Evidence Modernization in Oncology: A Regulatory Perspective

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Cancer Drug Development Forum

FDA Oncology RWE Program Overview

Established 2020

Program Statement

Collaboratively advance the appropriate use of real-world evidence in oncology product development to facilitate patient-centered regulatory decision-making.

Oncology RWE Program

Focus Areas

- Regulatory Review
- Regulatory Science Research
- Collaborations & Outreach
- Education & Engagement

FDA Oncology Real World Evidence Program

Regulatory Review

Completed ~200 Oncology RWE consults across FDA centers

Regulatory consults for Oncology RWD increasing over time

Drugs (CDER)

Devices (CDRH)

Biologics (CBER)

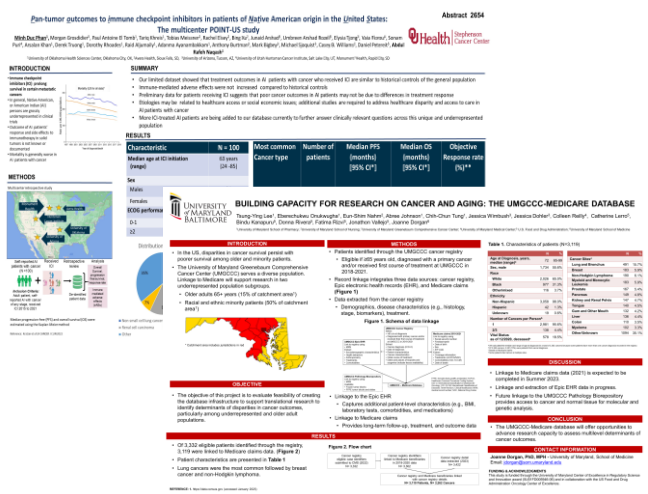
TEAM ForRWD
Translational Evaluation and Assessment of Methods to Facilitate use of Oncology RWD

Regulatory Science Research

Initial Program Strategic Goals

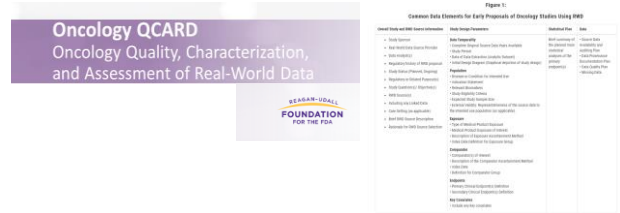
Enhance Source Data

- ALLIANCE, mCODE
- UMGCCC-Medicare Database
- OU AI/AN Database
- ASH Collaborative



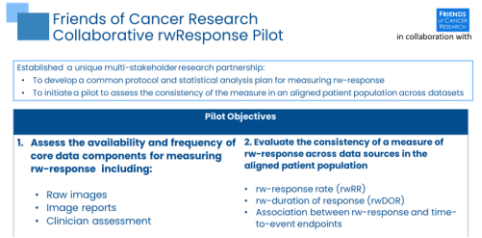
Standardize Submissions

- Oncology QCARD
  (Reagan Udall Foundation)



Develop Real World Endpoints

- rwResponse Study
  (Friends of Cancer Research)
- rwLugano Criteria
  (Cardinal Health)



REGULATORY OVERVIEW

Recently Released FDA RWE Guidances

Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products
Draft Guidance for Industry, September 2021

Data Standards for Drug and Biological Product Submissions Containing Real-World Data
Draft Guidance for Industry, October 2021

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry
Draft Guidance for Industry, November 2021

Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products
Draft Guidance for Industry, December 2021

Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products
Guidance for Industry, September 2022

Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products
Draft Guidance for Industry, February 2023

RWD Source
Submissions
Design

FDA RWE Program: https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

RWD and RWE for Regulatory Purposes

Effectiveness and/or Safety of a New Molecular Entity or Unapproved Product

Labeling Change(s) for an Approved Product

Postmarketing Requirement(s)/ Postmarketing Commitments(s)

Contextual Evidence (Natural History, Utilization, Patterns, or Trends)

Real-World Data: Key Factors→ Reliability and Relevance

For all study designs, it is important to ensure data **reliability** and **relevance**

Reliability

includes data ***accuracy***, ***completeness***, provenance, and ***traceability***

Relevance

includes the availability of key ***data elements*** (exposure, outcomes, covariates) and sufficient number(s) of representative patients

Alpelisib

Accelerated approval on 4/5/2022 for PIK3CA-Related Overgrowth Spectrum (PROS)

Indication: Treatment of patients ≥2 years of age with severe manifestations of PROS who require systemic therapy

Alternative Design Rationale	• Unfeasible to do clinical trial
Rare Disease	• Prevalence ~14 people per million
High Unmet Medical Need	• No approved therapies
Predefined Plans	• Study Objectives and Endpoints, SAP, Enrollment Guidance for EAP
Objective Outcome Validation	• Images available with Blinded Independent Central Review, durable response, ClinRo

Provide substantial evidence of effectiveness and a positive risk: benefit assessment

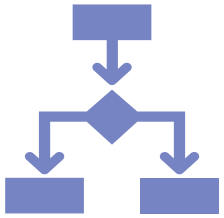
Use of RWD for Regulatory Purposes

Predefine

All essential elements of study

(design, analysis, conduct)

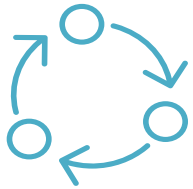
Describe



How each element was ascertained

from selected RWD source(s)

Address



Issues essential to determining reliability and relevance

of the data in the protocol (including ability for auditing)

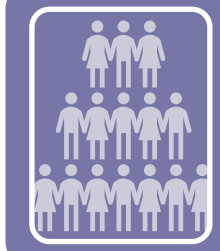
Consult

Confer with FDA prior to start of study

Target population, linkages, exposure, covariate, outcome ascertainment & validation

Current State

Complex and Restrictive



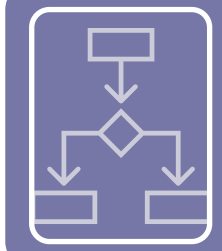
Resource Intensive

Highly Burdensome

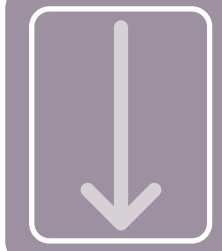
- Patients
- Providers

Future State

More streamlined and generalizable



Targeted
Objective-focused
Approaches



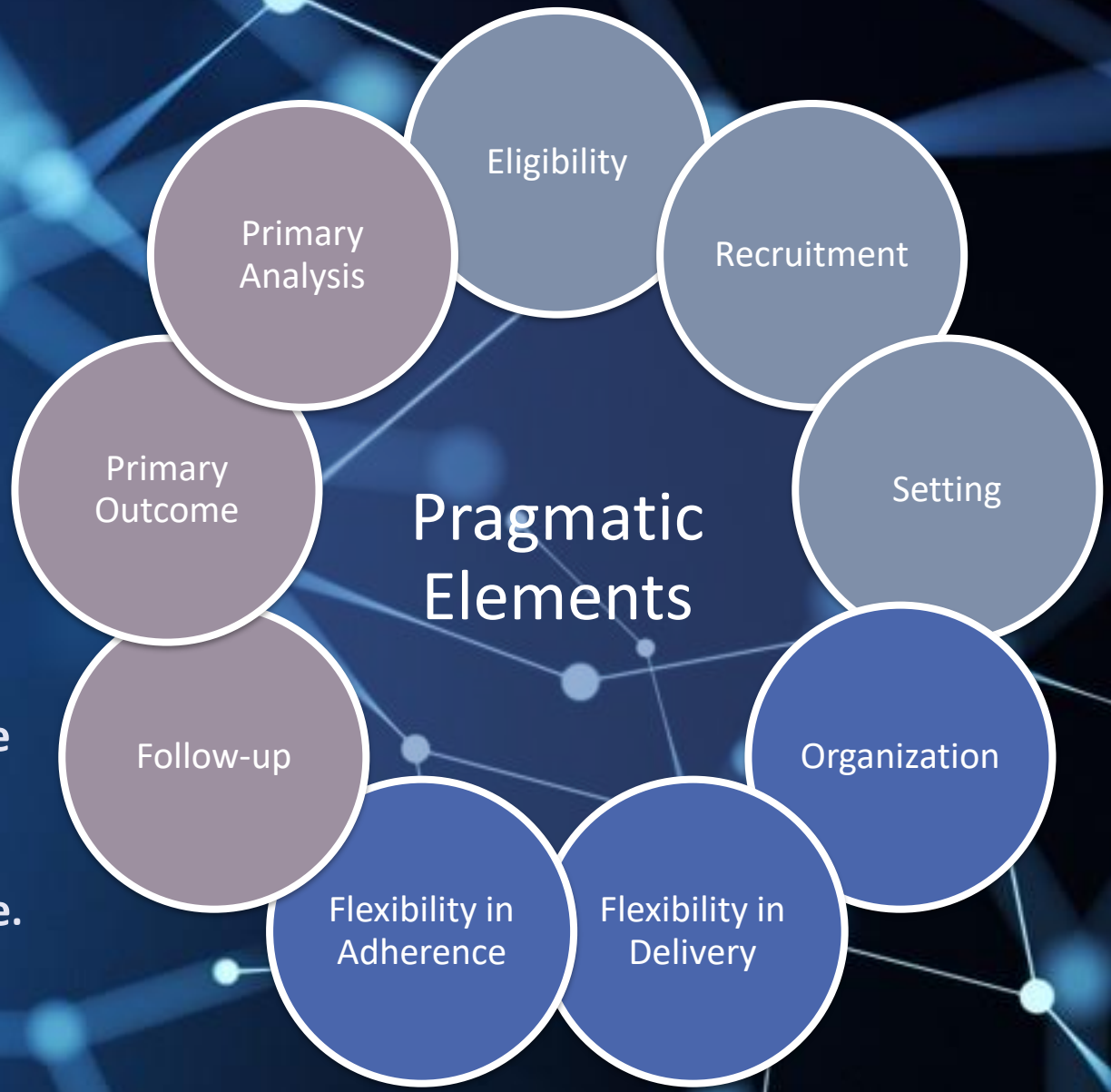
Closer to Routine Care

- Increased Access
- Appropriate Flexibilities

OCE Project Pragamatica

Objective

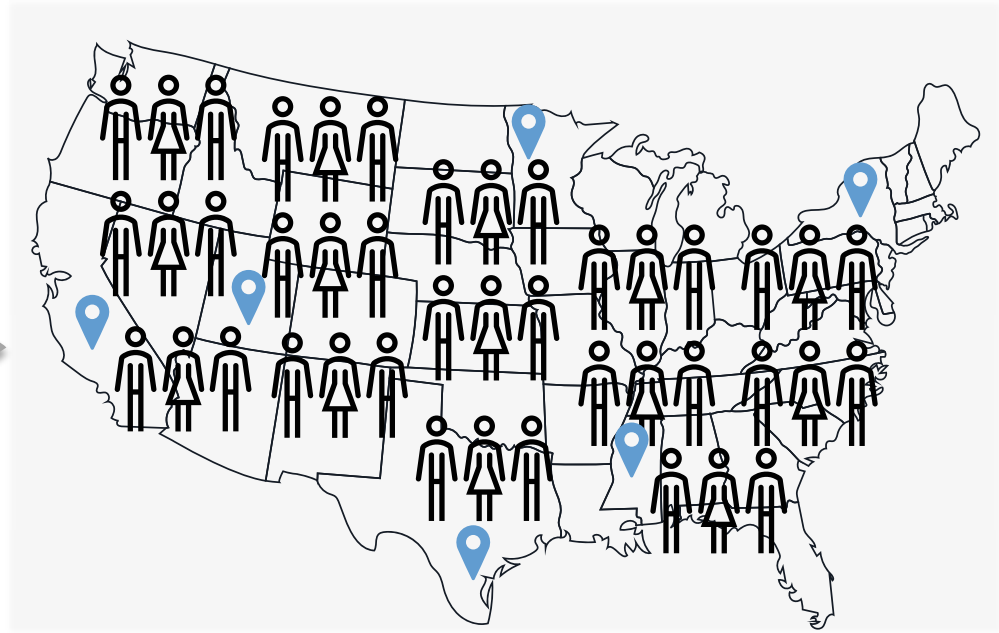
Advancing evidence generation for approved oncology medical products by exploring innovative trial design approaches that introduce functional efficiencies and patient centricity through integration with real-world routine clinical practice.



Enhancing Generalizability

Clinical Trials

Real World US Population



Possibilities

Challenges

Oncology RWD

Possibilities

- Rapid Characterization of Emergent Public Health Needs
- Innovative Prospective Designs
- rwResponse Data Ascertainment and Validation
- Understanding Drug Effects in Underrepresented Populations

Challenges (and Progress)

- Source Data and Quality
- Causal Inference in Noninterventional Studies
- Availability and Analysis of Raw Imaging Data


Enhance Regulatory Review
Advance Regulatory Science

Oncology QCARD

Oncology Quality, Characterization, and Assessment of Real-World Data

REAGAN-UDALL FOUNDATION FOR THE FDA

Background: Oncology review divisions receive a high volume of RWD containing submissions in a non-standardized format

Issue: Initial RWD submissions provide insufficient information to allow for substantive review and evaluation with continuous need for clarification (e.g., consistent gaps, repeated sponsor questions)

Objective: Provide structure that can support the inclusion of sufficient information for initial characterization of oncology RWD submissions

Benefit: Increasing efficiencies and facilitating more effective communication

OCE Scientific Collaborative

Clin Cancer Res. 2021 Oct 1;27(19):5161-5167. doi: 10.1158/1078-0432.CCR-20-4429.

The FDA Oncology Center of Excellence Scientific Collaborative: Charting a Course for Applied Regulatory Science Research in Oncology

Julie A Schneider [1], Yutao Gong [1], Kirsten B Goldberg [1], Paul G Kluetz [1 2], Marc R Theoret [1 2], Laleh Amiri-Kordestani [2], Julia A Beaver [1 2], Lola Fashoyin-Aje [1 2], Nicole J Gormley [2], Adnan A Jaigirdar [1 3], Steven J Lemery [1 2], Pallavi S Mishra-Kalyani [4], Gregory H Reaman [1], Donna R Rivera [1], Wendy S Rubinstein [1 5], Harpreet Singh [1 2], Rajeshwari Sridhara [1], Richard Pazdur [1 2]

- Cell/gene and personalized neo-antigen-based therapies for cancer
- Health equity and special populations
- Immuno-oncology
- Oncology patient-focused drug development
- Oncology safety
- Oncology trial designs, endpoints and statistical methodologies
- Pediatric oncology
- Precision oncology
- Rare cancers

OCE Projects

Project ASIATICA (ASian americans, nATive hawaiian, and other paCific islAnders) aims to bring focus and awareness to Asian Americans, Native Hawaiians, and Other Pacific Islander (AA & NHPI) patients with cancer.

Project Catalyst provides guidance and educational resources that help support informed anticancer therapy development to expedite the availability of directed and novel cancer treatments to the public, working primarily with small pharmaceutical companies and academic life science incubators and accelerators.

Project Community is a public health outreach initiative established for patients living with cancer, survivors, advocates, families, and people living in underserved urban and rural communities who are at greater cancer risk.

Project Confirm is an initiative to promote the transparency of outcomes related to accelerated approval for oncology indications

Project Equity is a public health initiative to ensure that the data submitted to the FDA for approval of oncology medical products adequately reflects the demographic representation of patients for whom the medical products are intended.

Project Facilitate is a single point of contact call and information center created to help oncology healthcare providers or regulatory professionals submit an Expanded Access Request for an individual patient with cancer through FDA's Expanded Access Program.

Project FrontRunner aims to encourage drug companies to consider the most appropriate line of treatment setting when developing new cancer therapies, such as in earlier clinical settings.

Project Livin' Label is an educational initiative that aims to foster broad understanding of the associated oncology product label and increase awareness of recent oncology drug FDA approvals in the cancer community.

Project Orbis provides a framework for concurrent submission and review of oncology products among international partners.

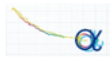
Project Optimus is an initiative to reform the dosage optimization and dosage selection paradigm in oncology drug development.

Project Patient Voice is an online platform for patients and caregivers along with their healthcare providers to look at patient-reported symptom data collected from cancer clinical trials.

Project Point/Counterpoint provides a new version of the Oncologic Drugs Advisory Committee (ODAC) briefing document that combines the company's and the FDA's positions in a single document.

Project Pragmatica seeks to introduce functional efficiencies and enhance patient centricity by integrating aspects of clinical trials with real-world routine clinical practice through appropriate use of pragmatic design elements.

Project Renewal is a public health initiative that aims to update the prescribing information (i.e., labeling) for certain older oncology drugs to ensure information is clinically meaningful and scientifically up to date



Project SignifiCanT (Statistics in Cancer Trials) promotes collaboration and engagement among diverse stake holders to further the design and analysis of cancer clinical trials with the goal to advance cancer therapies.

Project Silver is a public health initiative to increase representation of older adults (65 years and older) in cancer clinical trials with the goal of improving their treatment, care, and outcome through evidence base data.

Project Socrates provides educational opportunities for hematology/oncology fellows, basic and translational scientists, junior faculty, and others interested in learning more about regulatory science and drug development.

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- CDRH

Thank you!

Additional Questions?

Please email OCERWE@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION