Using Cancer Surveillance Data to Advance Science: Monitoring for a Potential Safety Signal for Approved Drugs Through Linkage Studies

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Presentation Objectives

• Provide background on the study
• Describe cancer registry enrollment
• Describe the outcomes of the first two linkages
• Describe the resources required to enroll registries and perform the linkage
• Describe the challenges associated with implementing a multiyear, multistate data linkage
Forteo Patient Registry

• Forteo (teriparatide) was initially approved in 2002 in the 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

• In July 2009, as a condition of approval for a new indication (use) for Forteo, the FDA required the implementation of a voluntary, prospective registry to estimate the incidence of osteosarcoma in patients receiving treatment with Forteo
Forteo Patient Registry

• Eligibility criteria for enrollment
  – Aged 18 years or older
  – Received a Forteo delivery device during the 2009-2014 enrollment period

• Patient participation
  – Complete a pre-enrollment form to indicate interest
  – Confirm having taken Forteo
  – Complete a registration form and provide a small amount of personal information required for linkage
  – Sign a consent form to allow state cancer registries to link the patient’s information to the cancer registry database
Study Background

• 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

• Data from the Forteo Patient Registry database will be linked with a minimum of 25 state cancer registries annually from 2010-2021
Methods for Cancer Registry Recruitment

• RTI-HS invited cancer registries in all 50 states plus DC to participate in May 2009
• States that expressed interest were contacted and their specific requirements for study approval were assessed
• An Access database was created to track the recruitment process
• All necessary applications and agreements (IRB, data use committee, cancer registry, etc.) were submitted to individual state cancer registries

DC = Washington, District of Columbia; IRB = institutional review board; RTI-HS = RTI Health Solutions.
Cancer Registry Recruitment Plan

RTI invites registries to participate in first linkage

Registry interested in participating?

Yes

RTI works with registry contact to prepare all required documentation

No further contact with registry

No

RTI finalizes submission package and sends to registry

Registry requests modifications

Yes

RTI facilitates modifications and resubmits to registry

No

RTI works with registry contact to obtain all required approvals and place a work agreement

State is “linkage-ready”
Results - Cancer Registry Recruitment Efforts

- RTI-HS invited all 50 states plus DC to participate
  - 42 initially expressed interest in participating
  - 9 were unable to participate or were not interested
- Of the 42 states that initially expressed interest
  - 28 indicated approval by their local IRB would be necessary
  - 14 indicated they could defer to RTI’s IRB approval
- Based on information provided by interested registries, at least 78 unique reviews would be required for these 42 states
  - Reviews included local IRB, cancer registry, Data Use Committee, Department of Health, etc.
Results - Time Required to Become Linkage-Ready

• States were considered “linkage-ready” once all required approvals were obtained and a work agreement was in place

• Average time from submission of the first application to the date the registry was linkage-ready
  – 27 states that participated in the first linkage in 2010
    • 94 days (range 10 days to 195 days)
  – 10 additional states that participated for the first time in the 2011 linkage
    • 309 days (range 119 days to 547 days)
State Cancer Registry Status as of May 31, 2012

Participation by State:
- Participated in 2011 linkage (n = 37)
- Approval in process (n = 2)
- Not currently able to participate (n = 12)
Results for 2010 and 2011 Linkages

• 2010 linkage
  – 27 states participated; 70% of the US population 18+ years
  – 6,338 patients in FPR linked with 431 adult osteosarcoma
    patients diagnosed 1 January 2009 or later
  – No matches found

• 2011 linkage
  – 37 states participated; 85% of the US population 18+ years
  – 16,365 patients in FPR linked with 961 adult osteosarcoma
    patients diagnosed 1 January 2009 or later
  – No matches found

• 2012 linkage: planned for August/September
Resources Required – RTI

• Study team required to enroll registries and conduct linkage:
  – Senior epidemiologists
  – Research epidemiologists
  – Research assistants
  – Statistical analysts
  – Support staff (legal, office of research protection, administrative)
Resources Required – Cancer Registries

• Cancer registry involvement in the application process varied by registry
  – 14 deferred to RTI’s IRB
  – 28 required a local IRB approval
  – 3 were required to complete and submit the application themselves
  – Many reviewed the initial application and provided feedback on RTI’s submission
    • Several then submitted the application to their IRB on behalf of RTI

• For the linkage, registries needed someone to attend the RTI linkage training session and to perform the linkage
Lessons Learned

- Study approval at individual registries is an iterative process
- Although RTI could use core standardized text for common questions on applications, the level of detail and wording must be customized extensively to accommodate the format specific to each registry
- Some IRBs or registries require customization
  - State-specific forms had to be included in initial mailings to patients (CA, OR)
Conclusions

• Data from cancer registries play a significant role in this drug safety surveillance study and have the potential to play an even greater role.

• The results from the first two linkages indicate that it is possible for a large number of registries to concurrently perform a data linkage.
  – However, significant resources are required and there are substantial challenges in conducting multistate studies.
Conclusions

• In the absence of a national cancer registry with patient-level identifying data in the US, many studies, especially those investigating rare cancers, will require the participation of multiple state cancer registries.

• Processes that would facilitate future studies:
  – Standardized review packages across registries
  – Deferral to a central IRB
THANK YOU!

- Thanks to all our registry contacts who have made it possible to conduct this multistate, multiyear linkage study.