Long-Term Cancer Surveillance: Five-Year Update for the Forteo Patient Registry Data Linkage Study

Presented at the 2015 NAACCR Annual Conference, Charlotte, North Carolina

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Objectives of This Presentation

Provide the following information about the Forteo Patient Registry:

1. Summary of the study background, objectives, and design
2. Overview of the cancer registry and patient enrollment processes
3. Interim results after 5+ years of patient enrollment and completion of five annual data linkages
Background

What is teriparatide?

• A medication similar to natural parathyroid hormone
• It stimulates formation of new bone and increase in bone mineral density and bone strength
• It is a self-injected daily therapy approved for use for up to 2 years
• It was initially approved in 2002 in the US for treatment of postmenopausal women with osteoporosis and for men with low bone mineral density at high risk of fracture
• The treatment indication was expanded in 2009 to include glucocorticoid-induced osteoporosis
Background

• In rat toxicology studies, teriparatide caused a dose-dependent increase in the incidence of osteosarcoma
• Due to the rat toxicology studies, the FDA required a postapproval surveillance study as a condition of drug approval (Osteosarcoma Surveillance Study)
• In 2009, the FDA required the addition of a prospective patient registry as condition of approval for the new indication (Forteo Patient Registry)
• Adult osteosarcoma is rare
  – Among adults aged 18 years or older, incidence is 2.7 cases per million population per year (SEER data)
  – Therefore, the study requires a large number of Forteo users and participation by a large number of state cancer registries
Study Objective and Design

Forteo Patient Registry Data Linkage Study

• Primary objective
  – To estimate the incidence of osteosarcoma in patients who have received treatment with Forteo

• Study design
  – Voluntary, prospective cohort study of adults (aged ≥ 18 years) residing in the US who receive a Forteo delivery device during the enrollment period (2009-2019) and who provide voluntary consent to have their personal data linked to cancer registry data
  – Annual linkage with state cancer registries is planned for 15 years (2010-2024)
  – 12 ICD-O-3 histology codes are used to define osteosarcoma: 9180-9187 and 9192-9195 (all primary sites allowed)
  – Registries include diagnosis years 2009 and later in an annual cumulative linkage file
Cancer Registry Enrollment

- All 50 state cancer registries in the US plus the registry in Washington, DC, were invited to participate in May 2009.
- Registries were considered “linkage-ready” once all required applications (IRB and other) had been approved and all agreements were in place.
- The first registry was linkage-ready in January 2010.
- The 41st registry was linkage-ready in May 2013.
- The average time for registries to become linkage-ready was 5 months and ranged from 10 days to over 18 months.
Patient Enrollment Overview

Patient is prescribed Forteo

Patient receives information about how to enroll in the Forteo Patient Registry

Patient provides pre-enrollment information to RTI

Patient meets pre-enrollment criteria (not previously enrolled, has started Forteo, etc.)

No

Patient not enrolled in registry

Yes

RTI removes duplicate cases; mails informed consent, $5 compensation, and registration form to patient

RTI receives informed consent and registration form within 3 weeks

Yes

Patient becomes part of registry

No

RTI call center places reminder call (maximum of 2 reminder calls per patient)

Annual linkage with participating cancer registries

Annual analysis and reporting to Advisory Board
### Patient Enrollment Status as of March 31, 2015

<table>
<thead>
<tr>
<th>Enrollment as of March 31, 2015</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total pre-enrollment forms received</td>
<td>60,126</td>
</tr>
<tr>
<td>Ineligible</td>
<td>1,603</td>
</tr>
<tr>
<td>Active refusal</td>
<td>2,971</td>
</tr>
<tr>
<td>Total patients pre-enrolled (percentage of forms received)</td>
<td>55,552 (92%)</td>
</tr>
<tr>
<td>Total patients mailed registration packets prior to 14 days before data cut</td>
<td>54,887</td>
</tr>
<tr>
<td>Total patients registered (response rate)(^a)</td>
<td>47,988 (83%)</td>
</tr>
</tbody>
</table>

\(^a\) Response rate = number registered/(number active refusals + number mailed registration packets)
Interim Results – Fifth Annual Linkage with State Cancer Registries

Completed October 14, 2014; 41 US state cancer registries, covering 92% of the adult US population.

No incident cases of osteosarcoma were found in Forteo users

Forteo Patient Registry Database
(N = 42,544)

Cancer registries databases
(N = 3,171)
Characteristics of the First Five Annual Data Linkages

Osteosarcoma Cases Diagnosed in 2009 or Later

<table>
<thead>
<tr>
<th>Year of Linkage</th>
<th>Number of Participating Registries (% US Coverage, Aged 18+ Years)</th>
<th>Cases From Cancer Registries</th>
<th>Forteo Patient Registry Enrollees</th>
<th>Matches Found by Registries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>27 (70%)</td>
<td>431</td>
<td>6,338</td>
<td>0</td>
</tr>
<tr>
<td>2011</td>
<td>37 (85%)</td>
<td>961</td>
<td>16,365</td>
<td>0</td>
</tr>
<tr>
<td>2012</td>
<td>38 (87%)</td>
<td>1,641</td>
<td>26,810</td>
<td>0</td>
</tr>
<tr>
<td>2013</td>
<td>41 (92%)</td>
<td>2,408</td>
<td>34,869</td>
<td>0</td>
</tr>
<tr>
<td>2014</td>
<td>41 (92%)</td>
<td>3,171</td>
<td>42,544</td>
<td>0</td>
</tr>
</tbody>
</table>

- As of the fifth linkage, the study had accumulated an estimated 100,000 person-years of follow-up, adjusted for estimated mortality
Conclusions

• Participation from a large number of cancer registries and patients is especially important in the US to monitor for rare cancers following uncommon drug exposures.

• Interim results from this study provide no evidence of an increased incidence of osteosarcoma in patients taking teriparatide.

• However, even with the large size of this registry, the amount of follow-up is relatively early considering the planned length of the study.

• The study will continue to accumulate information in the coming years.
THANK YOU

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