

RTI HEALTH SOLUTIONS®

New Directions in Using Cancer Registry Data: 5-Year Results From a Drug Safety Surveillance Study of Adult Osteosarcoma

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2009 NAACCR Meeting
San Diego, California
June 18, 2009

LEADING RESEARCH...
MEASURES THAT COUNT

What is RTI International?

Headquarters: Research Triangle Park, NC

- **Independent, not-for-profit research organization**
- **Established in 1958**
- **Over 2,500 researchers and support staff**
- **Government and commercial clients**
- **Extensive research in life and social sciences**



Background:

US Adult Osteosarcoma Surveillance Study

- In a preclinical rat toxicology study, Forteo caused a dose-dependent increase in the incidence of osteosarcoma.
- No such signal has been seen in clinical experience.
- FDA required a postapproval surveillance study as a condition of drug approval.
- At the time of initial marketing in 2002, this 10-year postmarketing study was initiated to better understand the long-term safety of Forteo.

Background: What is Forteo (teriparatide)?

- Forteo is a medication similar to the natural parathyroid hormone.
- Forteo stimulates formation of new bone and increase in bone mineral density and bone strength.
- Approved in 2002 in the United States (US).
- Used in men and postmenopausal women with osteoporosis who are at high risk for fractures.
- Forteo is injected daily for up to 2 years.

Study Objectives

- **Primary**

- Identify approximately 40% of newly diagnosed cases of osteosarcoma among men and women aged 40 years and older, starting 90 days after the first marketed use of the drug and for a duration of at least 10 years.
- Identify incident osteosarcoma cases, if any, who have a history of treatment with the drug of interest.

- **Secondary**

- Systematically collect, for descriptive epidemiologic purposes, additional patient information including demographics, other drug treatments, potential risk factor information, and comorbid conditions.

Study Design Overview

- **Study design**
 - Surveillance study initiated in 2002
- **Selection criteria**
 - Adults aged 40 years and older
 - Diagnosed with osteosarcoma (12 ICD-O-3 codes) or 5 other prespecified ICD-O-3 codes where the primary site equals bone
- **Case ascertainment:** cancer registries
- **Data collection modality:** telephone interview
- **Analysis:** compare observed exposure with expected exposure
- **Precision:** sufficient size to detect a tripling in risk by end of study

Data Collected

- **Data collected from cancer registries**
 - Date of diagnosis, cancer site, morphology, grade
 - Patient demographics
 - Age, sex, race, vital status
- **Data collected from patient (or proxy) interview**
 - Patient demographics
 - Age, sex, race
 - Drug exposure
 - Prior use of teriparatide
 - Known risk factors for osteosarcoma
 - Prior exposure to radiation, history of Paget's disease
 - Other possible risk factors for osteosarcoma
 - History of other cancers, prior injury or infection at tumor site, agricultural/occupational pesticide exposure, petrochemical exposure, family history of osteosarcoma

Progress in Meeting Study Objectives as of March 31, 2009

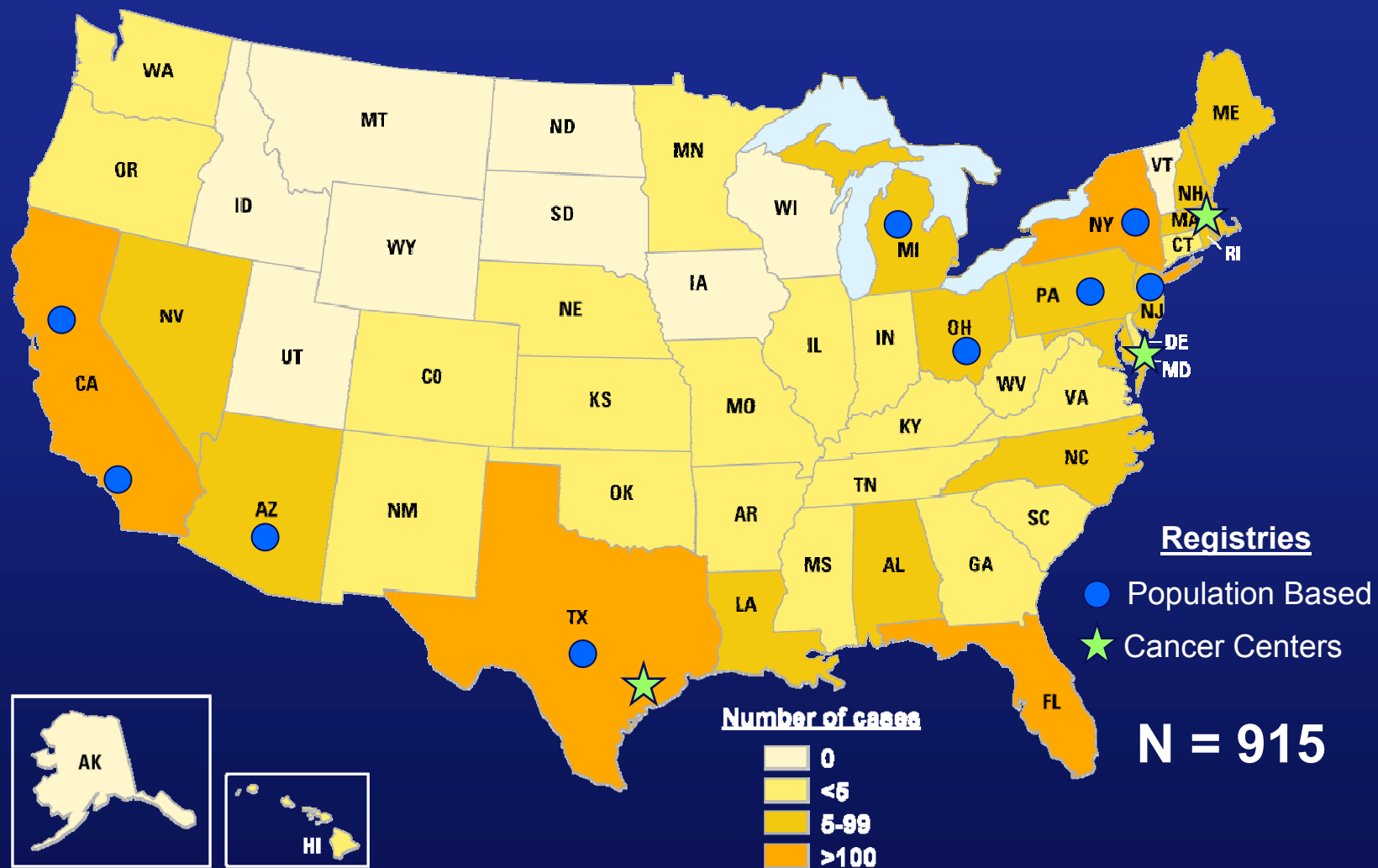
- **Primary objectives**

- No valid cases of teriparatide exposure have been reported
- 63% (n=915) of all 2003-2007 US cases identified
- 24% (n=346) of all 2003-2007 US cases interviewed

- **Secondary objective**

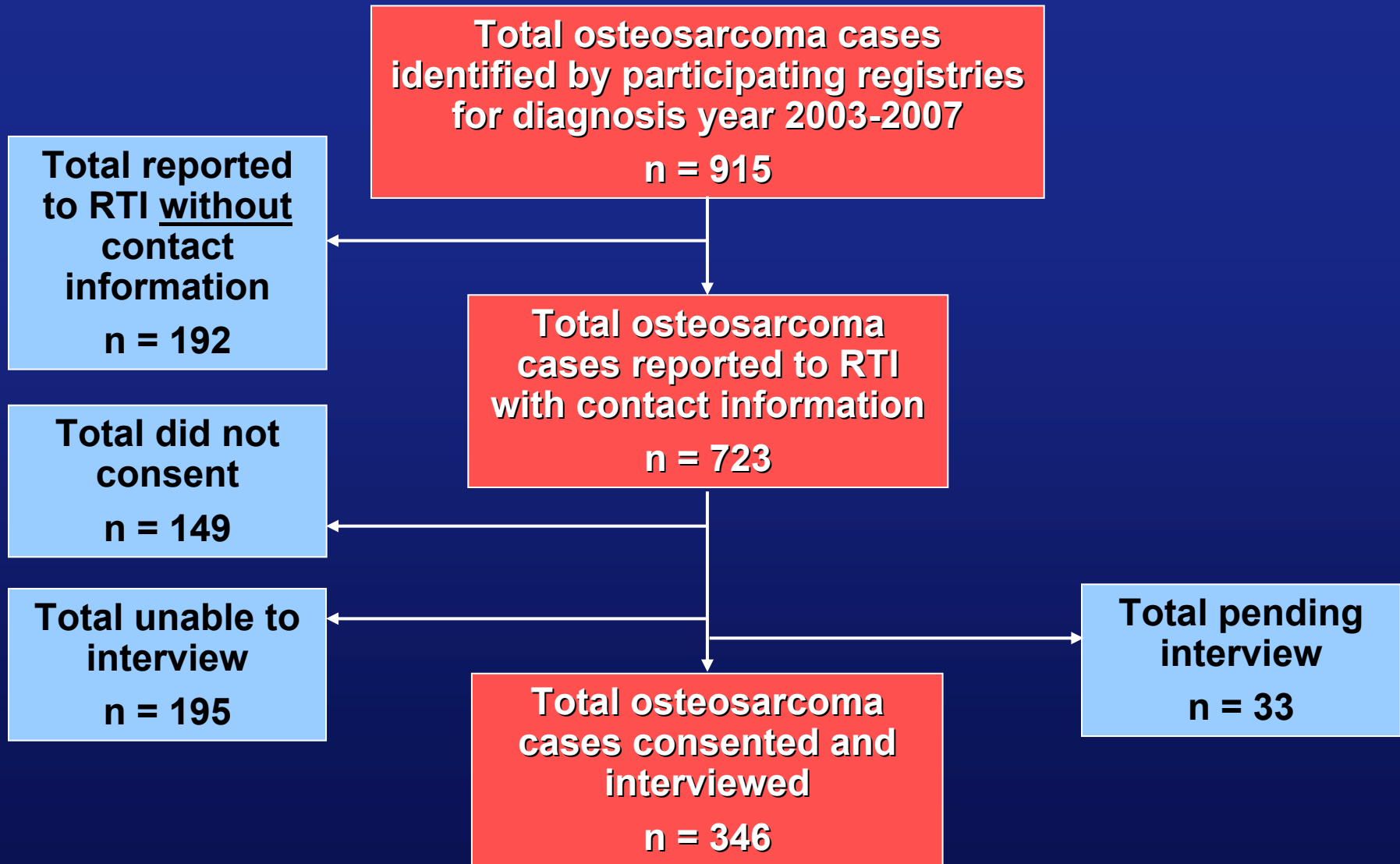
- Descriptive data on patient characteristics are available on 915 patients identified from registries
 - 346 patient or proxy interviews completed

Distribution of Osteosarcoma Cases Identified by Registries and Registry Sites



Data as of March 31, 2009

Osteosarcoma Results as of March 31, 2009



Reporting and Interviewing Status to Date

| Registries | ID'd 2003 - 2007 | % Reported Cases | # Interviewed | % Interviewed ^a |
|----------------------------|---------------------|---------------------|------------------|-------------------------------|
| Arizona Registry | 21 | 2% | 9 | 43% |
| CA Registry | 148 | 16% | 63 | 43% |
| LA SEER | 42 | 5% | 23 | 55% |
| Florida Registry | 119 | 13% | 37 | 31% |
| Harvard ^b | 47 | 5% | 19 | 40% |
| Johns Hopkins ^b | 3 | 0% | 1 | 33% |
| MI Registry | 75 | 8% | 24 | 32% |
| NC Registry | 40 | 4% | 23 | 58% |
| NJ Registry | 32 | 3% | 11 | 34% |
| NY Registry | 126 | 14% | 54 | 43% |
| Ohio Registry | 50 | 5% | 12 | 24% |
| PA Registry | 75 | 8% | 28 | 37% |
| MD Anderson ^b | 90 | 10% | 36 | 40% |
| Texas Registry | 47 | 5% | 6 | 13% |
| TOTAL | 915 | 13% | 346 | 38% |

^a Percentage interviewed (#Interviewed/#Identified); ^b Cancer center serves multiple states.

Distribution of Osteosarcoma ICD-O-3 Codes Among Identified Cases

| | Identified, N = 915 |
|--|---------------------|
| 9180 Osteosarcoma NOS | 68% |
| 9181 Chondroblastic osteosarcoma | 12% |
| 9182 Fibroblastic osteosarcoma | 9% |
| 9183 Telangiectatic osteosarcoma | 2% |
| 9184 Osteosarcoma in Paget's disease | 4% |
| 9192 Parosteal osteosarcoma | 3% |
| 9193 Periosteal osteosarcoma | 1% |
| 9185 Small cell osteosarcoma | 1% |
| 9186 Central osteosarcoma | < 1% |
| 9187 Intraosseous well-differentiated osteosarcoma | < 1% |
| 9194 High-grade surface osteosarcoma | < 1% |
| 9195 Intracortical osteosarcoma | 0% |

Data as of March 31, 2009

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Osteosarcoma Site Reported from Registries

Skull/face/mandible = 144

Rib/sternum/clavicle = 56

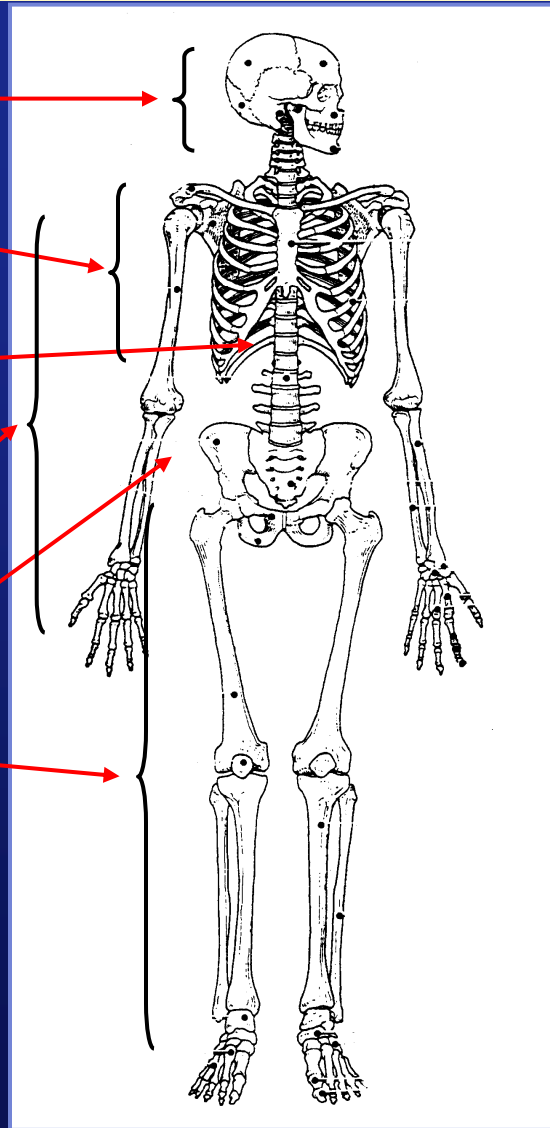
Vertebrae = 37

Scapula/hand/arm = 93

Pelvis/coccyx = 149

Leg bones = 268

Bones and joints,
site not specified = 39



Site not equal to bone = 129

Brain = 2
Sinuses = 4
Gum/salivary gland = 3
Larynx = 1
Bronchus/pleura = 3
Heart = 1
Breast = 22
Liver = 1
Large intestine = 1
Urinary bladder = 3
Genital/peritoneum = 5
Skin = 1
Connective tissue = 78
Site not specified = 4

N = 915

Comparison With SEER Data for Osteosarcoma Cases Where Site is Not Equal to Bone

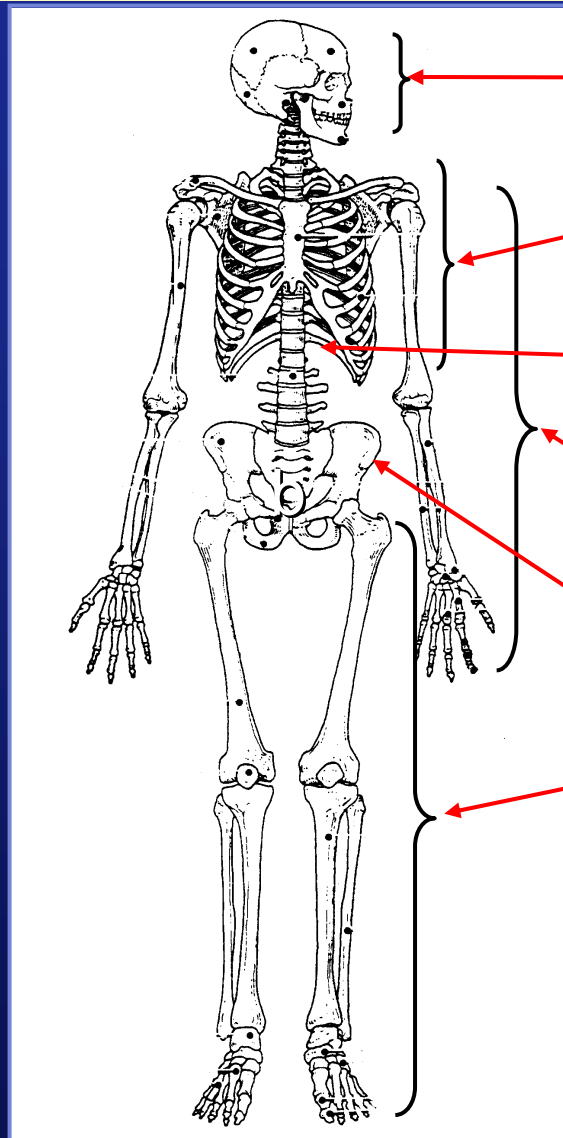
| Cancer Site | 1992-2003 SEER Osteosarcoma Cases n (%) | US Osteosarcoma Surveillance Study Cases n = 129 ^a n (%) |
|----------------------------|--|---|
| Brain | 0 (0) | 2 (0.22) |
| Breast | 15 (2.33) | 22 (2.40) |
| Bronchus | 3 (0.47) | 2 (0.22) |
| Genital & peritoneum | 5 (0.78) | 1 (0.11) |
| Gum | 2 (0.31) | 2 (0.22) |
| Heart | 1 (0.16) | 1 (0.11) |
| Larynx | 0 (0) | 1 (0.11) |
| Liver | 1 (0.16) | 1 (0.11) |
| Urinary bladder | 5 (0.78) | 3 (0.33) |
| Soft and connective tissue | 106 (16.43) | 78 (8.52) |

^a excludes 16 “other” sites where site is not equal to bone

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Other Bone Tumors Reported From Registries n = 342

| ICD-O-3 Codes | ID'd by Registries n (%) |
|---------------------------------|-----------------------------|
| Sarcoma NOS | 80 (23%) |
| Spindle cell sarcoma | 32 (9%) |
| Fibrosarcoma | 26 (8%) |
| Malignant fibrous histiocytoma | 91 (27%) |
| Dedifferentiated chondrosarcoma | 113 (33%) |



Skull/face/mandible = 20

Rib/sternum/clavicle = 26

Vertebrae = 19

Scapula/hand/arm = 51

Pelvis/coccyx = 78

Leg bones = 134

Bones and joints,
site not specified = 15

Results

Osteosarcoma Cases Interviewed (n = 346)

- **Demographics**

- Average age: 60 years, range 40 to 93 years
- Sex: 53% male
- Race: 83% white
- Vital status: 22% deceased

- **Distribution of known risk factors (self-report or proxy)**

- 69 (20%) exposure to radiation
- 22 (6%) history of Paget's disease

Results, Continued

Osteosarcoma Cases Interviewed (n = 346)

- **Distribution of possible risk factors (self-report or proxy)**
 - 90 (26%) history of other cancers
 - 69 (20%) previous injury or infection at tumor site
 - 94 (28%) agricultural/occupational pesticide exposure
 - 47 (14%) occupational petrochemical exposure
 - 20 (6%) family history of osteosarcoma

Tumor Site vs. Radiation Site

| | Tumor sites reported from registries | Site of radiation reported during interview |
|------------------------------|--------------------------------------|---|
| Matched Cases (n = 55/69) | Skull/face/mandible (n = 15) | Head/neck |
| | Sternum/clavicle (n = 3) | Head/neck |
| | Ribs/sternum/clavicle (n = 6) | Chest/breast |
| | Breast | Chest/breast |
| | Scapula/hand/arm (n = 3) | Shoulder/arm/hand |
| | Scapula/Hand/ arm bones | Chest/breast |
| | Vertebrae | Head/neck |
| | Vertebrae | Lung |
| | Vertebrae (n = 2) | Abdomen/pelvis |
| | Pelvis/sacrum/coccyx (n = 8) | Abdomen/pelvis/prostate |
| | Leg bones (n = 3) | Rectum/pelvis/prostate |
| | Leg bones (n = 3) | Knee |
| | Connective & soft tissue (n = 4) | Groin/prostate |
| | Connective & soft tissue (n = 4) | Chest/breast/shoulder/axilla |

Tumor Site vs. Radiation Site

| | Tumor sites reported from registries | Site of radiation reported during interview |
|-------------------------------------|---|---|
| Unmatched Cases (n = 12/69) | Skull/face/mandible | Lung |
| | Ribs/sternum/clavicle | Pelvis |
| | Scapula/arm/hand (n = 2) | Pelvis/prostate |
| | Scapula/arm/hand | Spine |
| | Pelvis/sacrum/coccyx (n = 2) | Head/neck |
| | Leg bones | Head/neck |
| | Leg bones | Chest/breast |
| | Connective & soft tissue (n = 2, finger, hip) | Chest/breast |
| | Connective & soft tissue (groin) | Head/neck |
| Unable to Match Cases (n = 2/69) | Bones & joints NOS | Head/neck |
| | Leg bones | No recorded response |

Summary

- There have been no reports of teriparatide exposure
- Osteosarcoma NOS was the most common tumor type, followed by chondroblastic osteosarcoma and fibroblastic osteosarcoma
- Most common tumor sites were the leg bones, followed by the pelvis/coccyx and the skull/face/mandible
- 129 (14%) of the osteosarcomas occurred in a site other than bone, consistent with SEER data

Summary, Continued

- **We observed a link between radiation site and tumor site, consistent with prior research**
- **One out of five patients reported prior injury or infection at the site of the tumor, warranting consideration in future studies**

Thank You!

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