Navigating the Registry-Specific Approval Process for a Long-Term Drug Safety Surveillance Study

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ABSTRACT

Background: The Forteo Patient Registry Study was initiated in 2009. In this ongoing study, data from patients taking teriparatide who voluntarily enroll in the Registry are linked with data from participating state cancer registries annually to determine the incidence of osteosarcoma.

Objective: To describe the variation of state cancer registry approvals required for participation in this linkage study.

Methods: Cancer registries in all 50 states and the District of Columbia were invited in May 2009 to participate in the study. Registries interested in participating provided information regarding necessary approval requirements (e.g., Institutional Review Board [IRB], Data Privacy Board, Registry, and Data Use Committee). RTI-HS collaborated with interested registries to submit all necessary applications for study approval.

Results: In total, 41 state cancer registries expressed an interest in participating. For the first annual linkage in 2010, 27 registries had obtained all approvals and participated in the linkage. In 2011, 37 registries participated, and in 2012, 38 state cancer registries, covering 86% of the US population aged 18 years and older, participated. Applications are under review for the 3 registries not currently participating. We will describe the variation in the approval process (whether local IRB review is required, and if so whether it was expedited or full review, and what type of additional reviews were required), among the participating registries in this multiyear linkage study.

Conclusion: Cancer registry participation in postmarketing safety studies is critical for surveillance studies examining cancer outcomes. Understanding the process for engaging multiple cancer registries in these types of studies will be important for future researchers and cancer registries to maximize collaboration and timely conduct of studies.

INTRODUCTION

- Teriparatide (Forteo) was initially approved in the United States (US) in 2002 for treatment of postmenopausal women with osteoporosis and for men with low bone mineral density at high risk for bone fractures.
- In rat toxicology studies, teriparatide caused increases in bone mass and a dose-dependent increase in the incidence of osteosarcoma.[1]
- In July 2009, as a condition of approval of a new indication for teriparatide, the Food and Drug Administration required the implementation of a voluntary, prospective registry to estimate the incidence of osteosarcoma in patients receiving treatment with teriparatide.
- The Forteo Patient Registry was established in 2009. Patients learn about the Forteo Patient Registry in a variety of ways, including the product packaging. Patients are invited to contact the Forteo Patient Registry to join. Following patient consent, patient identifying information and confirmation of teriparatide use are captured and maintained during the course of the study (see Figure 2). Each year, information from all enrolled patients is linked with participating cancer registries to identify any newly diagnosed cases of osteosarcoma.
- Following training, each cancer registry performs the annual data linkage using a standardized linkage algorithm.
- Data linkages will occur on an annual basis until 2021.
- The study requires a large number of patients who have received treatment with teriparatide from across the US and participation by a large percentage of US cancer registries, particularly those covering large populations, because adult osteosarcoma is rare (2.7 cases per million persons per year[2]).
- Participation of cancer registries is dependent on approval processes that are determined by each registry and its affiliated organizations.

AIMS

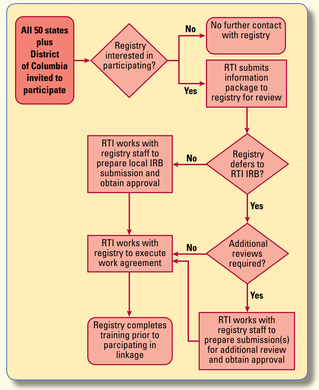
- The aims for this poster are to describe the variation of state cancer registry approvals required for participation in this linkage study and to provide a summary of the first three annual data linkages.

METHODS

Registry Recruitment

- The RTI International (RTI) IRB approved the study in 2009, and approval is renewed annually.
- In May 2009, RTI Health Solutions (RTI-HS) invited cancer registries in all 50 states and the District of Columbia to participate.
- States that expressed interest were contacted, and their specific requirements for study approval were assessed.
- RTI-HS developed standardized text describing the Forteo Patient Registry study procedures, data protection, and patient privacy safeguards. This text was used in the application process for individual registries and in response to questions anticipated by the IRB and Data Use Committees. Standardized text then was tailored to the needs of the individual cancer registries.
- All necessary applications and agreements for study approval, including ethics and data use agreements, were submitted to individual state cancer registries.
- States were considered "linkage ready" once all required approvals were obtained and a work agreement between the cancer registry and RTI-HS was established.
- Figure 1 shows the process for recruiting cancer registries into the study.

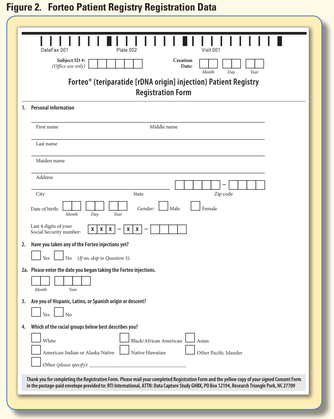
Figure 1. Registry Recruitment Process



Linkage

- Cancer registries were trained to use a standard Link Plus (v2.0) linkage algorithm. This algorithm was created and tested by RTI-HS in collaboration with three registries that reviewed the algorithm and procedures.[3]
- Selected data from enrolled patients' registration forms (Figure 2) are sent to participating state cancer registries annually via a secure FTP for the linkage.
- Cancer registries use cumulative files from their databases that include cases of adult osteosarcoma diagnosed January 1, 2009, or later to link with data from the Forteo Patient Registry.
- A standardized form is used to document results of the linkage, including the number of osteosarcoma cases in the cancer registry database and whether any cases matched with the Forteo Patient Registry participants provided by RTI-HS.
- The first three annual linkages between the Forteo Patient Registry database and participating registries were completed in September 2010, 2011, and 2012. The fourth linkage will be completed in September 2013.

Figure 2. Forteo Patient Registry Registration Data


Data Fax ID?
Plate ID?
Visit ID?
Subject ID #: (Office use only)
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: X X X – X X – ____
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 GHSE, PO Box 12194, Research Triangle Park, NC 27709

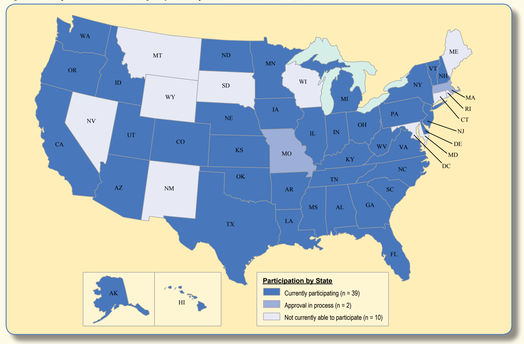
RESULTS

- Results have been updated since the abstract submission deadline to include linkage-ready states as of March 31, 2013.

Registry Recruitment

- As of March 31, 2013, of the 51 state cancer registries invited to participate, 39 were participating (Figure 3).

Figure 3. Map of State Cancer Registry Participation as of March 31, 2013



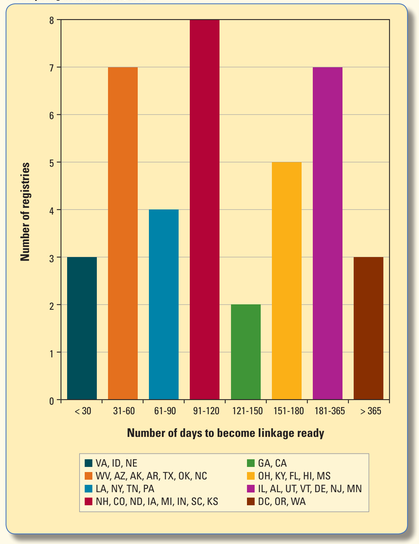
- Of the 39 registries that are currently linkage ready, 71 separate approvals of varying types were required (Table 1).
  - In some states, a single application was reviewed and approved by multiple groups (e.g., both the cancer registry and the department of health). In other states, a separate application was required for each group.
  - Additionally, many registries required more than a single contractual agreement. In some cases, a data use or other type of agreement was required by the cancer registry. RTI required that all registries sign a work agreement.

Table 1. Registry Approval Requirements for the 39 Linkage-Ready States

Table header	Defer to RTI'S IRB		Local IRB Approval		Total
	No Additional Approvals Required	Additional Approvals Required	No Additional Approvals Required	Additional Approvals Required	
Number of states	1	13	4	21	39
Number of approvals required	0	15	4	52	71

- Figure 4 shows the wide range of time (in days) required by the 39 participating states to become linkage ready.
  - For some states, applications were submitted prior to the 2010 linkage, but approvals were not received in time for the state to participate in that linkage.
  - In some instances, although IRB or other approvals were quickly received, it took several months to place all necessary data use and work agreements due to required reviews by state legal or contract departments.
- The average time for the 39 participating states to become linkage ready was 149 days (range, 10–547 days).

Figure 4. Time (in Days) From First Submission to Linkage-Ready Status for 39 States Participating as of March 31, 2013



Linkage

- Table 2 provides a summary of the first three linkages
- As of March 31, 2013, 39 cancer registries were linkage ready and will be participating in the fourth annual linkage occurring in September 2013.
- During the first three linkages, no matches between the Forteo Patient Registry and the databases from participating cancer registries were identified.
- The number of participating cancer registries and corresponding percentage of the US population covered have increased each year.

Table 2. Summary of the First Three Annual Data Linkages

Year	Number of Patients from Forteo Patient Registry	Number of Osteosarcoma Cases From Participating Registries	Participating Registries	US Adult (Aged ≥ 18 Years) Population Covered	Number of Matches
2010	6,338	431	27	70%	0
2011	16,365	961	37	85%	0
2012	26,810	1,641	38	86%	0

CONCLUSIONS

- The results of the first three linkages with Forteo Patient Registry data indicate that it is feasible for a large number of states to perform a multi-year data linkage concurrently, using a standard data linkage algorithm.
- After three annual linkages, no matches have been found where enrolled patients receiving treatment with teriparatide were subsequently diagnosed with osteosarcoma. The study will continue with linkages through 2021.
- Due to the disparate study requirements among the cancer registries and their affiliated institutions, significant time and resources are required to enroll states in the study, with some states requiring longer than a year to become linkage ready. However, information required by each cancer registry is very similar.
- Population-based studies that use data from state cancer registries play a significant role in drug safety surveillance activities.
- A standardized research application and approval process for all state cancer registries would facilitate greater efficiency for the research and registry communities, potentially enabling additional long-term studies to be performed.

REFERENCES

1. Vahle JL, Long GG, Sandusky G, Westmore M, Ma YL, Sato M. Bone neoplasms in F344 rats given teriparatide [rhPTH(1-34)] are dependent on duration of treatment and dose. Toxicol Pathol. 2004 Jul-Aug;32(4):426-38.
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3. Harris DH, Midkiff K, Gilsenan A, Andrews E. Public health surveillance collaboration: establishing a linkage algorithm with cancer registries for the Forteo patient registry. Poster presented at the North American Association of Central Cancer Registries Annual Conference; June 2010. Quebec City, Quebec, Canada.

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