Complementary Observational Studies Assessing the Incidence Of A Rare Cancer Outcome by Linking State Cancer Registry Data to Large Pharmacy Claims Databases in the United States

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ABSTRACT

Background: There are many challenges to conducting traditional post-marketing surveillance studies for rare cancer outcomes including precise case identification, exposure assessment, longitudinal follow-up, and sufficient study size. Using two large pharmacy claims databases to identify exposure and linking to cancer registries to determine outcome is one novel approach currently being implemented in an ongoing safety surveillance program.

Objective: To describe methods using two pharmacy claims databases linked to state cancer registries to assess the incidence of osteosarcoma, a rare bone cancer, among patients taking teriparatide and a comparison group.

Methods: Two population-based pharmacy claims databases, a federal health insurance program and a commercial outpatient pharmacy database, are used to identify drug exposure and assemble the appropriate study cohorts. Cancer diagnosis information is obtained by linking the cohorts with state cancer registry databases who use the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) codes. Incidence of cancer among the exposed and unexposed cohorts will be estimated and compared.

Results: Approximately 30 different state cancer registries initially agreed to participate in these linkage studies. The process for conducting the linkages between two different pharmacy claims databases and individual state cancer registries must be tailored to meet data privacy and other local requirements for all data sources. For one pharmacy claims database, a deterministic linkage using a direct identifier will be implemented either through a trusted third party or by the individual registry. For the other pharmacy claims database, linkage will be conducted using de-identification technology.

Conclusions/Implications: Using large pharmacy claims databases to obtain drug exposure information and linking with cancer registries to determine cancer outcomes minimizes the possibility of misclassification of the tumor type and has the potential to improve monitoring for patient safety without imposing burden on the patient.

BACKGROUND

Long-term post-marketing surveillance studies are used routinely to monitor safety and to quantify the occurrence of safety outcomes among patients being treated with specific medications compared with similar patients with different or no treatment. Challenges to conducting traditional post-marketing surveillance studies for rare cancer outcomes include adequate case identification, exposure assessment, longitudinal follow-up, and sufficient study size.

During the drug testing process, the medicine in Forteo® caused some rats to develop a bone cancer called osteosarcoma. At the request of the US Food and Drug Administration and the European Medicines Agency, a retrospective study was initiated in the US and Europe at the time of approval. The study initiated in Europe lasted 10 years and has completed. The US study is an ongoing 15-year surveillance study collaborating with US cancer registries to identify and interview patients newly diagnosed with osteosarcoma to determine any with a prior history of Forteo treatment. In 2009, at the time of approval for new indication for treatment of glucocorticoid induced osteoporosis, Lilly initiated a new prospective US voluntary registry program for patients taking Forteo. Patients are followed through annual data linkages with participating US state cancer registries.

METHODS

STUDY DESIGN

- A federal health insurance program and a commercial outpatient pharmacy database are being used to identify drug exposure and will be linked with outcome data from state cancer registries.
- Incidence of cancer among the exposed and unexposed cohorts will be estimated and compared using incidence rate ratios.

DATA SOURCES

State Cancer Registries

- All cancer registries in the US are invited to participate in the study.
- A deterministic linkage will include a cohort of Forteo users and matched comparators with qualifying dispensed pharmacy claims matched on demographic variables across the claims study cohorts and cancer registry data.

Commercial Claims Database – IMS LRx

- The IMS Health longitudinal prescription database (LRx) consists of patient-level dispensed prescriptions that enable patient prescription filling behavior to be tracked across time, payers, and pharmacies.
- Forteo users aged 18 years and older will be matched to nonusers based on demographic and baseline characteristics.
- The LRx captures prescriptions purchased through all methods of payment (e.g., cash, Medicaid, third party).

Medicare - RTI

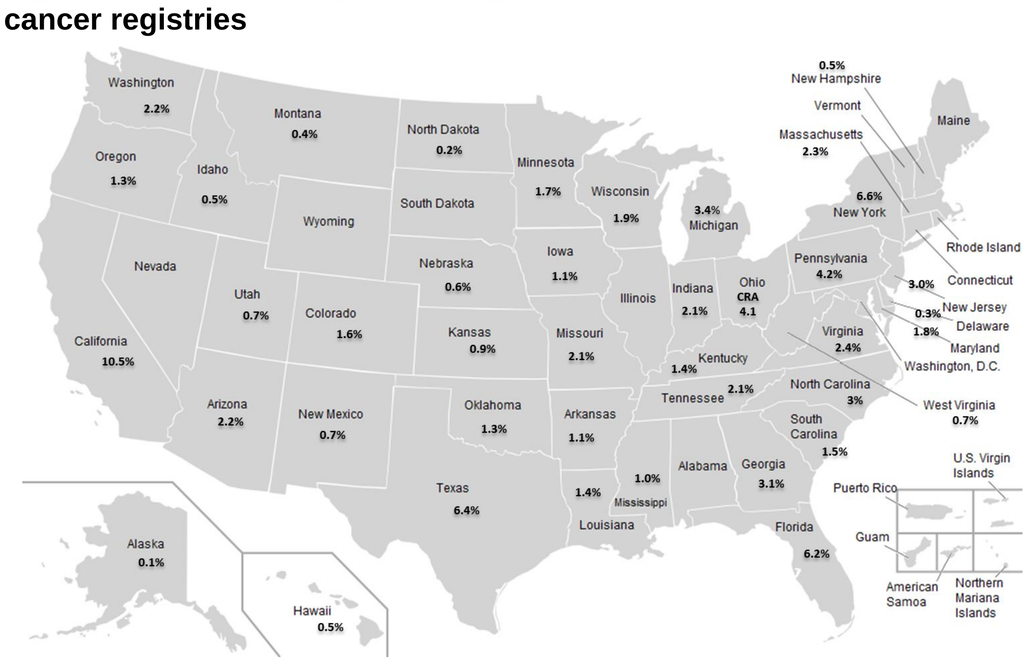
- Medicare is a federally sponsored health insurance program in the US that offers health coverage to 47 million people, including 39 million people aged 65 years or older and 8 million nonelderly people with a permanent disability (Cubanski et al., 2010).
- Forteo users aged 65 years and older will be matched to nonusers based on demographic and baseline characteristics.
- Medicare consists of Part A, which is hospitalization insurance; Part B, which covers physician services and outpatient care; and Part D, which is outpatient prescription drug coverage.

Data Linkages

- Drug exposure data will be ascertained from prescription drug claims using LRx and Medicare databases.
- Osteosarcoma diagnosis data outcome will be ascertained through linkage with state cancer registry data.
- Ascertaining exposure via prescription claims removes the possibility of recall bias and provides more information relating to duration of use than self-report. Ascertaining outcome through cancer registries minimizes the possibility of misclassification of the cancer diagnosis.
- Study teams will not have access to any personal health information. This will be managed by a trusted third party in each study.

METHODS (continued)

Figure 1. Map including percentage of the US population covered by state cancer registries



Study Outcome

Table 1. ICD-O-3 diagnosis codes used to identify osteosarcoma

Code	Description	Code	Description
9180/3	Osteosarcoma NOS	9186/3	Central osteosarcoma
9181/3	Chondroblastic osteosarcoma	9187/3	Intraosseous well differentiated Osteosarcoma
9182/3	Fibroblastic osteosarcoma	9192/3	Parosteal osteosarcoma
9183/3	Telangiectatic osteosarcoma	9193/3	Periosteal osteosarcoma
9184/3	Osteosarcoma in Paget's disease of bone	9194/3	High-grade surface osteosarcoma
9185/3	Small cell osteosarcoma	9195/3	Intracortical osteosarcoma

DATA FLOW DIAGRAMS

Figure 2. Commercial Claims Study

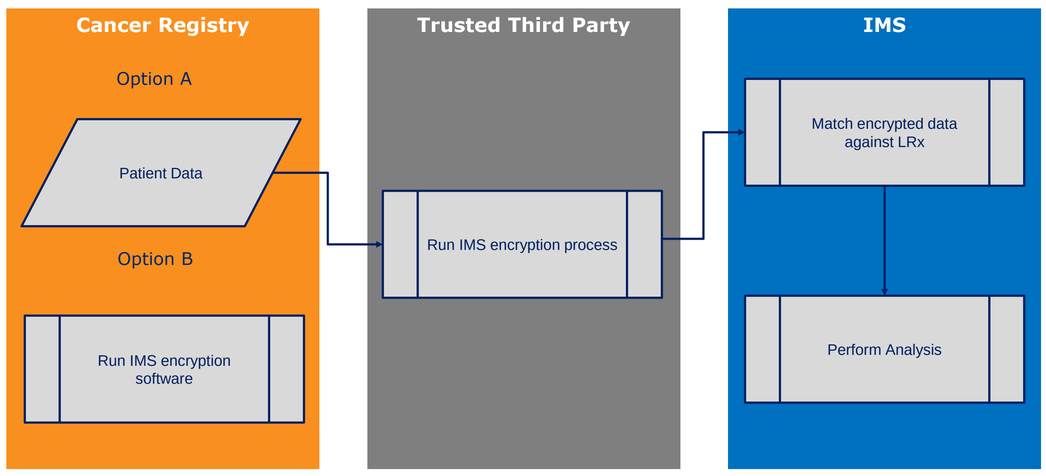
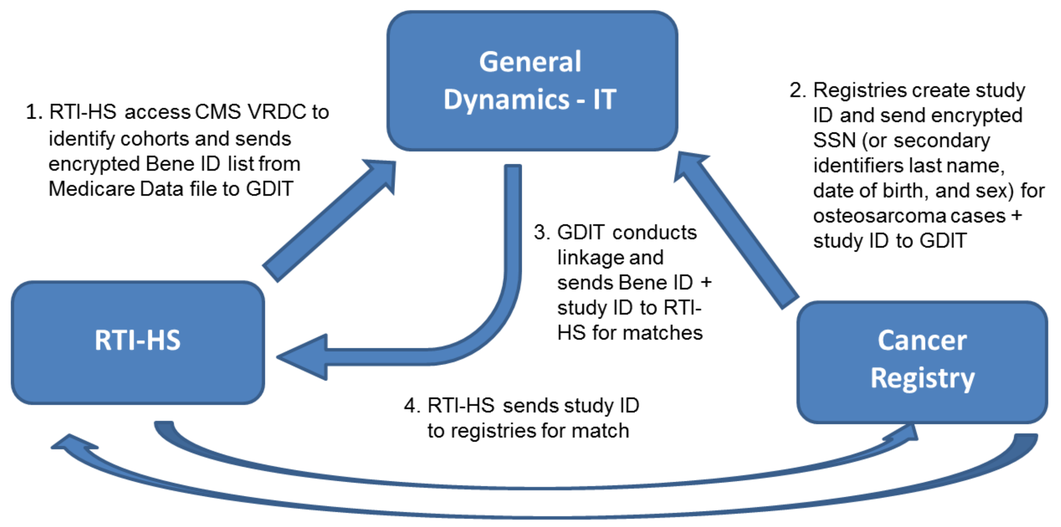


Figure 3. Medicare Database Study



Bene ID = Medicare beneficiary ID; ID = identification; RTI-HS = RTI Health Solutions; SSN = Social Security number

CONCLUSIONS

- Linkage studies allow for monitoring important drug safety issues with minimal patient burden.
- Large pharmacy claims databases are not anticipated to be biased with regard to the study outcome, and cancer registry data are the most accurate and complete population-based source of cancer outcomes.
- This study approach improves our ability to further investigate osteosarcoma, a rare outcome.

Conflict of Interest

- N. Kellier-Steele and D. Masica are full-time employees of Eli Lilly and Company, the study sponsor, and hold stock in Eli Lilly and Company.
- K. Midkiff, D. Harris, A. Gilsenan, D. Harris, and E. Andrews are full-time employees of RTI Health Solutions, which received funding from Eli Lilly and Company to conduct this study. The contract between RTI Health Solutions and the sponsor includes independent publication rights. RTI conducts work for government, public, and private organizations, including pharmaceutical companies.

Reference

Cubanski et al. Health Aff (Millwood). 2010;Sep;29(9):1725-33

32nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management, August 25-28, 2016; Dublin, Ireland

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