Issues that Perplex Us: Atypical Femur Fractures
What to do in Clinical Practice

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Disclosures

Industry:
• Amgen, Ipsen, Regeneron (grants to institution for research studies and/or honoraria)

Non-industry:
• International Society of Clinical Densitometry – 2019 Position Development Conference task force member (in charge of AFF guidelines); Canadian Panel Chair
• ASBMR International Task Force on AFF, member
• Endocrine Society – clinical practice guideline committee member
• Osteoporosis Canada – clinical practice guideline committee member
Learning Objectives

At the end of the session, participants will be able to:
1) Identify an atypical femur fracture
2) Discuss risk of developing atypical femur fracture
3) Manage patients with atypical femur fractures
IDENTIFY AFF

ATYPICAL FEMUR FRACTURE
Atypical femur fractures (AFF)

- low-trauma stress fractures
- in subtrochanteric or shaft region of the femur
- specific radiographic findings
- associated with bisphosphonates and denosumab therapy
Hip Fractures

- Subcapital neck fracture
- Transcervical neck fracture
- Intertrochanteric fracture
- Subtrochanteric fracture
- Fracture of the greater trochanter
- Fracture of the lesser trochanter
Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Report of a Task Force of the American Society for Bone and Mineral Research

Elizabeth Shane, David Burr, Bo Abrahamsen, Robert A Adler, Thomas D Brown, Angela M Cheung, Felicia Cosman, Jeffrey R Curtis, Richard Dell, David Dempster, Thomas A Einhorn, Harry K Genant, Piet Geusens, Klaus Klaushofer, Kenneth Koval, Joseph M Lane, Fergus McKiernan, Ross McKinney, Alvin Ng, Jeri Nieves, Regis O’Keefe, Socrates Papapoulos, Howe Tet Sen, Marjolein CH van der Meulen, Robert S Weinstein, and Michael Whyte


Elizabeth Shane, David Burr, Bo Abrahamsen, Robert A Adler, Thomas D Brown, Angela M Cheung, Felicia Cosman, Jeffrey R Curtis, Richard Dell, David W Dempster, Peter R Ebeling, Thomas A Einhorn, Harry K Genant, Piet Geusens, Klaus Klaushofer, Joseph M Lane, Fergus McKiernan, Ross McKinney, Alvin Ng, Jeri Nieves, Regis O’Keefe, Socrates Papapoulos, Tet Sen Howe, Marjolein CH van der Meulen, Robert S Weinstein, and Michael P Whyte
AFF: ASBMR Case Definition 2013

• Major features (4 out of 5 criteria):
  1. Below lesser trochanter, above supracondylar flare
  2. Little or no trauma
  3. Transverse (or mostly transverse) or short oblique configuration
  4. Non-comminuted (or minimally comminuted)
  5. Complete fractures extend through both cortices and may have a medial spike; Incomplete fractures involve only the lateral cortex
  6. Localized periosteal or endosteal reaction of the lateral cortex

• Minor features (none required):
  1. Generalized increase in cortical thickness
  2. Delayed healing
  3. Prodromal symptoms such as dull aching pain in groin or thigh
  4. Bilateral fractures and symptoms
Imaging
2013 (2014) ASBMR Case Definition for Incomplete AFF

• Major features (4 out of 5 criteria):
  1. Below lesser trochanter, above supracondylar flare
  2. Little or no trauma
  3. Transverse (mostly) or short oblique configuration
  4. Non-comminuted (minimally)
  5. Complete fractures extend through both cortices and may have a medial spike; Incomplete fractures involve only the lateral cortex

• Minor features (none required):
  1. Generalized increase in cortical thickness
  2. Delayed healing
  3. Prodromal symptoms such as dull aching pain in groin or thigh
  4. Bilateral fractures and symptoms

- Lucent line on X-rays or CT or uptake on bone scan
Imaging using other modalities

Plain X-rays

Bone Scan

MRI

DXA
International Society for Clinical Densitometry 2019 PDC – Detection of AFF

1) Full-length Femur Imaging (FFI) for detection of AFF

2) Reporting physicians to comment on presence or absence of abnormalities in the spectrum of AFFs for all hip and femur scans

3) Consider bilateral FFI in patients who have had 3 or more years of potent antiresorptive therapy, especially in those on long term glucocorticoid therapy

Cheung AM et al; JCD 2019; 22 (4): 506-516
Which of these is an incomplete AFF?

1.) Patient D

2.) Patient E

3.) Patient F
Fig. 2. Densitometer-based full-length femur imaging (FFI). (a) Single-energy scan showing beaking (arrows). (b) Dual-energy scan showing focal cortical periosteal and endosteal reactions at the lateral cortex (arrow; image: courtesy of Diane Krueger). (c) Image from densitometer-based full-length femur imaging (FFI).
RISK

ATYPICAL FEMUR FRACTURE
Trends in Incidence of Subtrochanteric Fragility Fractures and Bisphosphonate Use Among the US Elderly, 1996–2007

Zhong Wang and Timothy Bhattacharyya

Intramural Research Program, National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA
Trends in Incidence of Subtrochanteric Fragility Fractures and Bisphosphonate Use Among the US Elderly, 1996–2007

Zhong Wang and Timothy Bhattacharyya
Intramural Research Program, National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA
“In the context of declining typical hip fractures among the US elderly, we observed small but significant increases in the incidence of subtrochanteric fragility fractures”

“we estimated that for every 100 or so reduction in typical femoral neck or intertrochanteric fractures, there was an increase of one subtrochanteric fragility fracture.”
Incidence of Complete AFFs

Ontario CANADA Data

~1-2/1000 py after 6 - 7 years

Kaiser Permanente California Data

~1/1000 py after 8 - 9.9 years
Risk Factors for AFFs

• Younger women
• Osteopenic (can vary)
• Asian race
• Long duration of BP therapy
• Multiple anti-resorptive medications
• Glucocorticoid use
• Rheumatoid arthritis
• Varus hip angle, bow-leg deformity, small diameter
Risk Factors for AFFs

A  AFFs According to Age

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Incidence Rate (per 10,000 person-yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–64</td>
<td>0.8 (AFF=37)</td>
</tr>
<tr>
<td>65–74</td>
<td>2.2 (AFF=124)</td>
</tr>
<tr>
<td>75–84</td>
<td>2.4 (AFF=99)</td>
</tr>
<tr>
<td>≥85</td>
<td>1.0 (AFF=17)</td>
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</table>

B  AFFs According to Race or Ethnic Group

<table>
<thead>
<tr>
<th>Race</th>
<th>Incidence Rate (per 10,000 person-yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>6.0 (AFF=132)</td>
</tr>
<tr>
<td>Black</td>
<td>0.2 (AFF=94)</td>
</tr>
<tr>
<td>White</td>
<td>1.1 (AFF=46)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.2 (AFF=3)</td>
</tr>
<tr>
<td>Other or Unknown</td>
<td>0.9 (AFF=3)</td>
</tr>
</tbody>
</table>
Risk Factors for AFFs

**C** AFFs According to Cumulative Bisphosphonate Exposure

<table>
<thead>
<tr>
<th>Years of Bisphosphonate Use</th>
<th>Incidence Rate (per 10,000 person-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25</td>
<td>0.1 (AFF=4)</td>
</tr>
<tr>
<td>0.25 to &lt;3</td>
<td>0.6 (AFF=35)</td>
</tr>
<tr>
<td>3 to &lt;5</td>
<td>2.5 (AFF=90)</td>
</tr>
<tr>
<td>5 to &lt;8</td>
<td>6.0 (AFF=93)</td>
</tr>
<tr>
<td>≥8</td>
<td>13.1 (AFF=95)</td>
</tr>
</tbody>
</table>

**D** AFFs According to Time since Bisphosphonate Discontinuation

<table>
<thead>
<tr>
<th>Months since Discontinuation of Bisphosphonate</th>
<th>Incidence Rate (per 10,000 person-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not yet used</td>
<td>0 (AFF=1)</td>
</tr>
<tr>
<td>≤3</td>
<td>4.5 (AFF=200)</td>
</tr>
<tr>
<td>&gt;3 to 15</td>
<td>1.8 (AFF=46)</td>
</tr>
<tr>
<td>&gt;15 to 48</td>
<td>0.6 (AFF=18)</td>
</tr>
<tr>
<td>&gt;48</td>
<td>0.5 (AFF=12)</td>
</tr>
</tbody>
</table>
Pathogenetic Mechanisms

• Effect of suppression of bone remodeling on:
  • Bone’s material properties – collagen, AGEs, increased tissue mineral density etc.
  • Healing of stress fractures

• Relationship of hip and lower limb geometry

• Genetic susceptibility – collagen abnormality, low bone turnover at baseline, etc...
Defect in osteoclast function
Pycnodysostosis: CTSK gene
Osteopetrosis: TCFR51,
OSTM1, PLEKHM1, SNZ210,
TNFS11, TNFRSF11A, CAII,
CLCN7 genes

Defect in mevalonate pathway
GGP51 gene

Defect in osteoclast function
Bone remodeling unit
Bone matrix

Defect in osteocyte function
X-linked osteoporosis: PLS3 gene

Defect in collagen synthesis and structure
Osteogenesis imperfecta: COL1A1,
COL1A2, CRTAP, LEPR1, PP1B, SERPINH1,
FKBP10, PLOD2, SP7 genes

Mineralization defect
Hypophosphatasia: ALPL gene
X-linked hypophosphatemia: PHEX gene

Defect in osteoblast function
Osteoporosis pseudoglioma syndrome: LRP5 gene
AFF: Key Clinical Feature

**ASBMR Task Force review**

- 75% have prodromal pain
  - These features are fundamentally different from common osteoporotic femur fractures and strongly suggest a distinct pathogenesis

**Ontario AFF Cohort (n~400)**

- ~80-85% have prodromal symptoms: pain, ache, weakness, loss of function
MANAGE PATIENTS

ATYPICAL FEMUR FRACTURE
Surgical Management: IMR

Complete AFF treated with lateral compression plate, with subsequent failure and ultimately treated with a Gamma nail.
Current ASBMR Task Force Recommendations

STOP
anti-resorptive therapy
(bisphosphonates and denosumab)

IMAGE
Contralateral femur
Kaiser Permanente Southern California Data

Incidence Rate (per 10,000 person-yrs)

- Not yet used: 0 (AFF=1)
- ≤3: 4.5 (AFF=200)
- >3 to 15: 1.8 (AFF=46)
- >15 to 48: 0.6 (AFF=18)
- >48: 0.5 (AFF=12)

Months since Discontinuation of Bisphosphonate

Black DM et al, NEJM, August 2020; 383 (8): 743-753
Current ASBMR Task Force Recommendations

FOR INCOMPLETE AFFs ➔
Consider prophylactic nailing
+/- teriparatid

>>Decrease weight-bearing (treat like a stress fracture)
IMPLICATIONS FOR YOUR OSTEOPOROSIS PRACTICE

ATYPICAL FEMUR FRACTURE
POINTS to consider:

• Fractures are common

• Bisphosphonates, denosumab, teriparatide, romosozumab are all effective therapies

• Use a sequential combination of anabolic and antiresorptive therapy

• Adverse effects (such as MVFx, AFF, ONJ) are rare
Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline

Richard Eastell, Clifford J Rosen, Dennis M Black, Angela M Cheung, M Hassan Murad, Dolores Shoback


Published: 25 March 2019   Article history ▼
International Society for Clinical Densitometry
2019 PDC – Detection of AFF

1) Full-length Femur Imaging (FFI) for detection of AFF

2) Reporting physicians to comment on presence or absence of abnormalities in the spectrum of AFFs for all hip and femur scans

3) Consider bilateral FFI in patients who have had 3 or more years of potent antiresorptive therapy, especially in those on long term glucocorticoid therapy
How do we communicate the real risk to patients?

1. Low:
   - Complete AFFs – ~1/1000 patient years after 6-10 years
   - Incomplete AFFs -- ? ~1/100

2. Drug treatment according to fracture risk – benefit/risk ratio

3. Reassess drug therapies after 3-5 years, consider drug holiday for stable moderate (and ? high) risk patients
Special Considerations for Asians

**AFFs and Hip Fractures According to Race or Ethnic Group**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>AFFs Incidence Rate (per 10,000 person-yr)</th>
<th>Hip Fractures Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>6.0 (N=132)</td>
<td>81.2 (N=6712)</td>
</tr>
<tr>
<td>Black</td>
<td>0.2 (N=2)</td>
<td>1.1 (N=94)</td>
</tr>
<tr>
<td>White</td>
<td>20.4 (N=387)</td>
<td>39.7 (N=387)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.2 (N=46)</td>
<td>39.3 (N=1451)</td>
</tr>
<tr>
<td>Other or Unknown</td>
<td>0.9 (N=3)</td>
<td>32.7 (N=103)</td>
</tr>
</tbody>
</table>

Black DM et al, NEJM, August 2020; 383 (8): 744-753
Important Points

1. AFFs are rare (but incomplete AFFs may be more common)

2. Patients at high risk for osteoporotic fracture should be treated

3. Stop potent antiresorptive therapies for patients with AFFs

4. Consider bisphosphonate drug holidays for those who have been on potent bisphosphonates after 3-5 years, especially those who are not at high risk for fractures.
If your patient has an AFF:

1. stop potent antiresorptive therapy
2. decrease weight bearing activities
3. consider bone formation therapies if patients need therapies to prevent osteoporotic fractures
Summary

1) Identify an atypical femur fracture
2) Discuss risk of developing atypical femur fracture
3) Manage patients with atypical femur fractures
4) Implications for your practice in Osteoporosis
Thank you!

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Visit: osteoconnections.com

Facebook/OsteoporosisUHN

Twitter/OsteoUHN; Twitter/AngelaMCheung
Other imaging modalities

- X ray
- CT scan
- Bone scan
ISCD 2019 PDC: Detection of iAFFs

1. Can DXA systems detect iAFFs or abnormalities in the spectrum of AFF?

2. What densitometer-based test should be used for the detection of abnormalities in the spectrum of AFF, and how should it be analyzed, interpreted and reported?

3. In which patient population should densitometer based full length femur imaging (FFI) be used to screen for abnormalities in the spectrum of AFF?
ISCD 2019 PDC: Detection of iAFFs

1. Can DXA systems detect iAFFs or abnormalities in the spectrum of AFF? **YES**

2. What densitometer-based test should be used for the detection of abnormalities in the spectrum of AFF, and how should it be analyzed, interpreted and reported? **FFI**

3. In which patient population should densitometer based full length femur imaging (FFI) be used to screen for abnormalities in the spectrum of AFF?
ISCD Official position 2: (i.e. how should we screen? How should we report?)

- If the purpose is to detect abnormalities in the spectrum of AFF, then full length femur imaging (FFI) is recommended over both default-length femur imaging and extended-length femur imaging.

1. Can DXA systems detect iAFFs or abnormalities in the spectrum of AFF? **YES**

2. What densitometer-based test should be used for the detection of abnormalities in the spectrum of AFF, and how should it be analyzed, interpreted and reported? **FFI**

3. In which patient population should densitometer based full length femur imaging (FFI) be used to screen for abnormalities in the spectrum of AFF?

   Consider those on >3 yrs of potent anti-resorptive therapy, especially those on glucocorticoid therapy

Management of osteoporosis care of patients who need dental surgery. Considerations related to ONJ

Arthur C. Santora II, MD, PhD

Clinical Associate Professor of Medicine
Division of Endocrinology, Metabolism and Nutrition
Rutgers Robert Wood Johnson Medical School
Disclosures

Merck & Co. Inc.
• Former employee – Stock, pension

Entera Bio, Ltd.
• Chief Medical Officer / Consultant

Myovant Sciences
• Consultant

CSR Pharma Group Inc.
• Consultant
Objectives

Review

• Cased definition of Osteonecrosis of the Jaw (ONJ)
• Epidemiology of ONJ
  • Association of drugs that inhibit osteoclasts with ONJ
• Mechanism of action and pharmacokinetics of bisphosphonates and denosumab

ONJ risk management in osteoporosis patients

• Prior to starting treatment
• During long-term treatment
• Prior to an elective dental procedure
Case Definition of Osteonecrosis of the Jaw (ONJ)

- **ONJ** is defined as an area of exposed bone in the oral cavity that does not heal within 8 wk following identification by a healthcare provider in a patient who has not had radiation therapy in the craniofacial region or evidence of local malignancy.¹

- **AR**(antiresorptive-related)**ONJ** is defined as ONJ in a patient who has been receiving or has been exposed to a bisphosphonate or denosumab.¹

- **MR**(medication-related)**ONJ** is defined as ONJ in a patient who has been receiving or has been exposed to a bisphosphonate, denosumab or antiangiogenic therapy.¹,²

- **MRONJ, ARONJ and ONJ** often used interchangeably, and another name (e.g., osteomyelitis osteonecrosis) used to describe ONJ when there is no history of medication use)


Staging Antiresorptive-related ONJ

• Patients with **Stage 1** disease have exposed bone and are asymptomatic with no evidence of significant adjacent or regional soft tissue inflammation or infection.\(^1\)

• **Stage 2** disease is characterized by exposed bone with associated pain, adjacent or regional soft tissue inflammatory swelling, or secondary infection.\(^1\) (\(^2\)° is an assumption)

• **Stage 3** disease is characterized by exposed bone associated with pain, adjacent or regional soft tissue inflammatory swelling, or secondary infection, **in addition to** a pathologic fracture, an extraoral fistula or oral-antral fistula, or radiographic evidence of osteolysis extending to the inferior border of the mandible or the floor of the maxillary sinus.\(^1\)

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ONJ Incidence and Pathophysiology

Incidence

- Cancer: 1% to 2% / person-year (zoledronic acid and denosumab) 5- to 10-fold higher in combination with antiangiogenic agents

- Osteoporosis: 0.15% to < 0.001% / person-years of exposure

“The pathophysiology of ONJ is not well understood.”

- Case definition requires both bone necrosis and delayed healing
- Trauma (e.g., tooth extraction, dentures) and Infection may cause necrosis
- Neither bisphosphonates nor denosumab are established direct causes of bone necrosis
- Active osteoclasts are required for sequestration and sloughing of necrotic bone in the jaw

Risk Factors for ONJ in Patients with Osteoporosis

Tooth Extraction
Poor dental health
• Lack of routine care by a dentist
• Caries requiring extraction
• Periodontitis
• Chronic infection of bone
• Ill-fitting dentures
• Sjogren’s and other causes of decreased saliva
Tori / Exostoses - thin mucosa overlying periosteum
Smoking
Diabetes
Glucocorticoids – Infection and AVN
Factor V Leiden and other causes of thrombosis

Dental Implants may lead to diagnosis but may not be causal

Bisphosphonate Kinetics

Enteral Absorption, Intravenous Infusion

Non-Bone ECF

Plasma

Half-life is 1-2 hr

Urine

Terminal Elimination
Half-life is 10.9 yr

Bone Compartment

Bone Surface

Half-life is 3-5 wk

Bone ECF

Bone Matrix

Half-life is 5 yr

ECF

NOF 2021 Interdisciplinary Symposium on Osteoporosis (ISO2021)
Absorbed alendronate is rapidly cleared from blood ($T_{\frac{1}{2}} = 1-2$ hr)
- 50% rapidly excreted in urine
- No soft tissue accumulation
- 50% on bone surfaces concentrated under osteoclasts
- Only alendronate on bone surfaces under osteoclasts is pharmacologically active

Estimated $T_{\frac{1}{2}}$ on the surface of bone is 2 to 5 weeks
- Alendronate on the surface of bone is either
  - Slowly released into blood, or
  - Trapped ($\approx 65\%$ that initially distributed to bone) within newly formed bone where it is not pharmacologically active

Why are Drug Holidays Possible After Long-Term Bisphosphonate use?

• After treatment is interrupted, no “new” bisphosphonate is delivered to bone surfaces

• Bisphosphonate retained in bone that formed during prior dosing will be “recycled” and released after treatment is discontinued

• The amount of recycled drug is a function of previous daily/weekly dose and years of treatment

• Recycled bisphosphonate will prevent or at least slow post-treatment bone loss for months to years post treatment.
Estimated Bone Accumulation of Alendronate During Long-term Administration

Terminal Elimination $T_{1/2} = 12$ years
Oral Dose = 70 mg/wk
Bone Remodeling Changes after Discontinuation of Long-Term Bisphosphonate Treatment

• **Mathematical modeling** of alendronate release from bone suggests that the amount released will be insufficient to fully prevent bone loss if discontinued after 5 to 10 years
  
  • After 5 years of treatment with alendronate 70 mg weekly, the amount released from bone each week is approx. the same as that absorbed after a **12.8 mg weekly** dose
  
  • After 10 years of treatment with alendronate 70 mg weekly, the amount released from bone each week is approx. the same as that absorbed after a **17.5 mg weekly** dose

• **Clinical studies** of effects of discontinuation of long-term oral alendronate treatment on biochemical markers of bone remodeling and BMD have confirmed this prediction

Langdahl et al. J Bone Min Res 2012; 27: S120  
Black et al. JAMA. 2006; 296: 2927-38
Bone Resorption Increases Quickly After Long-Term Treatment is Discontinued

Patients Previously Treated with Bisphosphonates for ~5 Years

Urine NTx

Mean % Change from Baseline

Placebo

Alendronate 70 mg Weekly

Urine NTx = Urine N-Telopeptides of type 1 collagen to creatinine ratio (bone resorption marker). The figure represents the LS Geometric Mean ± SE.
Prior use of bisphosphonates: mean 6.0 years, median 5.2 years.

Presented at ASBMR Meeting in October 2012 Plenary Poster 0377
Langdahl et al. J Bone Min Res 2012; 27: S120
Bone Formation Increases After Long-Term Treatment is Discontinued

Patients Previously Treated with Bisphosphonates for ~5 Years

Serum N-Terminal Propeptide (P1NP)

P1NP = Serum N-Terminal Propeptide of Type 1 Collagen (bone formation marker)
The figure represents the LS Geometric Mean ± SE.
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Denosumab PK and PD

FIG. 1. Changes in a second morning void urinary NTX/creatinine (nmol BCE/mmol creatinine) over time. Mean and SE

FIG. 2. The serum concentration profile of AMG 162 (ng/ml) over time. Data are presented as mean and SE

ONJ Risk Management in Osteoporosis Patients
Prior to starting treatment ¹

Dental history and PE
- History of tooth extractions or periodontitis
- Missing or carious teeth
- Gum recession and/or inflammation

Current and prior dental care
- Personal oral hygiene
- Established relationship with a dentist with scheduled prophylaxis

Review ONJ as a potential risk with each patient and address modifiable risks (e.g., smoking)

Determine whether either dental extraction or implants are planned or needed
- Offer to communicate with your patient’s dentist/oral surgeon to coordinate dental and osteoporosis care
- Strongly consider delaying start of antiresorptive osteoporosis drugs until invasive dental procedures have been completed

Do not initiate antiresorptive osteoporosis drug therapy in a patient with an active dental abscess or osteitis/osteomyelitis until appropriately treated by a dentist/ oral surgeon. - long-term treatment with an appropriate antibiotic(s) often required

1. Personal “Expert Opinion” not experimentally validated
ONJ risk management in osteoporosis patients
During long-term treatment

• Review dental history and PE
• Confirm scheduled exams and prophylaxis by a dentist
• Determine whether either dental extraction or implants are planned
  • Offer to communicate with your patient’s dentist/oral surgeon to coordinate dental and osteoporosis care
• Review ONJ as a potential AE and discuss modifiable risk

1. Personal “Expert Opinion” not experimentally validated
ONJ risk management in osteoporosis patients
Prior to an elective dental procedure

Review dental history and PE
Determine what dental procedure(s) is/are planned
- Crowns and restorations with no bone trauma do not carry a risk of ONJ
- Some periodontal procedures are low-risk (patient’s periodontist should decide)

Dental Extractions and Implants
- Coordinate with dentist / oral surgeon
- Time procedure 6-months after prior denosumab dose and 9- to 12-months after prior zoledronic acid infusion
- Interrupt oral bisphosphonates 2 to 3 months prior to procedure
- Once dentist / oral surgeon confirms procedure site has healed, resume antiresorptive on schedule

Do not delay emergent dental procedures required to treat acute infections

1. Personal “Expert Opinion” not experimentally validated
ONJ Bibliography


