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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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

- Preclinical studies
- Clinical trials
- Risk of Adverse Event
- Post-approval studies
  - Retrospective
  - Prospective
- Individual adverse event report

RTI(b)(s)
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 specified 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

- **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
Participating US Registries and Residence of Cases Identified in the US: Adult Osteosarcoma Surveillance Study

Number of Cases*
- 0
- < 5
- 5–99
- ≥ 100

Registry
- ★ Cancer Center
- ○ Population based

*Cases with missing residence were excluded from this plot.
Patient Accrual Results as of March 31, 2011

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

Total reported to RTI without contact information
n = 294

Total did not consent
n = 197

Total unable to interview
n = 325

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

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

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

Total not yet meeting patient access requirements
n = 30

Total pending interview
n = 44

Total osteosarcoma cases consented and interviewed
n = 534
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 registry interviews completed
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 CasesInterviewed. 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
## Results: Distribution of Osteosarcoma Type

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

Data as of March 31, 2011
Primary Tumor Site Among US Osteosarcoma Interviewed Cases  \( N = 534 \)

- **Bone sites** = 450 (84%)
  - Skull/facet/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 = 3
  - Male genitals = 1
  - Urinary bladder = 1
  - Peritoneum = 4
  - Skin = 2
  - Connective tissue = 9
  - Site not specified = 2
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.
Thank You!

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