Oncology Center of Excellence Patient-Focused Drug Development Updates

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OCE Patient-Focused Drug Development (PFDD) Program

The Oncology Center of Excellence PFDD program fosters collaboration between FDA Centers and external stakeholders involved in patient outcomes research in cancer populations.

- Engage with patients and advocacy groups,
- Research the measurement of the patient experience,
- Develop science-based recommendations for regulatory policy.

The overarching goal is to identify rigorous methods to assess the patient experience that will complement existing survival and tumor information to better inform a cancer therapy's effect on the patient.

https://www.fda.gov/about-fda/oncology-center-excellence/patient-focused-drug-development

Oncology Center of Excellence
PFDD Program

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Actively engaging with patients and advocacy groups

Fostering research into measurement of the patient experience

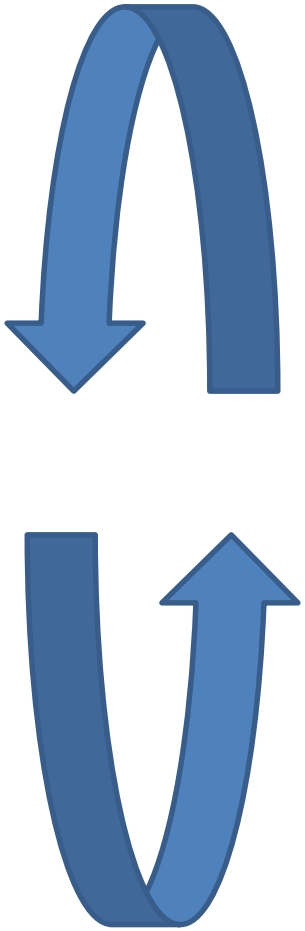
Generating science-based recommendations for regulatory policy

OCE PFDD Program

PFDD Education and Outreach
- Symposia/Workshops
- Reviewer Education
- Patient Engagement

PFDD Science
- Analysis and Presentation Methods
- Real-World COA Data
- Preference Data
- Wearable Devices

PFDD Regulatory Policy
- Consistency of advice
- SOPs, Guidances
- Review Practices



CDRH

CBER

CDER
- COA Staff
- Office of Biostatistics
- Office of Prescription Drug Promotion
- Office of Strategic Programs
- Office of Medical Policy

Outreach/Education

2018 and 2019 External Collaborations

Interagency:

National Cancer Institute (NCI), National Institutes of Health (NIH), Agency for Healthcare Research and Quality (AHRQ), Centers for Medicare and Medicaid Services (CMS)

Advocacy Groups:

Lungevity, Cancer Support Community, Friends of Cancer Research

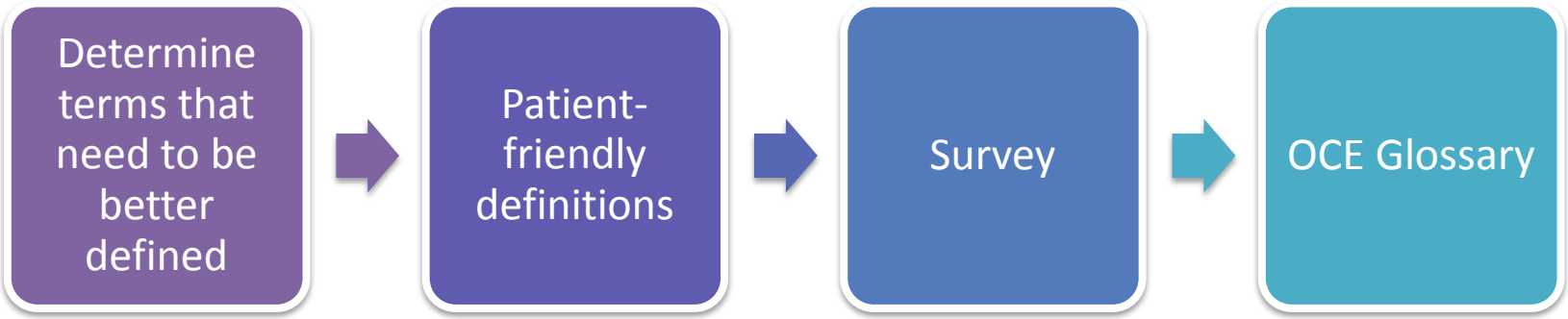
International Collaborations:

Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life, Standard Protocol Items: Recommendations for Interventional Trials Patient Reported Outcomes (SPIRIT-PRO), PRO Consortium ePRO Working Group, NCI Cancer Moonshot

Patient-Friendly Language Project

- An outside collaborative agreement with Cancer Support Community (CSC)
- Starting to create a list of clinical trial terms and definitions to include in OCE Glossary
- Querying patients through CSC and other means as well as querying industry and clinicians

Patient-Friendly Language Project



Example list of clinical trial terms

- Active Comparator Arm
- Adverse Event
- Drug-drug interaction
- Eligibility Criteria
- Wash-out period
- Protocol
- Randomized
- Endpoint
- Inclusion Criteria

Update on Efficacy Endpoint Definitions

- **Overall Survival** - The amount of time the patient is alive (with or without cancer) after the start of this treatment.
- **Progression Free Survival** - The average length of time after the start of treatment that patients are alive while the cancer does not grow or spread.
- **Disease Free Survival** - The length of time from the start of this treatment that patients show no sign of cancer.
- **Event Free Survival** - The amount of time after treatment ends that the patient remains free of complications from that treatment
- **Overall Response Rate** - The percentage of all patients whose cancer shrinks or disappears after treatment.
- **Treatment Discontinuation** - The amount time from when this treatment was started to when it was stopped.

Science

2018 and 2019 Science Collaborations

Research Collaborative Agreements

- Kaiser Permanente Northern California - *PanPROE accrual ongoing*
- Syapse- *Explore real-world toxicity*
- Cancer Support Community - *Query their patients*

Broad Agency Announcement

- BAA amendment - prospective study of physical function with ePRO and wearable devices- *accepting initial white papers*

2018 and 2019 Highlighted Publications

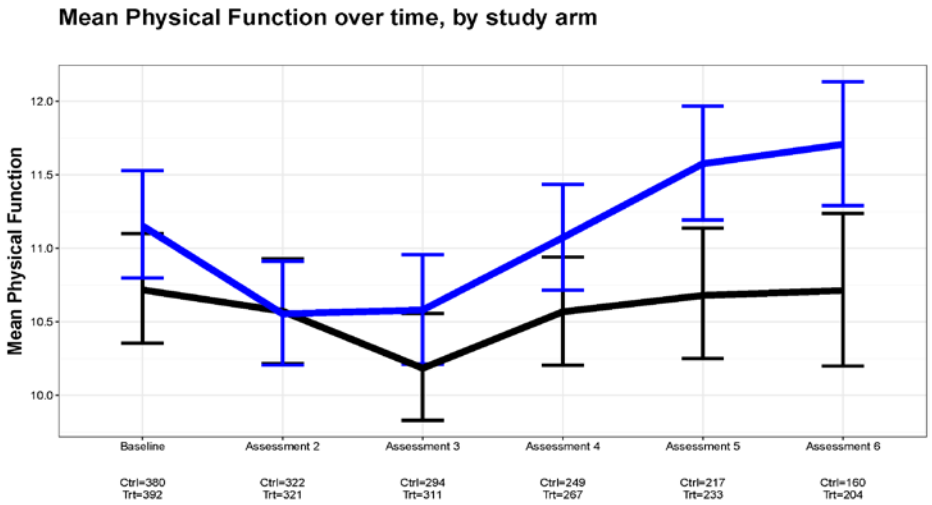
- Roydhouse, J.L., King-Kallimanis, B., Kluetz, P., Howie L., Singh, H. **Blinding and patient-reported outcome completion rates in US Food and Drug Administration Cancer Trial Submissions, 2007-2017**. (2018) *Journal of the National Cancer Institute.*
- Kim, J et al. **Use of PRO Measures to Inform Tolerability in Oncology Trials: Implications for Clinical Review, IND Safety Reporting, and Clinical Site Inspections.** (2018) *Clinical Cancer Research.*
- Roydhouse, J.L., Mallorie H. Fiero, and Paul G. Kluetz. **Investigating Potential Bias** in Patient-Reported Outcomes in Open-label Cancer Trials. (2019) *JAMA oncology*.
- Kim, J et al. **Patient-Friendly Language to Facilitate Treatment Choice for Patients with Cancer.** (2019), *The Oncologist*

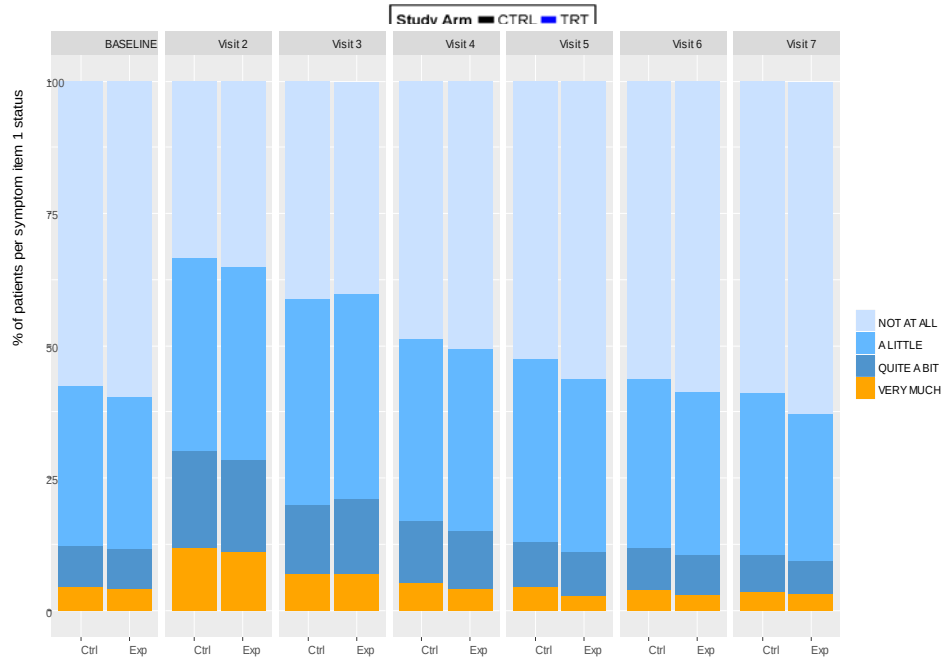
Policy

FDA Standard Information Request for PRO data

Includes:

- Patient Disposition
- PRO Completion Rates
- Mean subscale scores over time
- Change from baseline on subscales
- Descriptive bar charts for single item AEs





OCE PFDD Policies under consideration

1. PRO Measures to Inform Tolerability in Oncology Trials

2. Core COAs in Advanced or Metastatic Oncology Trials

Safety and Tolerability

1. Regulatory: Clinical Review: Does FDA ***require*** PRO data on symptoms be reviewed by clinical teams during trial conduct?

We do not dictate the depth of the PRO review during the conduct of cancer clinical trials

2. Regulatory: Safety Reporting: Will this data be considered safety data for purposes of FDA expedited IND safety reporting?

PRO data currently do not need to be reported as safety events to the FDA in the absence of a clinical evaluation

3. Regulatory: Inspections: How will FDA handle disparate PRO and Clinical results on a particular symptomatic adverse event?

PRO-CTCAE and CTCAE results are expected to be different. PRO-CTCAE results should not inform gaps or errors in CTCAE reporting during clinical site inspections.

Standard Approach to Core Outcomes

Core Clinical Outcomes

- Symptomatic adverse events & overall side effect impact
- Physical function & impact on work and leisure activities
- Disease-related symptoms

Assessment Frequency

Baseline, assessment frequency higher within first few treatment cycles

Instrument Selection

- PRO instrument fit for purpose
- Well-defined & reliable

Missing Data

- Procedures in place to mitigate missing data
- Reasons for missing data

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