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“First in Flight” or “When Pigs Fly” – Can Cancer Registries Play a Critical Role at the National Level in Studying Cancer as an Adverse Outcome from Drug Treatments?

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The power of knowledge.
The value of understanding.

Objectives of Presentation

1. Provide background on the increasing public interest in post–FDA-approval safety studies of medications and efforts to evaluate cancer as an adverse outcome of nononcological therapies
2. Present analysis conducted in FDA postmarketing-commitment database and examples of signals under study highlighting strengths and limitations related to identification of cancer
3. Discuss future vision of the cancer registry's role in the effort to reduce uncertainty around the risk of cancer from drug treatments

FDA = Food and Drug Administration.

Background

- Increasingly important public health issue
  - Aging population, Increasing medication use
  - Market withdrawals
- FDA and NCI public meeting in September 2014
- Timing and tools for evaluation of cancer risk in medications:
  - Preapproval
  - Postapproval
- What role do cancer registries currently play?

NCI = National Cancer Institute.

Review of FDA's Postmarketing Commitment Database

- **Purpose**: Identify cancer signals under study in postapproval setting for nononcological drugs
- **Method**: Reviewed PMC database for drugs with NDA/BLA approval after 1993 to describe those using cancer registries
- **Results**: Of 46 postmarketing commitments, we found two studies that mentioned using cancer registries to identify cancer
  - Most studies were using active patient follow-up or surveillance to attempt to identify cancer outcomes

BLA = Biologic License Application; NDA = New Drug Application; PMC = postmarketing commitment.

Potential Cancer Associations Under Study in the Postapproval Setting

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Warning: Long-Term Safety of Topical Calcineurin Inhibitors Has Not Been Established

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors…

Therapeutic Class	Generic Drug Name	Cancer Safety Concern	How is concern being studied?
Dermatologic Agents	Tacrolimus Pimecrolimus	Lymphoma, skin All malignancies	Long-term pediatric AD registries

- Atopic dermatitis (AD) registries are not using cancer registries to identify cancer outcomes

Potential Cancer Associations Under Study in the Postapproval Setting

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Warning: Serious Infections and Malignancies

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers…

Therapeutic Class	Generic Drug Name	How is concern being studied?
Biologic and Immunologic Agents	Adalimumab Certolizumab Etanercept Golimumab Infliximab	• Pediatric and adult Crohn's disease registry • Adult psoriasis registry • Cohort study of patients with psoriasis

- Patient registries are <u>currently</u> not using cancer registries to identify cancer outcomes

Potential Cancer Associations Under Study in the Postapproval Setting

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Warning: Potential Risk of Osteosarcoma

In rats, teriparatide caused an increase in the incidence of osteosarcoma, a malignant bone tumor.

Therapeutic Class	Generic Drug Name	How is concern being studied?
Endocrine/ Metabolic Agent	Teriparatide	Long-term patient registry; case-series

- Both studies of teriparatide are currently using cancer registries to identify cancer outcomes
- No national cancer registry; high burden to include a large number of cancer registries at states and cancer centers

Potential Cancer Associations Under Study in the Postapproval Setting

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Warning: Risk of Thyroid C-Cell Tumors

Exenatide extended-release causes thyroid C-cell tumors at clinically relevant exposures in rats. It is unknown whether BYDUREON causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans…

Therapeutic Class	Generic Drug Name	How is concern being studied?
Endocrine/ Metabolic Agent	Exenatide Exenatide extended release	Prospective cohort study Case-series

- Prospective study used claims: small number of events, short duration, lacks sensitivity and specificity
- Case-series using cancer registry: no national registry, high burden to include large number of registries

Potential Cancer Associations Under Study in the Postapproval Setting

Therapeutic Class	Generic Drug Name	Cancer Safety Concern	How is concern being studied?
Endocrine/ Metabolic Agent	Pioglitazone	Bladder	Long-term cohort study

- Study is currently using the Kaiser Permanente Northern California registry to identify cancer outcomes
- Interim results are uncertain, no national registry for determining outcome in a larger population

KPNC = Kaiser Permanente Northern California.

Conclusion

- What happens when we don't use cancer registry data?
  - Designs may not reduce the uncertainty
  - Prospective cohort studies for drug safety are expensive
  - We resort to data sources with inherent limitations (e.g. claims, EMRs)
- How can cancer registries help?
  - Cancer registry data have additional "untapped" public health value by reducing the uncertainty of the risk of cancer from drug treatments
  - Linking study cohorts from postapproval studies to cancer registries at a national level would provide a valid and efficient mechanism to quantify cancer risks
- Why aren't we using cancer registries?
  - Lack exposure information
  - Not linkable on a national level
  - Challenging to navigate approvals to encourage substantial population coverage

Possible Solutions/Examples

- National Death Index
- Virtual Pooled Registry Data Project
- United Kingdom (Clinical Practice Research Datalink [CPRD])
  - Increasing record linkage between clinical data, exposure information, and cancer registry data
- Nordic country registries
  - Finland
  - Sweden

Thank You!

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