

# Variations Among Cancer Registries in Accessing Patients for a Drug Safety Surveillance Study

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## ABSTRACT

**Background:** The Osteosarcoma Surveillance Study, a 15-year surveillance study monitoring for a potential safety signal of a possible association between teriparatide (an osteoporosis treatment) and osteosarcoma in humans, was initiated in 2003. Multiple state, SEER regional, and comprehensive cancer registries are actively participating in this study.

**Objectives:** To describe the variety of patient-access pathways (i.e., permissions required before a researcher can contact a potential study participant identified by the participating cancer registries) and the impact of each pathway on study interview completion rates.

**Methods:** In this study, incident cases of adult osteosarcoma diagnosed January 1, 2003, or later are identified through US cancer registries. Prior to contacting an eligible patient or proxy regarding participation in the study, RTI-HS adheres to the required patient-access pathway applicable to each cancer registry. Patient-access pathways include a mix of initial contact by the cancer registry or RTI-HS and active permission versus passive notification of physicians and/or patients.

**Results:** We will describe the various patient-access pathways required by the participating cancer registries. We will also provide results regarding the percentage of cases identified with contact information (and therefore eligible for telephone interview) among total cases identified and the interview completion rate for each patient-access pathway and registry.

**Conclusions:** Postmarketing drug safety surveillance for a rare outcome such as osteosarcoma requires the participation of multiple cancer registries to be effective. However, the heterogeneity in requirements to gain access to patients for studies requiring patient contact presents unique challenges to the success of these collaborations.

## BACKGROUND

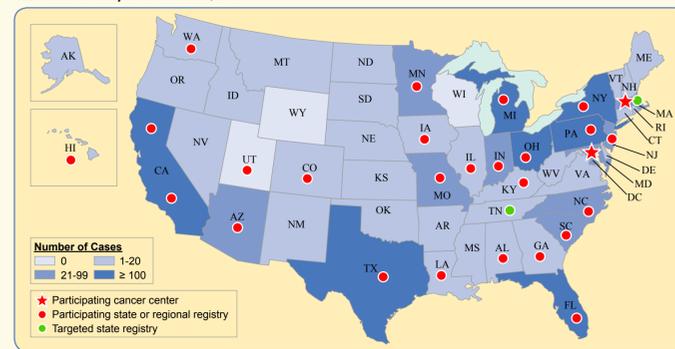
- Cancer registries are an essential partner in postapproval safety studies evaluating long-term safety of medications. However, they often have administrative, legal, or resource constraints that can impede their ability to participate in research beyond characterizing the cancer burden in their catchment area.
- Implementation of the HIPAA Privacy Rule,<sup>1</sup> local statutes, institutional review board priorities, and cancer registry data use restrictions create a mosaic of pathways researchers must follow for multisite studies before being allowed to contact patients to invite them to participate in observational research.
- An ongoing 15-year surveillance program provides a unique opportunity to characterize the diversity of pathways required by the participating cancer registries and describe their effect on the success of these collaborations for a patient contact study.
- Prior work suggests that the likelihood of successfully completing an interview with a patient (or proxy) is related to the complexity of the patient-access pathway, lag time in data reporting to researchers, and whether the patient was alive at the time the case was reported to researchers.<sup>2</sup>

### US Adult Osteosarcoma Surveillance Study

- At the request of the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), a retrospective safety surveillance study was initiated in the US and Europe.<sup>3,4</sup>
- The study was initiated in 2003 to monitor for a signal of a possible association between teriparatide, an injectable treatment for osteoporosis, and adult osteosarcoma.
- Current primary objectives:
  - To identify and interview 33% of newly diagnosed cases of osteosarcoma in adults aged 40 years and older in the US, for a duration of 15 years.
  - To determine incident cases, if any, in those who have a history of treatment with teriparatide.
- Case ascertainment is conducted by state, regional, or hospital-based cancer registries.
- Information is transferred to RTI by cancer registries that use locally approved patient-access pathways prior to sending patient contact information for identified cases.
- Exposure ascertainment is obtained by RTI via telephone interviews with the identified patient or, if patient is deceased, his or her proxy.
- The primary analysis is to compare observed teriparatide exposure (from interviews) versus the exposure expected in osteosarcoma patients assuming no increased risk is associated with exposure.
- The study will have sufficient precision to detect at least a tripling in the risk compared with the general population of similar age and sex by the end of the study, based on current assumptions regarding the rate of teriparatide use, participation of cancer registries, and interview completion rate.

Figure 1 shows the participating registries and locations of cases identified in the US Adult Osteosarcoma Surveillance Study.

Figure 1. US Registries Contributing Data and State of Diagnosis of Cases Identified in the US Adult Osteosarcoma Surveillance Study as of March 31, 2013



## OBJECTIVE

- To characterize the various types of patient-access pathways by each participating cancer registry and describe the impact the pathway has on interview completion rates by type of pathway and by individual cancer registry.

## METHODS

### Definitions

- Lag time:** The time between the date of diagnosis and the date the contact information is released to RTI is considered the lag time in our analysis.
- Full Release Population:** The group of patients provided to RTI by cancer registries where the registry may release contact information for approved research requests for the entire study population covered.
- Patient-access pathways:** The pathways are the series of steps (notifications that must be carried out and permissions obtained) completed by the local cancer registry before patient contact information can be released to RTI. Pathways also include the steps RTI must complete before contacting a patient regarding his or her interest in participating in the study.
  - Physician (MD) notification only (least restrictive) – RTI initiates contact:** RTI sends a notification about the study to the patient's physician. If the physician does not object to the patient being contacted for the study within a set time, RTI is allowed to initiate contact with the patient.
  - Only patient release required – Registry or RTI initiates contact:** If registry initiates contact, a patient permission form must be obtained by the cancer registry before the patient's contact information can be released to RTI. If RTI initiates contact, a patient release form must be obtained by RTI before telephone interviewers may contact the patient.
  - MD notification and patient release required – Registry initiates contact:** The physician is notified and allowed a set time to object, and the cancer registry must obtain a permission form from the patient before RTI may contact the patient to participate in the study.
  - MD permission to contact patient required – Registry or RTI initiates contact:** If the registry initiates contact, permission must be obtained from the physician before contact information can be released to RTI. If RTI initiates contact, permission from the physician must be obtained before RTI telephone interviewers may contact the patient. No patient release is required.
  - MD permission and patient release required (most restrictive) – Registry initiates contact:** The registry must obtain permission from both the physician and the patient before contact information for the patient is released to RTI.

### Design

- We conducted descriptive analyses for each individual cancer registry, showing the number of patients identified, the number reported to RTI with contact information, and the number interviewed. We then grouped the registries by patient-access pathway and repeated the analysis.
  - Descriptive Analysis 1: The interview rate was stratified by contributing cancer registries (Figure 2).
  - Please note that cancer registries with more restrictive patient-access pathways were added later during implementation of the study. RTI attempts to interview patients diagnosed as far back as January 1, 2003, for registries joining prior to 2012. RTI attempts to interview patients diagnosed as far back as January 1, 2007, for registries that joined in 2012 or later.
  - Descriptive Analysis 2: Individual contributing cancer registries were collapsed into the larger patient-access pathway categories and stratified by whether RTI or the cancer registry initiated contact, with the interview rate listed in descending order (Figure 3).
  - Descriptive Analysis 3: The interview rate was stratified by lag time for all cases where contact information for the Full Release Population was provided to RTI (Figure 4).

## RESULTS

- This is an ongoing study; results for this analysis include osteosarcoma and other cancers as defined in the study protocol. Data presented are current to March 31, 2013. Due to lag time in reporting from registries, cases diagnosed in 2012 or 2013 are not included in the data presented here. In addition, the states of Hawaii and South Carolina recently joined the study and were in the process of obtaining necessary permissions for these newly identified cases and therefore are not included in the analyses.
- A total of 18 cancer registries (14 state registries, 1 regional registry, and 3 medical center registries) had identified 2,913 cases of osteosarcoma and other cancers, of which 2,297 (79%) were reported to RTI with contact information and were therefore eligible to be interviewed.
- A total of 1,036 cases had been interviewed. None of the cases interviewed had been exposed to teriparatide prior to diagnosis of osteosarcoma and other cancers.

### Descriptive Analysis 1

- Figure 2 depicts the results of the interview rate for all patients identified, stratified by the contributing cancer registries. Cancer registries with the least restrictive pathway (MD notification only – RTI initiates contact) collectively had the highest interview rate.

Figure 2. Interview Rate Among All Cases Identified by Registries Contributing Data, Stratified by Patient-Access Pathway, in Descending Order of Interview Rate (N = 2,913)

Registry	Type of Patient-Access Pathway	Total Identified	Total Interviewed	Interview Rate <sup>a</sup> %
North Carolina	MD notification only – RTI initiates contact	163	96	59
Pennsylvania	Only patient release required – RTI initiates contact	251	106	42
California – LA SEER	MD notification only – RTI initiates contact	93	39	42
California (excluding LA)	MD notification only – RTI initiates contact	412	172	42
New York	MD notification and patient release required – Registry initiates contact	309	128	41
Arizona	MD notification only – RTI initiates contact	48	17	35
MD Anderson	Only patient release required – Registry initiates contact	146	51	35
Michigan	MD notification and patient release required – Registry initiates contact	186	64	34
Harvard	MD permission to contact patient required – Registry initiates contact	122	40	33
Missouri	Only patient release required – Registry initiates contact	92	30	33
Florida	Only patient release required – RTI initiates contact	355	112	32
New Jersey	MD permission and patient release required – Registry initiates contact	84	26	31
Ohio	MD permission to contact patient required – RTI initiates contact	128	38	30
Johns Hopkins	MD permission to contact patient required – RTI initiates contact	42	12	29
Minnesota	MD notification and patient release required – Registry initiates contact	127	31	24
Texas	MD permission to contact patient required – RTI initiates contact/ MD notification only – RTI initiates contact <sup>b</sup>	277	66	24
Iowa	MD notification and patient release required – Registry initiates contact	28	3	11
Indiana	MD permission to contact patient required – RTI initiates contact	50	5	10

LA = Los Angeles; SEER = Surveillance, Epidemiology, and End Results.  
<sup>a</sup> Interview rate among identified cases = (# interviewed)/(# identified by participating registries).  
<sup>b</sup> In December 2010, the Texas institutional review board approved converting the patient-access pathway from "MD permission to contact patient required" to "MD notification only." At that time, Texas had the lowest interview rate among the 16 registries contributing data to the study.

### Descriptive Analysis 2

- Figure 3 depicts the interview rate, grouped by patient-access pathway. The highest interview rate occurred with the least restrictive pathway (MD notification only), whereas lower response rates occurred with more restrictive pathways (MD permission to contact patient required and MD permission and patient release required).
- There was little variation in interview rate whether RTI or the registry initiated contact; however, registry-initiated MD permission contacts yielded higher interview rates compared with RTI-initiated MD permission contacts (33% vs. 25%).

Figure 3. Interview Rate Among All Cases Identified From Registries Contributing Data, Collapsed by Patient-Access Pathway, in Descending Order of Interview Rate (N = 2,913)

Type of Patient-Access Pathway	Total Identified	Total Interviewed	Interview Rate <sup>a</sup> %
MD notification only – RTI initiates contact (5 registries)	993	390	39
Only patient release required – RTI initiates contact (2 registries)	606	218	36
MD notification and patient release required – Registry initiates contact (4 registries)	650	226	35
Only patient release required – Registry initiates contact (2 registries)	238	81	34
MD permission to contact patient required – Registry initiates contact (1 registry)	122	40	33
MD permission and patient release required – Registry initiates contact (1 registry)	84	26	31
MD permission to contact patient required – RTI initiates contact (3 registries)	220	55	25

<sup>a</sup> Interview rate among identified cases = (# interviewed)/(# identified by participating registries).

### Descriptive Analysis 3

- Figure 4 depicts the impact of increased lag time on the interview rate for cases where contact information has been released to RTI for the Full Release Population by the cancer registry. Results show a consistent relationship between higher interview rates and shorter lag time.

Figure 4. Interview Rate by Lag Time for the Full Release Population<sup>a</sup> (n = 1,819)

Lag Time, Years	Total Reported to RTI With Contact Information	Total Interviewed	Interview Rate <sup>b</sup> %
0-1	629	277	44
1-2	691	249	36
2-3	213	68	32
> 3	286	69	24

<sup>a</sup> The Full Release Population is reported from the following registries: LA SEER, California, Texas, Florida, North Carolina, Indiana, Pennsylvania, Ohio, Arizona, and Johns Hopkins.  
<sup>b</sup> Interview rate among identified cases = (# interviewed)/(# reported to RTI with contact information).

## CONCLUSIONS

- There is an inverse correlation between complexity of the patient-access pathway and interview rate (i.e., as the patient-access pathway complexity increases, the interview rate decreases).
- Interview rates at registries where "MD permission to contact patient required" is the requisite patient-access pathway may be higher when the registry makes initial contact than when RTI makes initial contact because physicians may be more willing to respond to a local institution.
- As expected, interview rates were lower as the time between the date of diagnosis and the date contact information was reported to RTI increased.

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