

June 18, 2015

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

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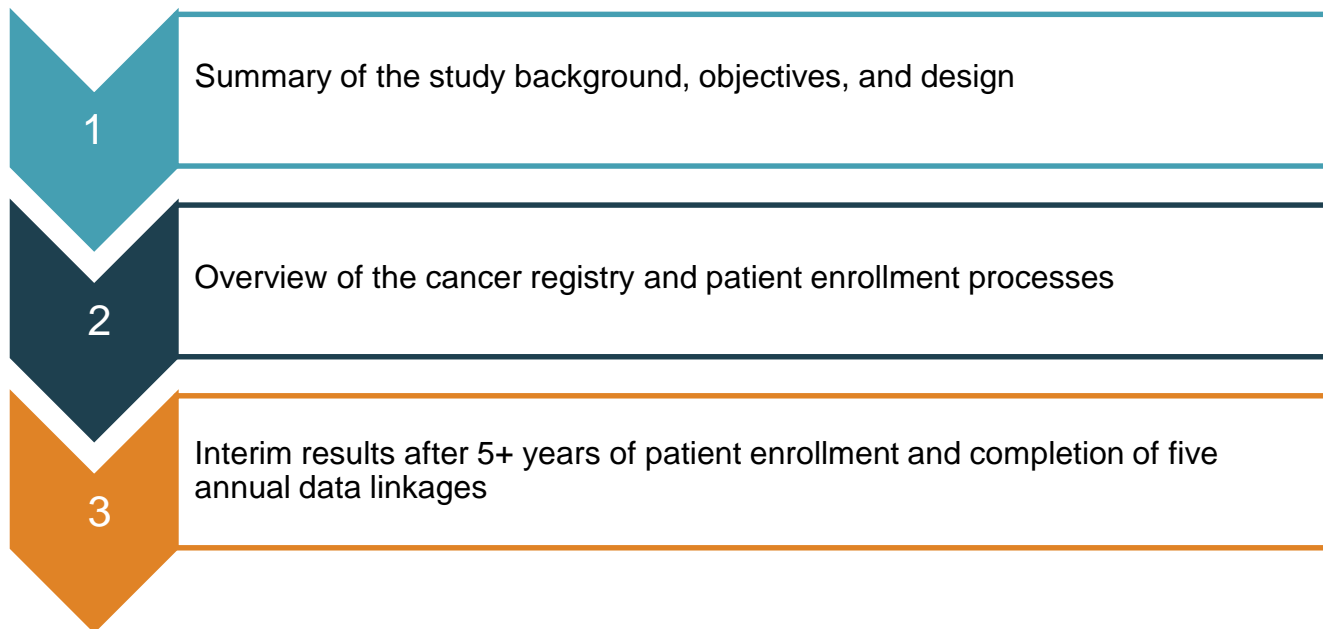
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The power of
The value of

knowledge.
understanding.

Objectives of This Presentation

Provide the following information about the Forteo Patient Registry:



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

- 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

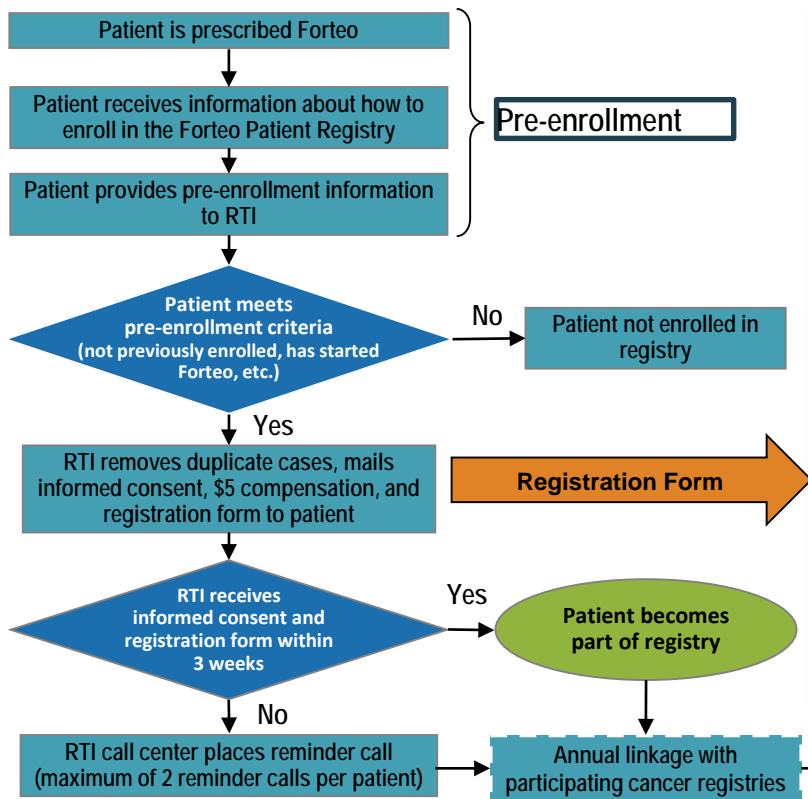
Forteo Patient Registry Data Linkage Study

- 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



Subject ID #:

Creation Date:

Month Day Year

Forteo® (teriparatide [rDNA origin] injection) Patient Registry Registration Form

1. Personal information

First name Middle name

Last name

Maiden name

Address

City State Zip code -

Date of birth:

Month Day Year Gender: Male Female

Last 4 digits of your Social Security number: - -

2. Have you taken any of the Forteo injections yet?

Yes No (If no, skip to Question 3).

2a. Please enter the date you began taking the Forteo injections.

Month Year

3. Are you of Hispanic, Latino, or Spanish origin or descent?

Yes No

4. Which of the racial groups below best describes you?

White Black/African American Asian

American Indian or Alaska Native Native Hawaiian Other Pacific Islander

Other (please specify):

Thank you for completing the registration form. Please mail your completed Registration Form and the yellow copy of your signed Consent Form in the postage-paid envelope provided to: RTI International, ATTN: Data Capture Study GHX, PO Box 12194, Research Triangle Park, NC 27709

Patient Enrollment Status as of March 31, 2015

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

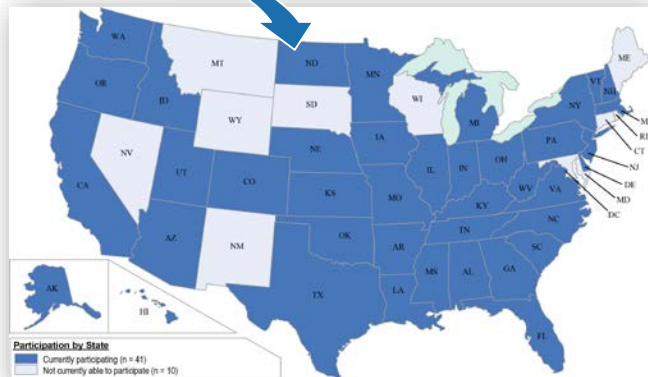
^a Response rate = number registered/(number active refusals + number mailed registration packets)

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



Forteo Patient Registry Database
(N = 42,544)



Cancer registries databases
(N = 3,171)

No incident cases of
osteosarcoma were
found in Forteo users

Characteristics of the First Five Annual Data Linkages

Osteosarcoma Cases Diagnosed in 2009 or Later

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

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

- 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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