Reimagining Cancer Care & Drug Development through Real-World Data Creation

flatiron

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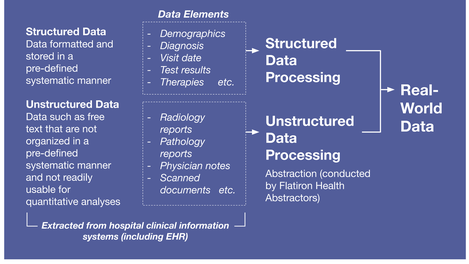
BACKGROUND & OBJECTIVES

- To date, the gold standard for evidence generation for oncology treatment has been prospective clinical trials; yet, the generalizability and representativeness of findings from clinical trials remain a challenge,[1-3] with only approximately 5% of cancer patients participating in clinical trials.[4,5]
- The potential applications of real-world data (RWD) in improving cancer care have become a growing focus in recent years. In Japan, while the development and application of RWD have gained traction in recent years, there remains room for improvement in data quality and methodological approaches.[6,7]
- This ongoing study therefore aims to contribute to improving cancer treatment and outcomes in Japan by constructing electronic health record (EHR)-based, longitudinal, patient-level RWD.

METHODS

- Flatiron Health is constructing oncology RWD by processing information extracted from clinical systems in Japanese hospitals.
- By leveraging over 10 years of experience in the US, and adapting the US-proven approach of abstraction,[8,9] Flatiron Health K.K. is developing local methodologies to curate high-quality oncology RWD in Japan (Figure 1).

Figure 1. Flatiron Health's real-world data curation approach.



FLATIRON HEALTH IN THE US

3.5M+ **Patient Records**
- **75%** from community practices
- **25%** from academic medical centers

> 200 **Community Cancer Centers**

8 **Academic Medical Centers**

Oncology RWD in 22 indications, with applications in:

23 **Regulatory submissions**
See Figure 2 for examples

> 15 **Health technology assessments (HTA)**

500+ **Peer-reviewed publications and conferences**
(e.g. JAMA, JCO, The Oncologist, ASCO, AACR)

PARTNERSHIPS:

U.S. FOOD & DRUG ADMINISTRATION — Research collaboration on the applications of RWD in regulatory decision-making[10]

NICE National Institute for Health and Care Excellence — Research collaboration on the use of EHR-derived RWD for HTA decision-making[11]

NCCN National Comprehensive Cancer Network® — Applications of RWD in clinical decision support[12]

Figure 2. Key regulatory and access approvals utilizing Flatiron Health's US RWD.[13-16]

FDA Label Update (2021)
Cetuximab (Erbitux)
New dosage regimen for metastatic colorectal cancer & squamous cell head and neck cancer

FDA Approval (2021); Natural history elucidated using RWD
Sotorasib (Lumakras)
New drug approved for KRAS G12C mutated locally advanced or metastatic non-small cell lung cancer

NICE Appraisal - Recommended (2023)
Mobocertinib (Exkivity)
New drug recommended for EGFR exon 20 insertion mutation-positive advanced NSCLC after platinum-based chemotherapy

CONTINUOUS ADVANCEMENT OF METHODOLOGIES AND QUALITY OF ONCOLOGY RWD

Assessing Data Quality in Flatiron Health RWD:

Relevancy
- **Availability**
- **Sufficiency**
- **Representativeness**

…of data within the appropriate **time period** to address a **given use case.**

Reliability
The degree to which data **represent the clinical concept intended,** as assessed by…
- **Accuracy**
- **Provenance**
- **Completeness**
- **Timeliness**

Improving Data Quality and Scope of Flatiron Health RWD

Linkage with the External Data Sources
- Linkage of EHR-derived data with other data sources including clinico-genomics data, claims data, obituary data and prospectively-collected data for specific use cases.

Development of NLP/ML approaches for effective unstructured data processing
- Leveraging natural language processing (NLP) and machine learning (ML), in addition to abstraction, for greater efficiency in unstructured data processing.[9,17]
- For example, an algorithm was developed for accurately extracting ECOG PS scores from unstructured data, improving data completeness from 61.5% to 75.6%[18]

FLATIRON HEALTH IN JAPAN: COLLABORATION WITH NATIONAL CANCER CENTER HOSPITAL EAST

Objective: To curate high-quality oncology RWD in Japan

Comparison with Flatiron Health's Approach in the US

	PATIENT CONSENT	DATA TRANSFER IN JAPAN	DATA PROCESSING IN JAPAN	PROVISION OF RWD Research-Ready Datasets
Approach	• Obtain relevant informed consent (IC) from eligible patients with a diagnosis of gastrointestinal cancers or other cancers. • Only the medical records of patients who provide IC will be utilized.	• Reduce sensitivity and securely share data with Flatiron Health K.K. • Data transfer approach customized to meet NCCHE's technical infrastructure and requirements.	• Medical records are appropriately de-identified in line with local legal, ethical and security requirements*. • De-identified data are processed locally via abstraction and other data processing approaches.	• The first Japan RWD products will be made available to researchers by the end of 2023.
Similarities	• Protecting patient privacy is central to all Flatiron Health activities • Handling of data privacy in accordance with relevant local ethics, privacy and legal requirements*		• Same high-quality, validated data processing approaches (harmonization, abstraction etc.)	• Rich longitudinal datasets based on unstructured and structured EHR data
Differences	• Obtaining IC from eligible patients, instead of the opt-out framework under the Health Insurance Portability and Accountability Act (HIPAA)	• Data transfer approach tailored to Japanese EHR systems, including local language and system requirements	• Abstraction and other data processing conducted in Japan, in line with local clinical context and in local language	• Data model adapted for local standard of care • Provided via the Flatiron Research Platform, based on the robust Trusted Research Environment framework's requirements[19]

Potential Use Cases Utilizing Flatiron Health Japan's RWD

- **Regulatory use cases (e.g. new drug application, label expansion)**
  - Characterize therapeutic context (e.g., treatment sequencing, testing patterns)
  - Characterize additional cohorts not included in clinical studies
  - Serve as a data source for external controls
  - Evaluation of real-world clinical endpoints such as progression-free survival (PFS), overall survival (OS), time to treatment discontinuation (TTD), time to next treatment (TTNT) etc. in the post-marketing setting
- **Integrated evidence generation**
  - Explore real-world treatment patterns, testing patterns, patient journey etc.
  - Evaluate comparative effectiveness and association between clinical outcomes, treatment or testing patterns and patients' demographic / clinical characteristics (e.g. age, gender, ECOG PS)
- **Methodological advancements**
  - Investigating approaches for improving quality, minimizing bias, and identifying fit-for-purpose, multinational applications of EHR-based RWD

* To safeguard patient privacy, handling of personal information and data privacy are conducted in accordance with the Declaration of Helsinki, the Ethical Guidelines for Life Science and Medical Research Involving Human Subjects, and the Act on the Protection of Personal Information in Japan.

PLANS FOR THE FUTURE

- RWD can play an important role in accelerating cancer research and improving outcomes. To date, high-quality, fit-for-purpose sources of RWD have not been readily available in Japan, but this novel collaboration aims to address this challenge. Flatiron Health Japan RWD are anticipated to inform cancer research and decision-making by clinicians, health authorities, and industry stakeholders.
- In addition to launching its first Japanese datasets in gastric and colorectal cancer in late 2023, Flatiron Health is also establishing a network of partnerships across the country, with the goal of curating a representative database of cancer treatments and outcomes across Japan. Data from these partnerships will be curated and made available for research in 2024 and beyond.
- Flatiron Health also aims to engage local regulatory authorities and other experts in Japan to discuss and establish best practices for the fit-for-purpose usage of RWD in supporting regulatory submissions and other use cases.

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