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Using Cancer Registry Data to Advance the Science of Drug Safety: Results from an Ongoing Postmarketing Drug Safety Surveillance Study of Adult Osteosarcoma

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LEADING RESEARCH…
MEASURES THAT COUNT

Objectives of Presentation

- **Provide brief introduction to drug safety methods**

- **Present one example of how cancer registry data are being used in drug safety and descriptive results from this ongoing study**

- **Demonstrate value of cancer registry data in augmenting traditional safety surveillance approaches**

Methods to Characterize the Risk of Adverse Events
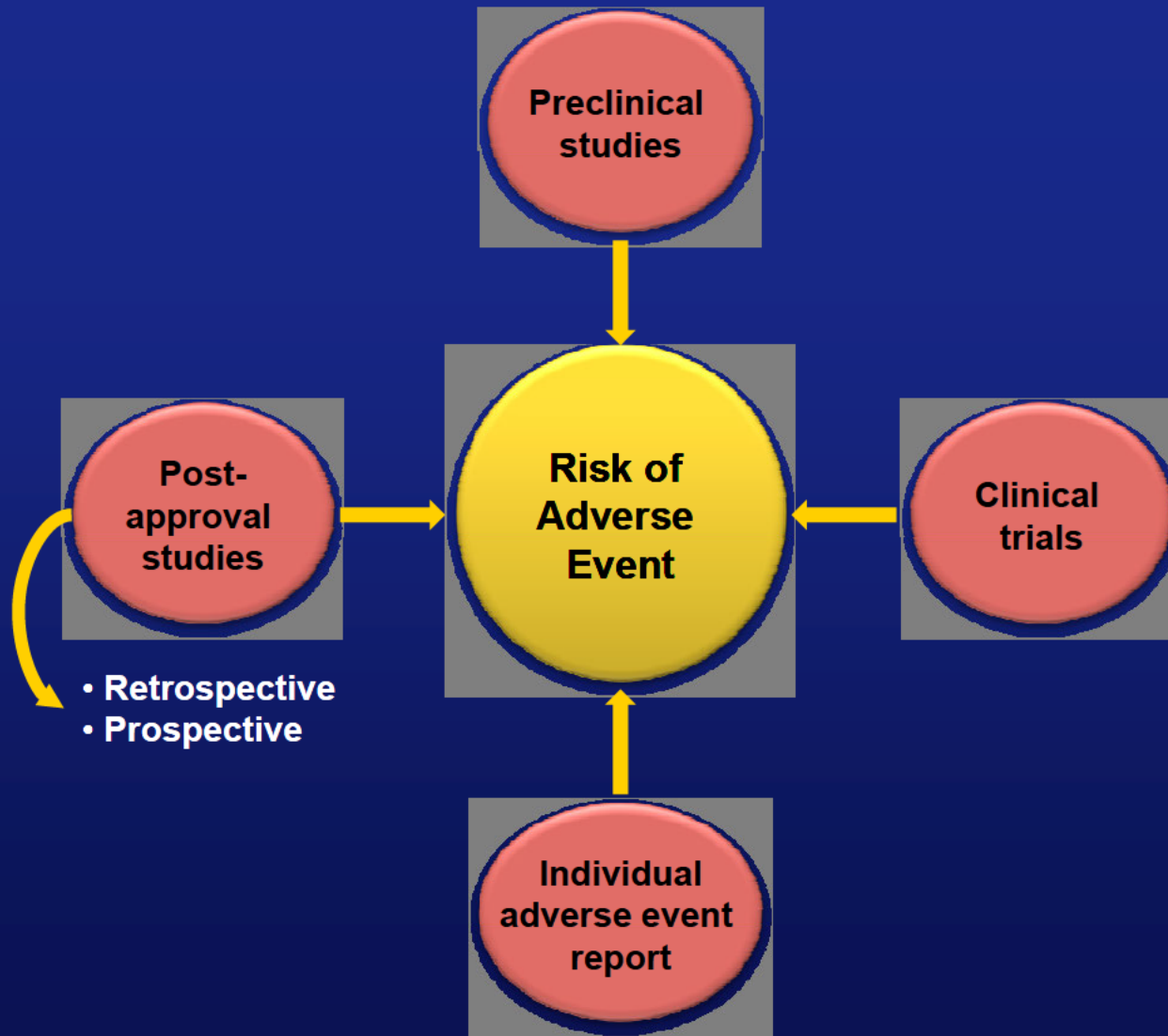
Example: What is Forteo (teriparatide)?

- **Forteo is a medication similar to 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**

Background:
US Adult Osteosarcoma Surveillance Study

- **In a preclinical rat toxicology study, Forteo caused an 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**

- **A postmarketing study was initiated at the time of initial marketing in 2002 to better understand the long-term safety of Forteo**

Study Objectives

- **Primary**

  – Identify approximately 33% 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 15 years

  – Determine incident osteosarcoma cases, if any, who have a history of Forteo treatment

Study Objectives

- **Secondary**
  - Systematically collect, for descriptive epidemiologic purposes, additional patient information:
    - Demographics
    - Other drug treatments
    - Potential risk factor information
   - Comorbid conditions

Study Design Overview

- **Selection criteria**
  - Adults aged 40 years and older
  - Diagnosed with osteosarcoma (12 ICD-O-3 codes) or 5 other ̧ reş ecified 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**

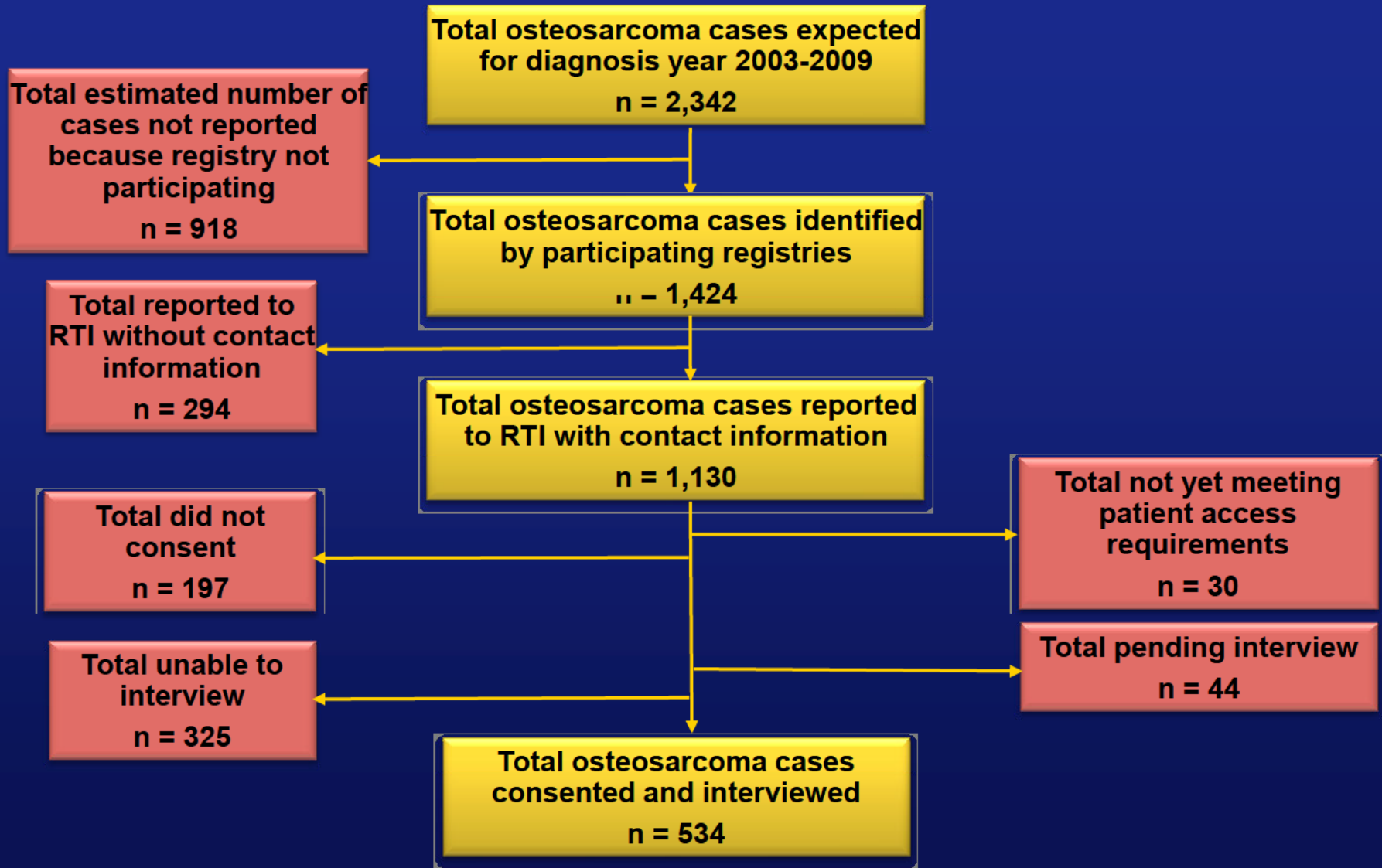RTI$(h)(s)$

Data Collected

- **Cancer registries:**
  - Date of diagnosis, cancer site, morphology, grade
  - Patient demographics
    - Age, sex, race, vital status
- **RTI:**
  - Patient demographics
    - Age, sex, race
  - Drug exposure
    - Prior use of Forteo
  - 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

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Participating US Registries and Residence of Cases Identified in the US: Adult Osteosarcoma Surveillance Study
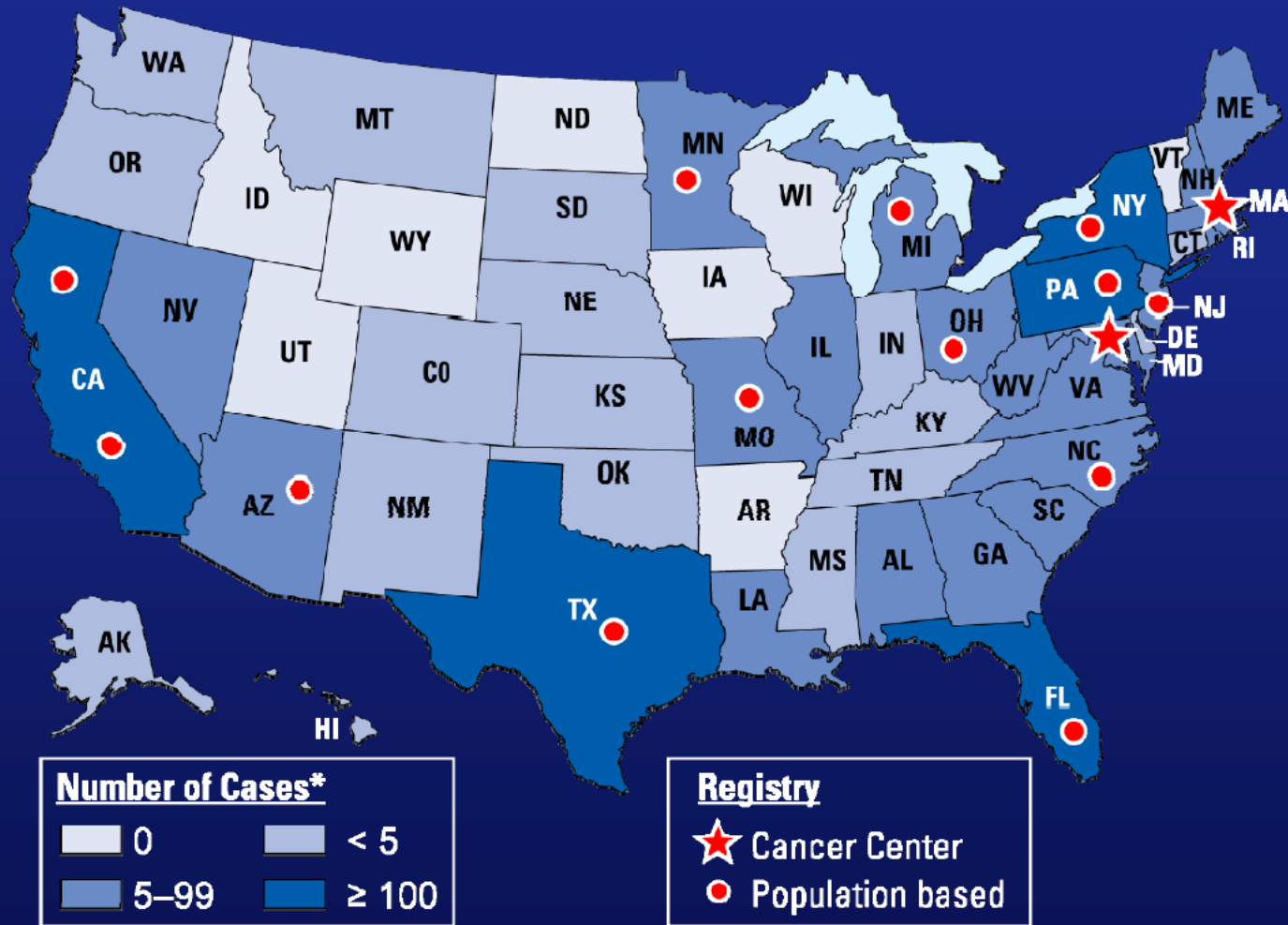
*Cases with missing residence were excluded from this plot.

Patient Accrual Results as of March 31, 2011

Total osteosarcoma cases expected for diagnosis year 2003-2009
n = 2,342

Total estimated number of cases not reported because registry not participating
n = 918

Total osteosarcoma cases identified by participating registries
n – 1,424

Total reported to RTI without contact information
n = 294

Total osteosarcoma cases reported to RTI with contact information
n = 1,130

Total did not consent
n = 197

Total not yet meeting patient access requirements
n = 30

Total unable to interview
n = 325

Total pending interview
n = 44

Total osteosarcoma cases consented and interviewed
n = 534

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Study Progress as of March 31, 2011

- **Primary objectives**

  - No cases of Forteo exposure prior to osteosarcoma diagnosis

  - 61% (n = 1,424) of all 2003-2009 US cases identified

  - 23% (n = 534) of all 2003-2009 US cases interviewed

- **Secondary objective**

  - Descriptive data on patient characteristics are available on 1,424 patients identified from registries

    - 534 patient or proxy interviews completed

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Results: Osteosarcoma Cases Interviewed (n = 534)

- **Demographics**
  - Average age: 61 years, range 40 to 93 years
  - Sex: 54% male
  - Race: 84% white
  - Vital status: 23% deceased

Results, Distribution of Self-Reported Risk Factors, Osteosarcoma Cases Interviewed (n = 534)
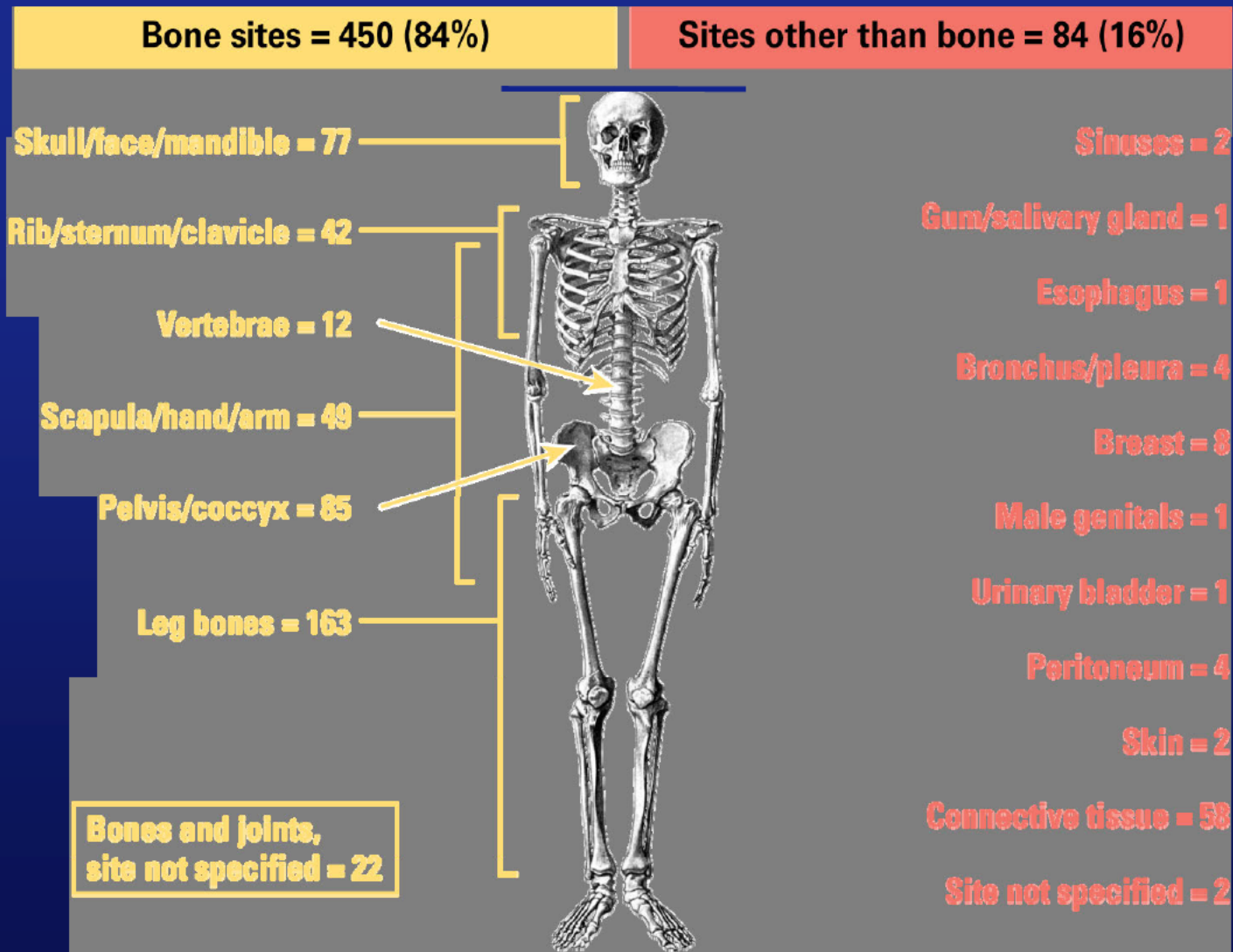
- **Known risk factors**
    - 106 (20%) exposure to radiation
    - 31 (6%) history of Paget's disease
- **Possible risk factors**
    - 141 (26%) history of other cancers
    - 133 (25%) agricultural pesticide exposure
    - 99 (19%) previous injury or infection at tumor site
    - 65 (12%) occupational petrochemical exposure
    - 33 (6%) family history of osteosarcoma

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Results: Distribution of Osteosarcoma Type

ICD-O-3 Codes	Interviewed, N = 534
9180 Osteosarcoma NOS	71%
9181 Chondroblastic osteosarcoma	12%
9182 Fibroblastic osteosarcoma	7%
9192 Parosteal osteosarcoma	3%
9183 Telangiectatic osteosarcoma	2%
9184 Osteosarcoma in Paget's disease	2%
9185 Small cell osteosarcoma	1%
9186 Central osteosarcoma	1%
9193 Periosteal osteosarcoma	< 1%
9187 Intraosseous well-differentiated osteosarcoma	< 1%
9194 High-grade surface osteosarcoma	< 1%
9195 Intracortical osteosarcoma	0%

Data as of March 31, 2011

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Primary Tumor Site Among US Osteosarcoma Interviewed Cases (N = 534)

Bone sites = 450 (84%)

- Skull/face/mandible = 77
- Rib/sternum/clavicle = 42
- Vertebrae = 12
- Scapula/hand/arm = 49
- Pelvis/coccyx = 85
- Leg bones = 163
- Bones and joints, site not specified = 22

Sites other than bone = 84 (16%)

- Sinuses = 2
- Gum/salivary gland = 1
- Esophagus = 1
- Bronchus/pleura = 4
- Breast = 8
- Male genitals = 1
- Urinary bladder = 1
- Peritoneum = 4
- Skin = 2
- Connective tissue = 58
- Site not specified = 2

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Summary

- **Based on the information reviewed to date, there does not appear to be a pattern indicative of causal relationship between Forteo treatment and osteosarcoma in humans**

- **Ongoing results expand on osteosarcoma information in the literature and assist in describing the distribution of other possible risk factors**

- **Data from this long-term research collaboration with cancer registries provide a powerful tool in the effort to advance the knowledge of long-term safety of Forteo**

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Thank You!

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