

Linking a Voluntary Patient Registry With US State Cancer Registries for Possible Signal Detection

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CONFLICT OF INTEREST STATEMENT

This study was funded by Eli Lilly and Company. N. Kellier and D. Masica are employees of Eli Lilly and Company. A. Gilsonan, E. Andrews, and D. Harris are employees of RTI Health Solutions, a nonprofit research organization that conducts research with multiple pharmaceutical companies and has an independent right to publish for this study.

BACKGROUND

- Forteo (teriparatide) was initially approved in 2002 in the United States (US) for treatment of postmenopausal women with osteoporosis and for men with low bone mineral density.
- In rat toxicology studies, teriparatide caused increases in bone mass and a dose-dependent increase in the incidence of osteosarcoma.
- Osteosarcoma is a rare bone cancer in humans; incidence in adults aged 18 years and older in the US is 2.7 cases per million population per year.¹
- In July 2009, as a condition of approval for a new indication (use) for Forteo, the Food and Drug Administration (FDA) required the implementation of a voluntary, prospective registry to estimate the incidence of osteosarcoma in patients receiving treatment with Forteo.

- The Forteo Patient Registry was established in 2009 to estimate the incidence of osteosarcoma in patients who have received treatment with Forteo and includes the following elements:
 - Patients aged 18 years and older who have used Forteo at least once and reside in the US are eligible to enroll.
 - Patients become aware of the registry from a variety of sources (see Methods) and can voluntarily elect to enroll, following simple pre-enrollment, consent, and enrollment processes.
 - A limited amount of information is collected to confirm exposure to Forteo and enable subsequent linkage with cancer registries.
 - Annually, the information from all enrolled participants is linked with all participating cancer registries to ascertain any incident cases of osteosarcoma.
 - Enrollment is planned for a total of 5 years, and linkage is planned for a total of 12 years.

OBJECTIVES

- The objectives for this poster are to describe patient recruitment methods, cancer registry linkage status, and progress of the voluntary Forteo Patient Registry.

METHODS

Patient Recruitment and Enrollment Methods

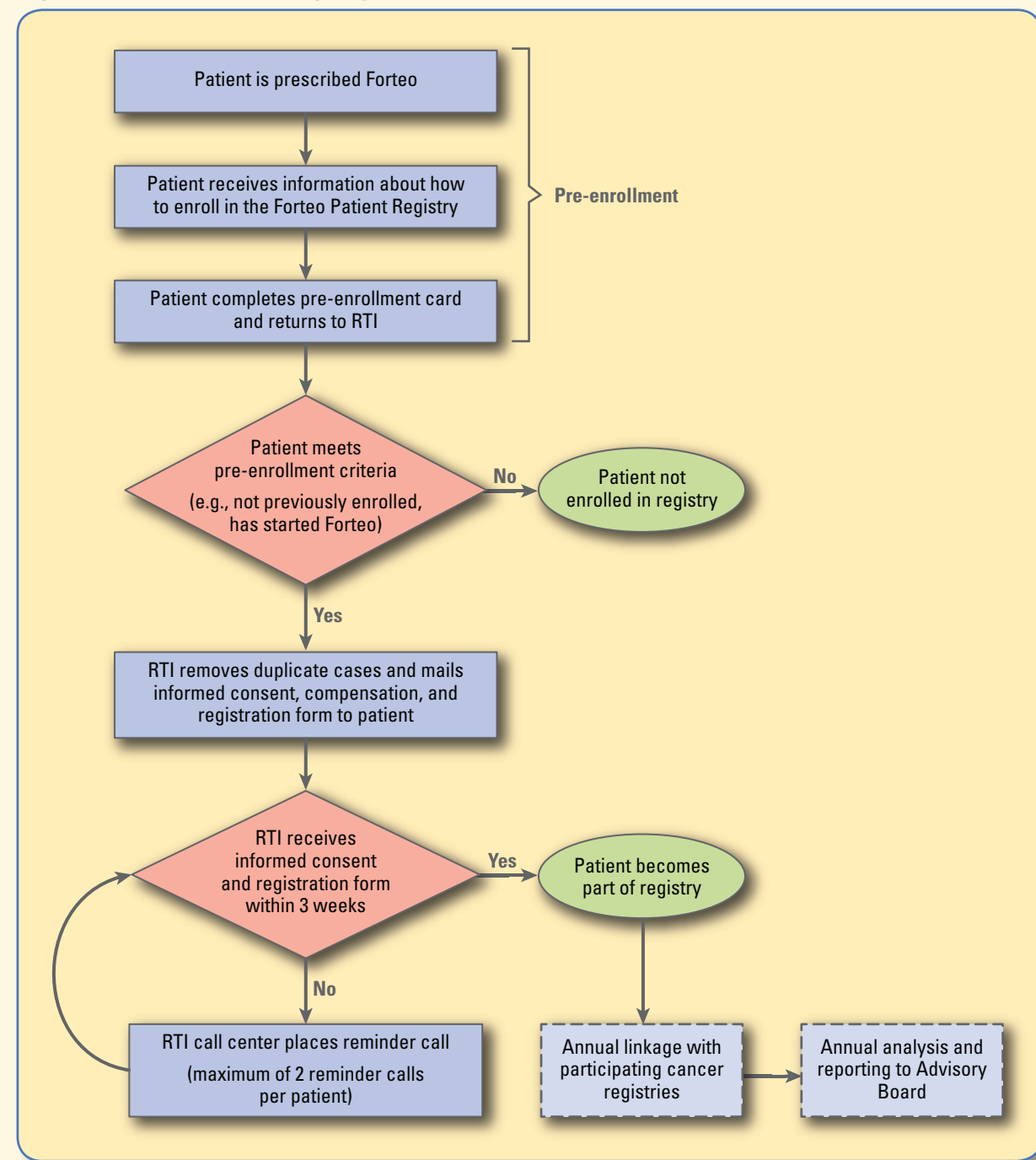
Patient Recruitment

- Multiple methods of recruitment have been implemented to facilitate patient recruitment. These include a study-specific Web site; a toll-free number; and including pre-enrollment forms in the Forteo device packaging, kits, and brochures distributed by physicians or nurses.
- The method for recruitment is tracked based on codes embedded on each of the individual pre-enrollment forms.

Patient Enrollment

- Eligible patients who express interest via a completed pre-enrollment form are mailed a registration form and informed consent form. Once completed forms are returned, the patients are considered registered, and their information is included in the annual linkage with state cancer registries.
- Figure 1 shows the study flow diagram.

Figure 1. Forteo Patient Registry Enrollment Overview



Cancer Registry Linkage

Cancer Registry Recruitment

- In May 2009, registries in all 50 states plus the District of Columbia were invited to participate in the Forteo Patient Registry.
- Of these, 42 expressed initial interest in participating.
- All necessary applications and agreements for study approval, including ethics and data use agreements, were submitted to individual state cancer registries that expressed interest.
- States were considered "linkage-ready" once all required approvals were obtained and a work agreement was established.

Linkage

- RTI International created and tested a standard linkage algorithm in collaboration with three registries that reviewed the algorithm and procedures.²
 - Link Plus (v2.0), a probabilistic matching software program available from the Centers for Disease Control and Prevention, was used to develop the algorithm.
 - Link Plus was selected because it was designed specifically for linking with state cancer registry data, is easy to use, and is readily accessible.
- Cancer registries were trained to use the algorithm via in-person and Web-enabled training sessions.
- Annually, registration data (Figure 2), including name, date of birth, last four digits of social security number, and race and ethnicity, from all eligible patients enrolled in the study are sent to all participating state cancer registries via a secure file transfer protocol (FTP).
 - Only the last four digits of the social security number are requested, to increase probability of response to this item on the registration form.
- State cancer registries are asked to create a linkage file to hold locally, which includes all incident osteosarcoma cases in adults aged 18 years and older diagnosed since January 1, 2009.

Figure 2. Forteo Patient Registration Form

Cancer Registry Variables Requested

- If a match occurs during linkage, the following variables are requested from the cancer registry:
 - Date of diagnosis
 - Age at diagnosis
 - Histology (International Classification of Diseases for Oncology [ICD-O] code)
 - State of residence at diagnosis
 - Site and laterality, where applicable
 - Stage
 - Grade

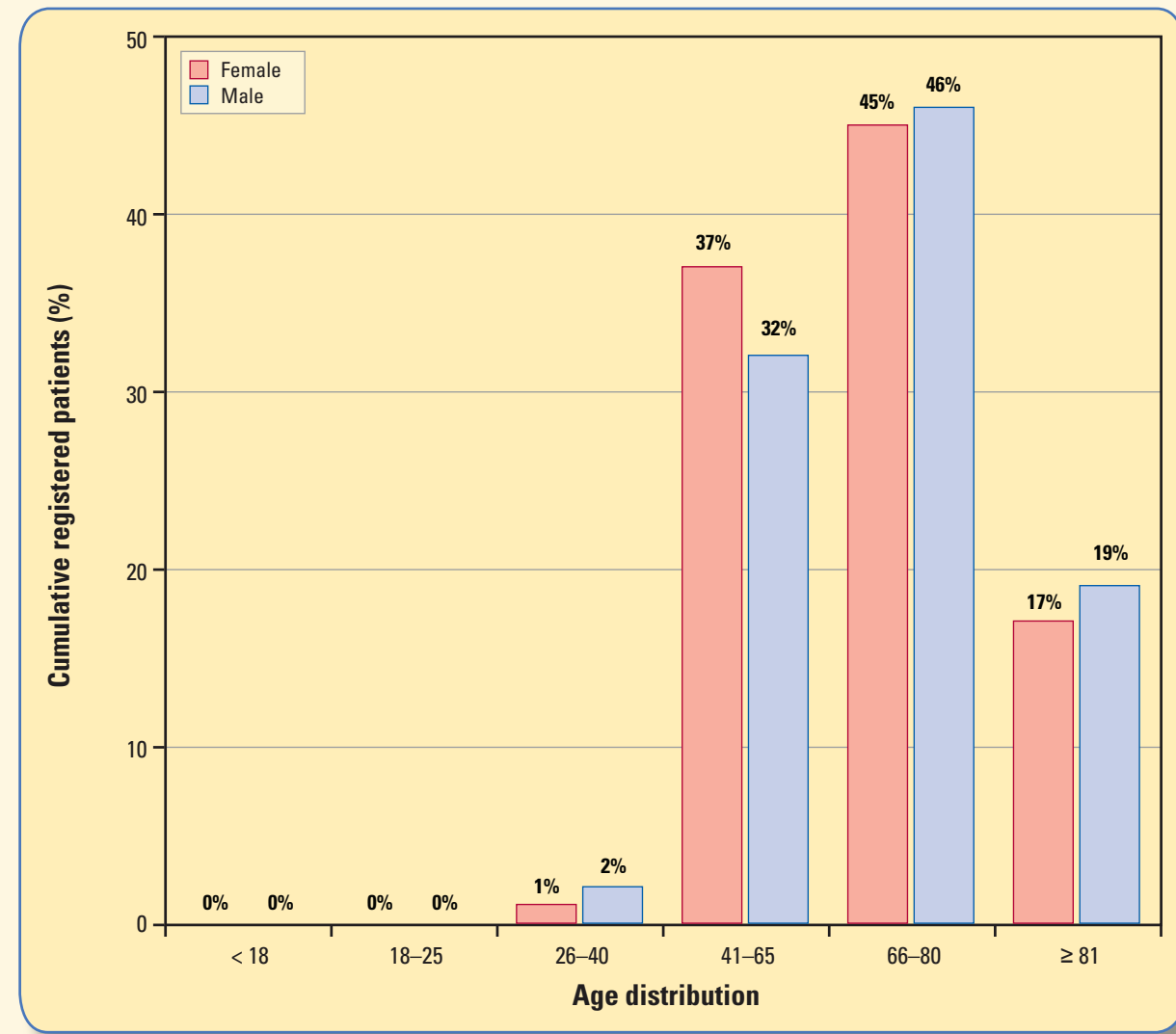
RESULTS

- Results are presented as of March 31, 2012, the latest available data at the time of the poster preparation. Data in the abstract are from December 31, 2011.

Patient Enrollment Status as of March 31, 2012

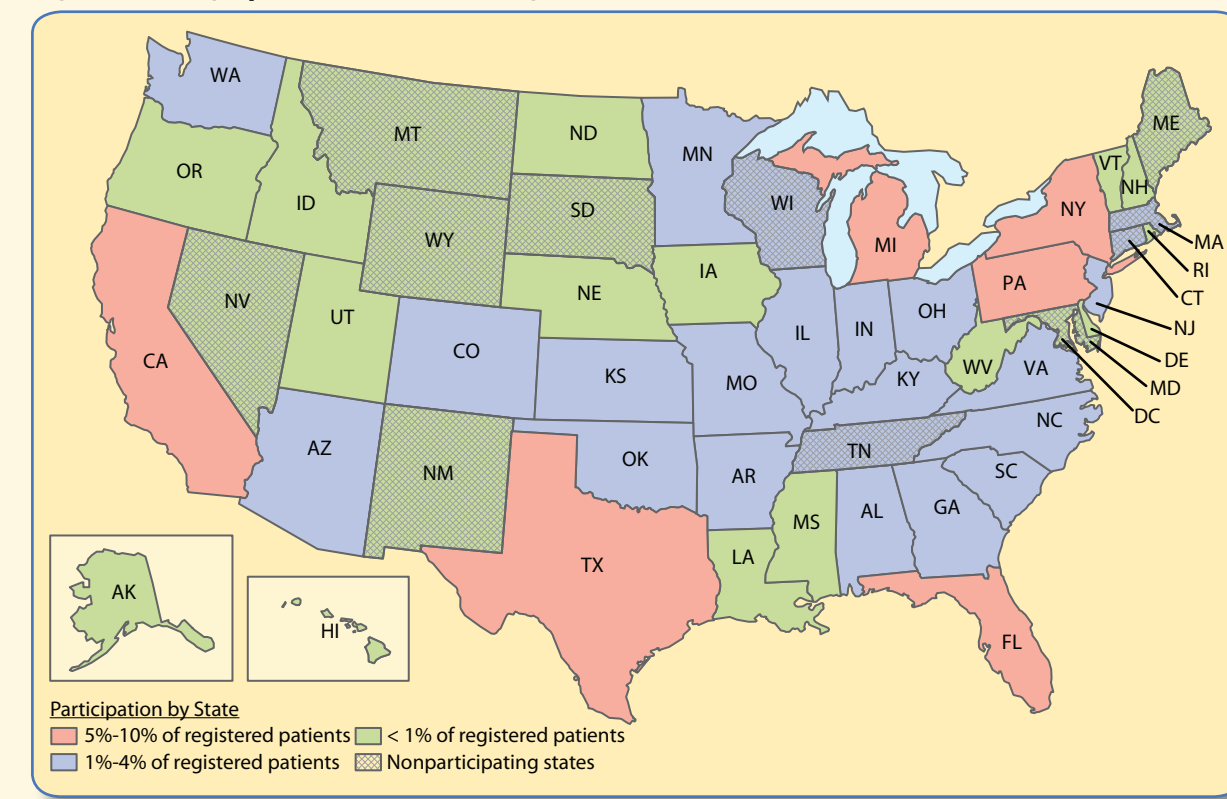
- As of March 31, 2012, a total of 24,492 patients have been registered.
- Figure 3 displays the distribution of age category stratified by sex of patients enrolled in the Forteo Patient Registry. Similar to the general Forteo user population, 90% of Forteo Patient Registry participants are female.

Figure 3. Age Distribution of Registered Patients Stratified by Sex, as of March 31, 2012 (N = 24,492)



- At least one patient from each state is included in the Forteo Patient Registry, and the distribution of patients is consistent with the size of the population in each state. (Figure 4).

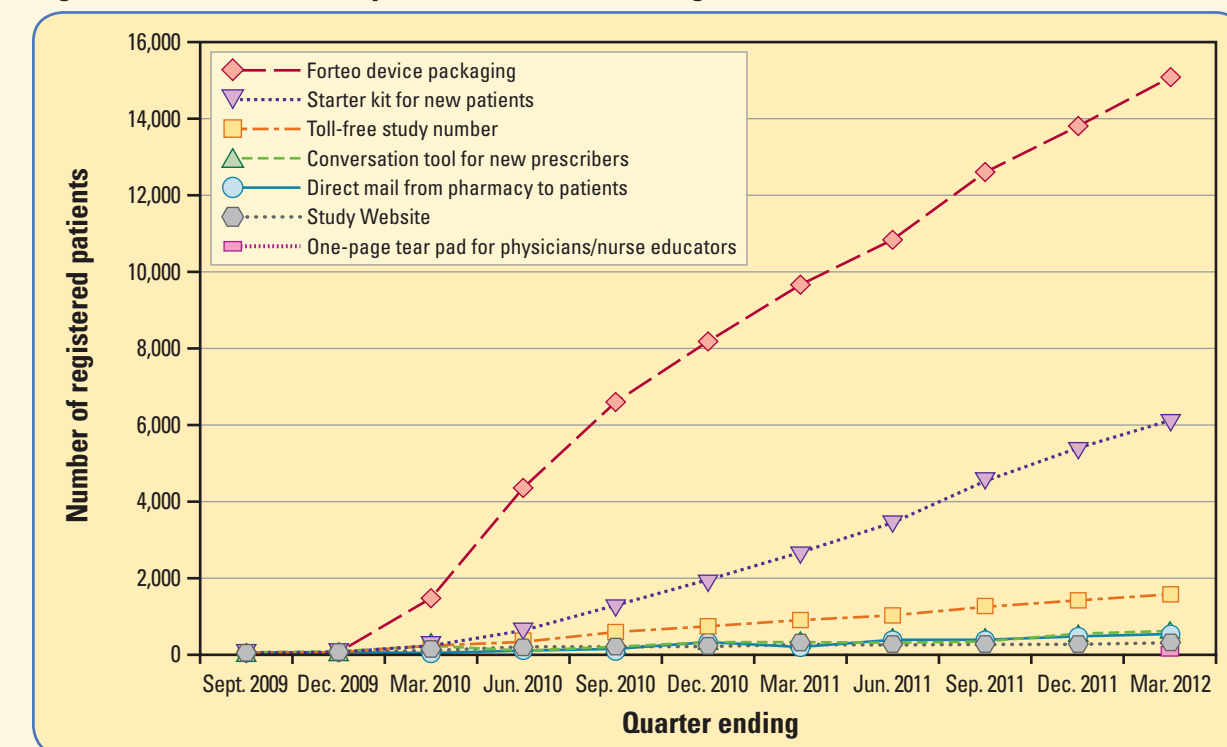
Figure 4. Geographic Distribution of Registered Patients



Trend in Method of Recruitment Among Registered Patients

- The predominant method for recruitment is the pre-enrollment form included in the Forteo device packaging (Figure 5).
- The second most common method for recruitment is the pre-enrollment form included in the starter kit, a kit that health care providers may choose to give to their new patients starting Forteo, which includes a Forteo device travel case and other informational materials.

Figure 5. Trend in Pathways for Recruitment for Registered Patients



Cancer Registry Linkage

- In September 2011, the second annual linkage was performed.
- 16,365 patients in the Forteo Patient Registry, representing approximately 14,551 person-years, were linked with a total of 961 adult osteosarcoma cases diagnosed since January 1, 2009, in the research database for each of 37 state cancer registries.
- These 37 states cover approximately 85% of the US population aged 18 years and older.
- As in the first annual linkage, no incident cases of osteosarcoma were identified among the patients registered in the Forteo Patient Registry. However, our ability to draw conclusions about the incidence of osteosarcoma in Forteo patients is limited due to the limited amount of patient follow-up time and short time from exposure to diagnosis currently available in the Forteo Patient Registry.
- Linkages with all registered patients will continue each year through 2021.

CONCLUSIONS

- Linking with a large proportion of US state cancer registries is feasible but requires significant effort and resources on the part of the researchers and cooperation by multiple individuals at each participating cancer registry.
- To date, two linkages have been performed using data from the Forteo Patient Registry, and no matches have been found between the registered patients and the osteosarcoma cases included in the state cancer registry linkage files in 2010 and 2011; no signal for osteosarcoma was detected among enrollees in the registry.
- Despite the fact that person-years of follow-up in the early years of linkage are limited and do not account for possible cancer latency, this linkage experience demonstrates the feasibility of this surveillance method for an uncommon exposure and rare cancer.

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