# **Characteristics of Adult Osteosarcoma Patients: Results From an Ongoing Postmarketing Drug Safety Surveillance Study**

# **ABSTRACT**

**Background:** Adult osteosarcoma is very rare (approximately 2 to 3 per million cases per year in adults aged 40 years and older), and few population-based or large case series studies are reported in the literature. To monitor for a potential signal of a possible association between teriparatide treatment and adult osteosarcoma, a 15-year surveillance study was initiated in 2002.

**Objectives:** To characterize the demographic profile plus environmental and treatment exposures in adult osteosarcoma patients from an ongoing surveillance study.

Methods: Incident cases of adult osteosarcoma diagnosed on or after January 1, 2003, are identified through populationbased state cancer registries and comprehensive cancer center registries in the United States (US). Currently, 15 US registries are participating (11 states, 1 Surveillance, Epidemiology and End Results [SEER], and 3 comprehensive cancer centers). Once cases are identified and consent is obtained, information about demographics, prior treatment with osteoporosis medications, and exposure to possible osteosarcoma risk factors is ascertained by telephone interview.

Results: As of September 2009, 979 cases of osteosarcoma diagnosed between January 1, 2003, and December 31, 2007, were identified and 365 interviews were completed (231 patients, 134 proxies). Characteristics were similar for interviewed and noninterviewed cases. Among all cases identified, mean age was 63 years, 49% were female, and 80% were white. Osteosarcoma not otherwise specified (NOS) (67%) and chondroblastic osteosarcoma (12%) were the most common morphologic types; leg bones (29%) were the most common anatomical tumor site, followed by the pelvis/sacrum (17%). Among those interviewed, reported prevalence of possible risk factors was 27% for prior history of cancer, 20% for history of radiation therapy, 20% for prior trauma or infection at site of cancer, and 6% for history of Paget's disease.

**Conclusions:** Data from this ongoing surveillance study are adding to the collective knowledge about adult patients with osteosarcoma. Results through the first 7 years of the study expand on information from the literature and describe the distribution of possible risk factors among adult osteosarcoma patients from a populationbased case series.

# BACKGROUND

- Teriparatide is a recombinant human parathyroid hormone analog approved in 2002 in the US for postmenopausal women with osteoporosis and for men with low bone mineral density at high risk for bone fractures with a 2-year treatment duration (during a patient's lifetime).
- In rat toxicology studies,<sup>1,2</sup> teriparatide caused exaggerated increases in bone mass and a dosedependent increase in the incidence of osteosarcoma.
- The estimated background incidence of osteosarcoma in adults aged 40 years and older is 2.5 cases per million per year.<sup>3</sup>
- Adjusted to the age-gender distribution of teriparatide patients,<sup>4</sup> the estimated incidence rate of osteosarcoma rises to 3.2 cases per million per year.
- The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), requested a signal detection study be initiated in the US and Europe.<sup>5</sup>

# US Adult Osteosarcoma Surveillance Study

- Initiated in 2002 to monitor for a signal of a possible association between teriparatide and adult osteosarcoma.
- Primary objectives:
- To identify and interview 33% of newly diagnosed cases of osteosarcoma in adults aged 40 and older in the US, for a duration of 15 years.
- To determine incident cases, if any, who have a history of treatment with teriparatide
- Secondary objective: Systematically collect, for descriptive epidemiology purposes, additional patient information, including demographics and data related to other risk factors for osteosarcoma.

# **OBJECTIVE**

• To characterize the demographic profile plus environmental and treatment exposures in adult osteosarcoma patients from the US surveillance study

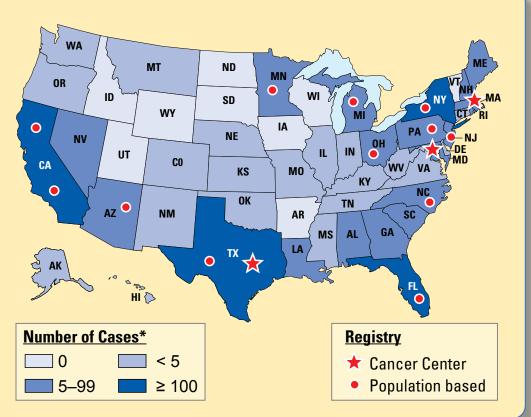
# METHODS

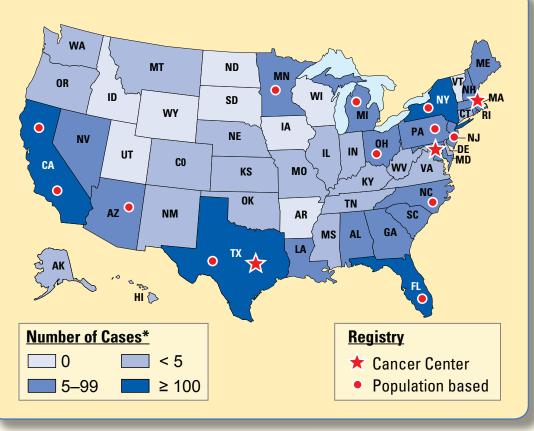
### Study Design

- Retrospective case series
- **Eligibility Criteria**
- Adults aged 40 years and older at time of diagnosis
- Diagnosed with osteosarcoma (12 ICD-O-3 codes) on or after January 1, 2003

# **Case Identification Setting**

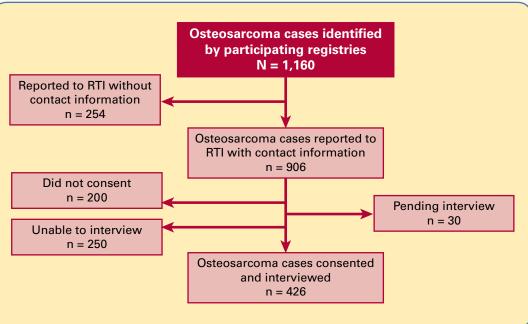
- Population-based cancer registries, comprehensive cancer treatment center cancer registries
- 15 US registries (11 state, 1 SEER, and 3 comprehensive cancer treatment centers) provided cases diagnosed between 2003 and 2008 (Figure 1)





- Known 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

# RESULTS



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Figure 1. Participating US Registries and Residence of Cases Identified in the US Adult Osteosarcoma Surveillance Study

Cases with missing residence were excluded from this plot (n = 3).

# **Data Collected From Cancer Registries**

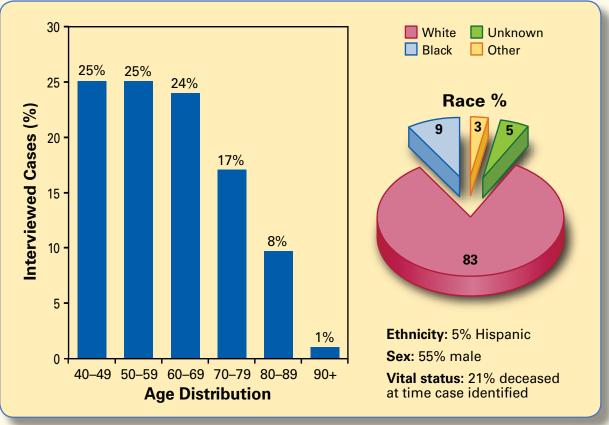
- Cancer information
- Date of diagnosis, cancer site, morphology, grade
- Data Collected From Patient (or Proxy) by Telephone Interview • Patient demographics:
- Age, sex, race, vital status
- Drug exposure:
- Prior use of teriparatide
- Prior exposure to radiation, history of Paget's disease
- Other possible risk factors for osteosarcoma:

• Results have been updated since the abstract was submitted and include data as of April 1, 2010.



- 426 cases were interviewed (Figure 2).
- Among cases interviewed, Figure 3 lists demographic information.
- Drug exposure:
- No cases reported exposure to teriparatide prior to osteosarcoma diagnosis.
- Among those cases with a prior exposure to radiation treatment (n = 82):
- 67% matched the anatomical site of the tumor as reported by the cancer registry
- 24% did not match
- 9% were indeterminate

Figure 3. Demographic Characteristics of Adult Osteosarcoma Cases Interviewed (N = 426) in the Osteosarcoma Surveillance Study



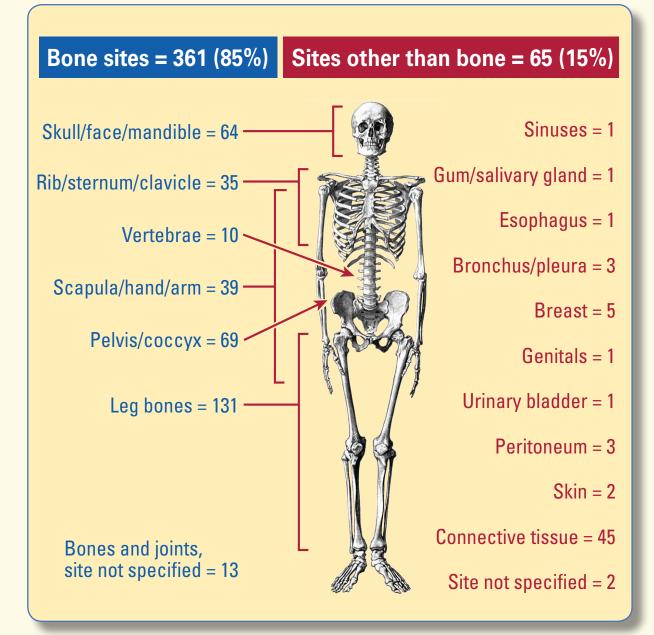
Average age (range): 60 years (40 to 93 years)

 
 Table 1. Self-Reported Prevalence of Exposures (and Characteristics) Among Interviewed Cases
(n = 426)

Exposure/Characteristic	n (%)
Lifestyle exposures	
Drank alcohol during 12 months prior to diagnosis	282 (66)
Smoked $\ge$ 100 cigarettes in their lifetime	221 (52)
Treatment, injury, and infection exposures	
Previous injury or infection at tumor site	87 (20)
Prior radiation treatment	82 (19)
Environmental exposures	
Agricultural pesticide exposure	100 (23)
Occupational petrochemical exposure	56 (13)
Occupational radiation exposure	29 (7)
Personal and family history	
History of other cancers	110 (26)
Family history of osteosarcoma	27 (6)
History of Paget's disease	25 (6)
Note: Known risk factors highlighted in red.	

Table 2. Distribution of Morphology Among Interviewed Cases (n = 426)	
Morphology	Interviewed n (%)
9180 Osteosarcoma NOS	303 (71)
9181 Chondroblastic osteosarcoma	56 (13)
9182 Fibroblastic osteosarcoma	29 (7)
9184 Osteosarcoma in Paget's disease	10 (2)
9192 Parosteal osteosarcoma	10 (2)
9183 Telangiectatic osteosarcoma	6 (1)
9186 Central osteosarcoma	5 (1)
9185 Small cell osteosarcoma	4 (1)
9187 Intraosseous well-differentiated osteosarcoma	2 (< 1)
9193 Periosteal osteosarcoma	1 (< 1)
9194 High-grade surface osteosarcoma	0 (0)
9195 Intracortical osteosarcoma	0 (0)

# Figure 4. Primary Tumor Site Among Interviewed Cases (n=426)



# **DISCUSSION AND CONCLUSIONS**

- There have been no reports of teriparatide exposure prior to osteosarcoma diagnosis.
- Osteosarcoma NOS was the most common tumor type, followed by chondroblastic osteosarcoma and fibroblastic osteosarcoma, representing over 90% of the cumulative distribution of cases.
- Most common tumor sites, in order, were the leg bones, pelvis/ coccyx, and the skull/face/mandible.
- 65 (15%) of the osteosarcomas occurred in a site other than bone.
- There was a link between radiation site and tumor site, consistent with prior research.
- 20% (87/426) of patients reported prior injury or infection at the site of the tumor, warranting consideration in future studies.
- These interim descriptive results expand on information from the literature and describe the distribution of possible risk factors among adult osteosarcoma patients from a populationbased case series.

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