillectomy with a 2-layer closure involving a buccal fat flap. E, He was noted to have maintained full mucosal coverage of the maxillary defect at 1 year postoperatively. F, The panoramic radiograph at 1 year postoperatively shows smooth margins of the maxillectomy defect.
Figure 1. A. Obvious exposed, necrotic bone in the right mandible in a patient previously treated with Fosamax who underwent multiple extractions after the initiation of Fosamax. B. The extent of the necrotic bone is appreciated on the panoramic radiograph, which also identifies a nonunion of the mandible. C. Computed tomography scans identify disease appearing to extend across the midline. D, E. Because of the presence of limited disease (stage I) in a nonunion of the mandible, a marginal resection of the right mandible was performed. F. The remaining mandible is noted to be bleeding favorably at the conclusion of the marginal resection. (Figure 1 continued on next page.)
Pedicled Buccal Fat Pad Flap as a Reliable Surgical Strategy for the Treatment of Medication-Related Osteonecrosis of the Jaw

Horatiu Rotaru, MD, DDS, PhD, * Min-Keun Kim, DDS, † Seong-Gon Kim, DDS, PhD, ‡ and Young-Wook Park, DDS, PhD

Purpose: The purpose of this study was to evaluate the coverage of the pedicled buccal fat pad flap (PBFP) and the long-term results of this treatment in patients with medication-related osteonecrosis of the jaw (MRONJ).

Patients and Methods: Ten patients (2 men and 8 women; average age, 72.9 yr old) diagnosed with MRONJ were selected. Patients were treated with a PBFP. Data from patients regarding MRONJ stage, defect size, bone exposure after surgery, operation time, admission period, duration of antibiotic therapy, recurrence of disease, and postoperative complications were analyzed retrospectively.

Results: Six patients were diagnosed with MRONJ stage 2, and 4 patients were diagnosed with MRONJ stage 3. The maximum defect in the study was 62 × 18 mm. Among the 10 patients, there was only 1 bony exposure, which occurred on postoperative day 2 after receiving the PBFP. This exposure might have been due to an incomplete resection of the affected bone. There were no severe donor site morbidities, and all patients showed satisfactory healing without incident.

Conclusions: According to this evaluation, the PBFP effectively covered a relatively large surgical defect. Complications were minimal, and there was no recurrence of bony exposure during follow-up. In conclusion, using the PBFP was a reliable treatment option for the management of denuded bone in patients with MRONJ.

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Exposure

age, 5.1 million patients over the age of 55 years received a prescription for a bisphosphonate in year 2008. A recent federal study estimated that the prevalence of BP exposure was 7 for every 100 US population receiving a prescription for a bisphosphonate in the outpatient setting for the treatment
Safety of Long-Term Bisphosphonate Therapy

Conclusion

In summary, osteoporosis is a serious condition that often leads to fractures, especially of the hip. Bisphosphonates are effective in reducing the incidence of hip fractures. However, since their introduction and subsequent widespread, long-term use, a number of less common, potentially serious adverse effects have been noted. This has raised questions regarding the optimal duration of use. It appears that bisphosphonate therapy can be safely discontinued after a number of years in some patients, but the appropriate patient population for discontinuation and optimal duration of therapy remains to be determined.

Esophageal Cancer and Bisphosphonates

Oral bisphosphonates can cause esophageal irritation and injury. Risk is reduced if patients drink water and remain upright after administration. Case reports of esophageal cancer after bisphosphonate use triggered additional study of cancer risk.37,39
Bisphosphonate drug holiday: who, when and how long

Dima L. Diab and Nelson B. Watts

Abstract: Bisphosphonates have been widely used in the treatment of osteoporosis with robust data from numerous placebo-controlled trials demonstrating efficacy in fracture risk reduction over 3–5 years of treatment. Although bisphosphonates are generally safe and well tolerated, concerns have emerged about adverse effects related to long-term use. For most patients with osteoporosis, the benefits of treatment outweigh the risks. Because these agents accumulate in bone with some persistent antifracture efficacy after therapy is stopped, it is reasonable to consider a ‘drug holiday.’ There is considerable controversy regarding the optimal duration of therapy and the length of the holiday, both of which should be based on individual assessments of risk and benefit.

Keywords: bisphosphonates, drug holidays, fractures, osteoporosis
DRUG HOLIDAYS IN THE TREATMENT OF OSTEOPOROSIS

For patients at fairly low risk of fracture, treatment can be stopped after 3-5 years. The drug holiday can be continued until there is significant loss of bone density or the patient has a fracture, whichever comes first.

For patients at moderate risk of fracture, bisphosphonate therapy can be stopped after about five years, and the drug holiday can be offered for 3-5 years or until there is significant loss of bone density or the patient has a fracture, whichever comes first.

For patients at high risk of fracture, bisphosphonate therapy should be continued for up to 10 years and a drug holiday can be offered for 1-2 years or until there is significant loss of bone density or the patient has a fracture, whichever comes first. A non-bisphosphonate treatment (e.g. raloxifene, teriparatide) may be offered during the holiday from the bisphosphonate.
Drug Holidays in the Treatment of Osteoporosis

These recommendations are based on a study with alendronate (Fosamax®) that recruited women who had five years of treatment in an earlier trial and signed them up for a second five-year study in which some were continued on treatment and others came off but were changed to placebo. In the second five-year period, for women who did not have osteoporosis initially or whose bone density increased out of the “osteoporosis” category, stopping treatment was not associated with an increased risk of fracture. However, for women whose hip T-score was consistent with osteoporosis at the start of the second five-year period (T-score -2.5 or below), fractures were twice as common in those who stopped after five years compared with those who continued treatment for 10 years.
Continuing Bisphosphonate Treatment for Osteoporosis — For Whom and for How Long?

Dennis M. Black, Ph.D., Douglas C. Bauer, M.D., Ann V. Schwartz, Ph.D., M.P.H., Steven R. Cummings, M.D., and Clifford J. Rosen, M.D.
Conclusions

- Benefits of therapy far outweigh risk of exposed bone or ONJ

- Prevention, clinician communication, and patient education are mandatory

- Conservative management…until ‘bigger' surgery is needed

- How long is long enough?
Outline

- Antiresorptive Medications
- BRONJ—BIONJ—ARONJ—MRONJ
- Pathophysiology
- Risk Factors
- Management Strategies
- Staging
- Discussion
- Conclusions
Follow-Up: The Faculty Practice

Former Employee Health Site near previous Health Center entrance at Wilmington Hospital
Opened in April 2012 for all patients (including CCHS employees)

Oral and Facial Surgery Center
Faculty Practice
2W44
302-320-5730
Wilmington Hospital Campus
Christiana Care Health System
Objectives

1/OMFS at CCHS

2/Practical Review of MRONJ
References

- AAOMS Position Paper on BRONJ. 2009
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