

US Osteosarcoma Surveillance Study

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CONFLICT OF INTEREST

This study was funded by Eli Lilly and Company. Nicole Kellier and Daniel Masica are employees of Eli Lilly and Company. David Harris, Kirk Midkiff, Alicia Gilsenan, and Elizabeth Andrews are employees of RTI Health Solutions, a nonprofit research organization that conducts research with multiple pharmaceutical companies and has an independent right to publish this study.

ABSTRACT

Background: The Osteosarcoma Surveillance Study, an ongoing 15-year drug safety surveillance study, was initiated in 2003 to monitor for a possible association between teriparatide treatment and osteosarcoma in adults aged 40 years or older in the United States (US).

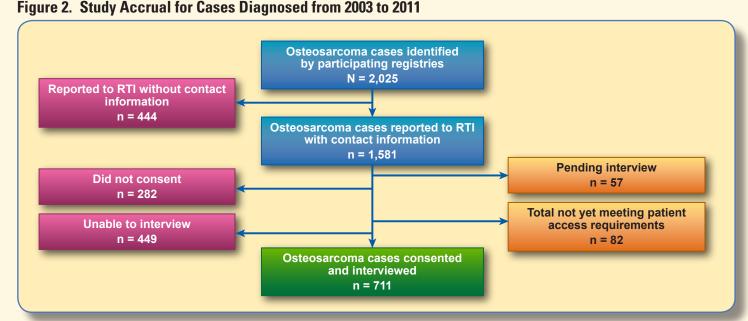
Objective: To provide an update on results, including descriptive characteristics of patients aged 40 years and older with osteosarcoma in the US.

Methods: Incident cases of adult osteosarcoma diagnosed on or after January 1, 2003, are identified through cancer registries in the US. After consent, case information, including demographics, prior treatment with medications, and exposure to possible risk factors, is ascertained via telephone interview. Medical record review is performed for a random sample each year to validate self-reported information.

Results: As of September 30, 2012, 1,729 patients diagnosed between 2003 and 2010 had been identified from the 16 participating cancer registries and 643 had been interviewed. Characteristics were similar for interviewed and noninterviewed patients. Among patients interviewed, mean age was 60 years, 47% were female, and 86% were white. Osteosarcoma, not otherwise specified (NOS) (72%) and chondroblastic osteosarcoma (11%) were the most common morphologic types; leg bones (31%) and pelvis/sacrum (16%) were the most common anatomical tumor sites. Reported prevalence of known risk factors was 20% for history of radiation and 6% for history of

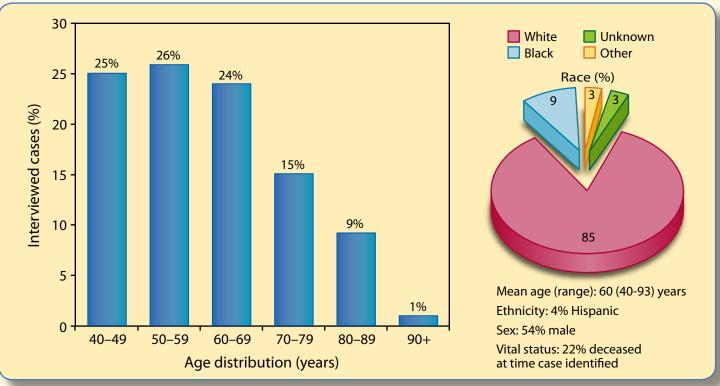
RESULTS

- Results have been updated since the abstract was submitted and include data as of June 30, 2013, the latest available data at the time of the poster preparation.
- There were no reported exposures to teriparatide before osteosarcoma diagnoses.



RTI = RTI International.

Figure 3. Demographic Characteristics of Adult Osteosarcoma Cases Interviewed in the US Adult Osteosarcoma Surveillance Study (N = 711)



Paget's disease of bone. The prevalence of other possible risk factors included 27% for prior history of cancer and 18% for prior trauma or infection at site of cancer. No patients reported use of teriparatide prior to the diagnosis of osteosarcoma.

Conclusions: Data from this 15-year surveillance study contribute to knowledge about the long-term safety of teriparatide. After 8 years of data collection, the study has not detected a pattern indicative of a causal association between treatment with teriparatide and osteosarcoma.

BACKGROUND

- Teriparatide is a recombinant human parathyroid hormone analog, approved in 2002 in the US for the treatment of postmenopausal women with osteoporosis who are at high risk for fracture and for increase in bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture. In 2009, the treatment indication was expanded to include treatment of men and women with glucocorticoidinduced osteoporosis who are at high risk for fracture.
- In preclinical studies in rats, teriparatide caused a dose-dependent increase in the incidence of osteosarcoma. No causal association has been seen in the clinical experience.
- Osteosarcoma is a rare bone cancer in humans, with an estimated background incidence in adults aged 40 years and older of 2.5 cases per million population per year.¹ Standardized to the age-sex distribution of patients receiving teriparatide,² the estimated incidence rate of osteosarcoma is 3.2 cases per million per year. ^{3,4}
- As a condition of approval, the US Food and Drug Administration and the European Medicines Agency requested a postapproval surveillance study be conducted (Osteosarcoma Surveillance Study).

US Adult Osteosarcoma Surveillance Study

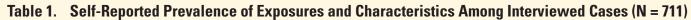
- Initiated in 2003 to monitor for a signal of a possible association between teriparatide, an injectable treatment for osteoporosis, and adult osteosarcoma.
- Primary objectives: (1) to identify incident cases of osteosarcoma, if any, who have a history of treatment with teriparatide and (2) to identify and interview 33% of newly diagnosed cases of osteosarcoma in adults aged 40 years and older in the US during a 15-year period.
- Secondary objective: to systematically collect, for descriptive epidemiology purposes, additional patient information, including demographics and data related to other risk factors for osteosarcoma.

OBJECTIVE

 To provide an update on results, including descriptive characteristics of patients aged 40 years and older with osteosarcoma in the US.

METHODS

 Incident cases of adult osteosarcoma diagnosed on or after January 1, 2003, are identified through cancer registries in the US. After consent, case information, including demographics, treatment with medications, and exposure to possible risk factors, is ascertained via telephone interview. Medical records of a random sample



Exposure/Characteristic	n (%)
Lifestyle exposures	
Drank alcohol during 12 months before diagnosis	466 (66%)
Smoked \geq 100 cigarettes in their lifetime	363 (51%)
Treatment, injury, and infection exposures	
Previous injury or infection at tumor site	132 (19%)
Prior radiation treatment	137 (19%)
Environmental exposures	
Agricultural pesticide exposure	170 (24%)
Occupational petrochemical exposure	88 (12%)
Occupational radiation exposure	51 (7%)
Personal and family history	
Personal history of other cancers	185 (26%)
Family history of osteosarcoma	39 (5%)
Personal history of Paget's disease of bone	40 (6%)

Note: Known risk factors are highlighted in red.

Table 2. Distribution of Morphology Among Interviewed Cases (N = 711)

Morphology	n (%)
9180 Osteosarcoma NOS	511 (72%)
9181 Chondroblastic osteosarcoma	79 (11%)
9182 Fibroblastic osteosarcoma	49 (7%)
9192 Parosteal osteosarcoma	20 (3%)
9183 Telangiectatic osteosarcoma	13 (2%)
9184 Osteosarcoma in Paget's disease	13 (2%)
9186 Central osteosarcoma	12 (2%)
9185 Small cell osteosarcoma	7 (1%)
9193 Periosteal osteosarcoma	4 (1%)
9187 Intraosseous well-differentiated osteosarcoma	2 (< 1%)
9194 High-grade surface osteosarcoma	1 (<1%)
9195 Intracortical osteosarcoma	0 (0%)

Figure 4. Osteosarcoma Site For Interviewed Cases (N = 711^a), as of June 30, 2013

Bone sites = 613 (86%)	Sites other than bone = 98 (14%)
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are reviewed each year to validate self-reported information.

Study Design

• Retrospective case series

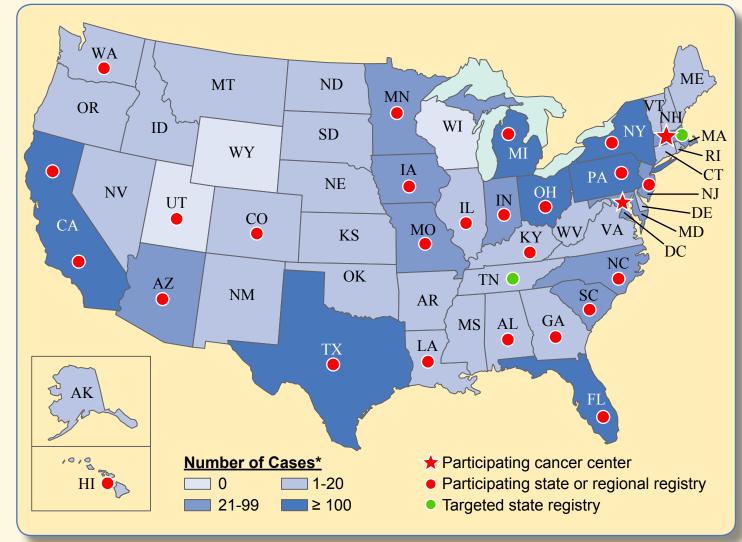
Eligibility Criteria

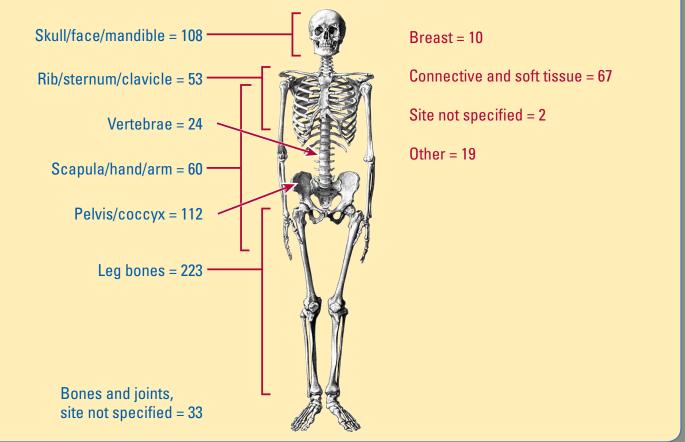
- Adults aged 40 years and older at time of diagnosis
- Diagnosed with osteosarcoma (12 ICD-O-3 codes) on or after January 1, 2003
 Case Identification Setting*
- Population-based cancer registries, comprehensive cancer treatment center cancer registries
- As of June 30, 2013, 29 US registries were actively participating in the study or were targeted for participation (Figure 1):
 - Twenty registries (17 state, 1 regional, and 2 comprehensive cancer treatment centers) provided cases diagnosed between 2003 and 2011
 - Nine registries are in the process of collecting data, finalizing work agreements, or reviewing applications
- **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
- Known risk factors for osteosarcoma
 - Exposure to radiation, history of Paget's disease of bone
- Other possible risk factors for osteosarcoma
 - History of other cancers, injury or infection at tumor site, agricultural/occupational pesticide exposure, petrochemical exposure, family history of osteosarcoma

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





^aNo interviewed cases have reported prior treatment with teriparatide.

DISCUSSION AND CONCLUSIONS

- There have been no reports of teriparatide treatment before an osteosarcoma diagnosis.
- At this time, we have adequate power to detect a risk, if it occurs, of one additional case per 104,000 treated patients (i.e., a four-fold increase in risk), without regard to latency.
- Osteosarcoma NOS was the most common tumor type, followed by chondroblastic osteosarcoma and fibroblastic osteosarcoma, representing over 90% of the cumulative distribution of cases.
- Consistent with what we would expect, the most common tumor sites, in order, were the leg bones, pelvis/coccyx, and the skull/face/mandible.
- Of the osteosarcomas reported by the cancer registries, 98 (14%) occurred in a site other than bone.
- Overall, 132 patients (19%) 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 population-based case series.

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* Due to a 9- to 18-month case identification and reporting lag time, cases diagnosed in 2012 and 2013 are not included in these analyses.

CONTACT INFORMATION

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