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How FDA is Using Patient Experience Data in the Determination of Risk and Benefit

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CDDF MULTI-STAKEHOLDER WORKSHOP on INVOLVING PATIENTS IN ONCOLOGY DRUG DEVELOPMENT

June 18-19 Amsterdam

Disclosures

- I have no financial relationships to disclose
- Examples of instruments are for discussion and not endorsement

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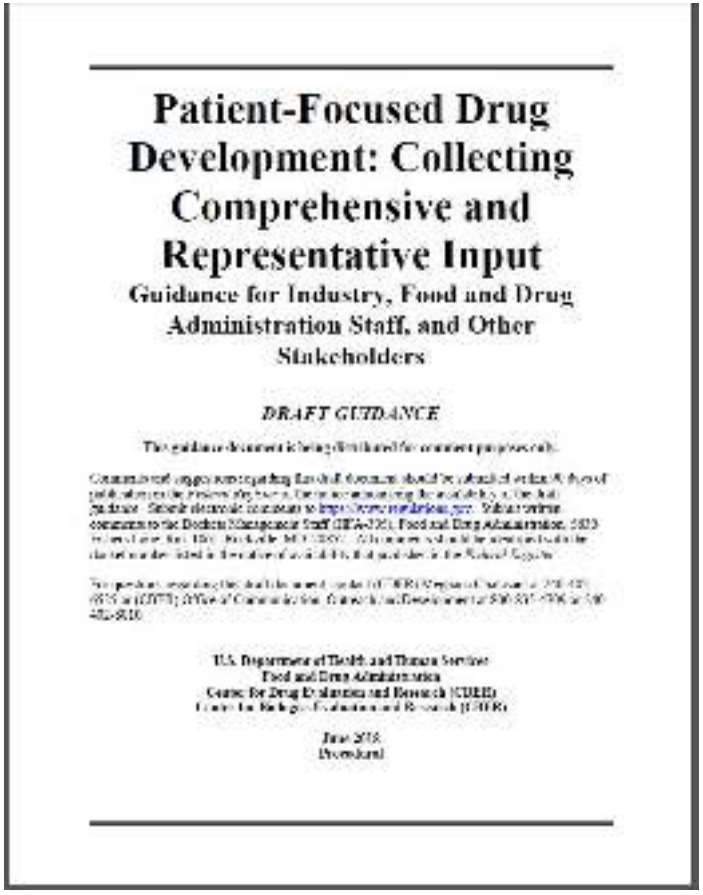
Topics Addressed in Series of Four Patient-Focused Methodological Guidances



Patient-Focused Drug Development: Collecting Comprehensive and Representative Input

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2018
Procedural

1

- Whom do you get input from, and why?
- How do you collect the information?

2

- What do you ask, and why?
- How do you ask non-leading questions that are well-understood by a wide range of patients and others?

3

- How do you decide what to measure in a clinical trial and select or develop fit-for-purpose clinical outcome assessments (COAs) ?

4

- Once you have a COA measurement tool ways to collect data using the tool, what is an appropriate clinical trial endpoint?

Slide courtesy of Meghana Chalasani

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Progress Update

PFDD Guidance 1: Collecting Comprehensive and Representative Input

- Workshop held on December 18, 2017
- Issued Draft Guidance in June 2018

PFDD Guidance 2-3: Methods to Identify What is Important to Patients and Select, Develop or Modify Fit-for-Purpose Clinical Outcome Assessments

- Workshop held on October 15-16, 2018
- Discussion Document published

PFDD Guidance 5: Developing and Submitting Proposed Draft Guidance Relating to Patient Experience Data

- Workshop held on March 19, 2018
- Issued Draft Guidance in December 2018

Workshop on Enhancing Patient Input on Clinical Trials

- Workshop held on March 18, 2019
- Convened by CTTI

Slide courtesy of Meghana Chalasani

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Oncology Center of Excellence
PFDD Program

Bellinda King-Kallimanis, PhD

Paul Kluetz, MD

Janice Kim, PharmD

Actively engaging with patients and advocacy groups

Fostering research into measurement of the patient experience

Generating science-based recommendations for regulatory policy

OCE Guidances

Two guidances that will provide information on:

1. PRO Measures to Inform Tolerability in Oncology Trials

2. Core COAs in Advanced or Metastatic Oncology Trials

21st Century Cures Act

Under 21st Century Cures Act Title III, Subtitle A, **Section 3001**, FDA is required to:

> *"make public a brief statement regarding the patient experience data and related information, if any, submitted and reviewed as part of the application."*

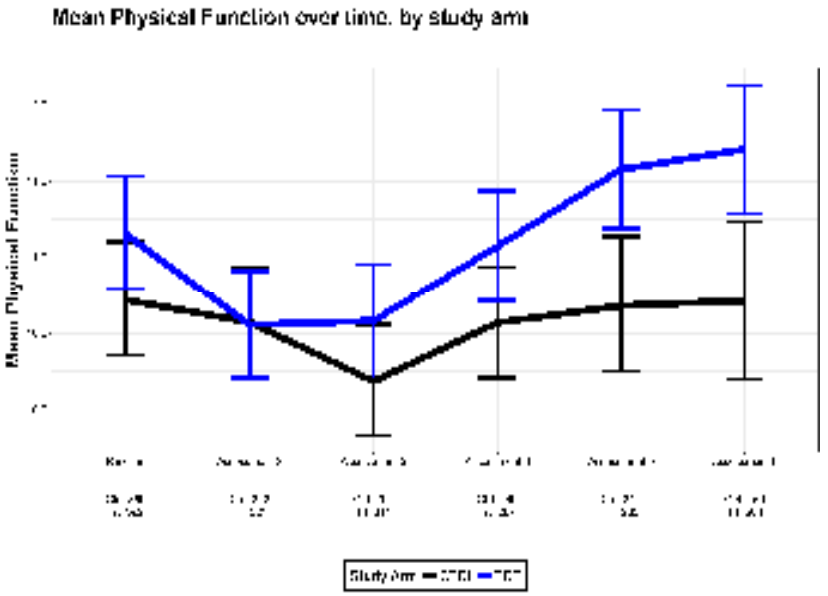
Under 21st Century Cures Act Title III, Subtitle A, **Section 3004**, FDA is required to publish no later than June 1 of 2021, 2026, and 2031:

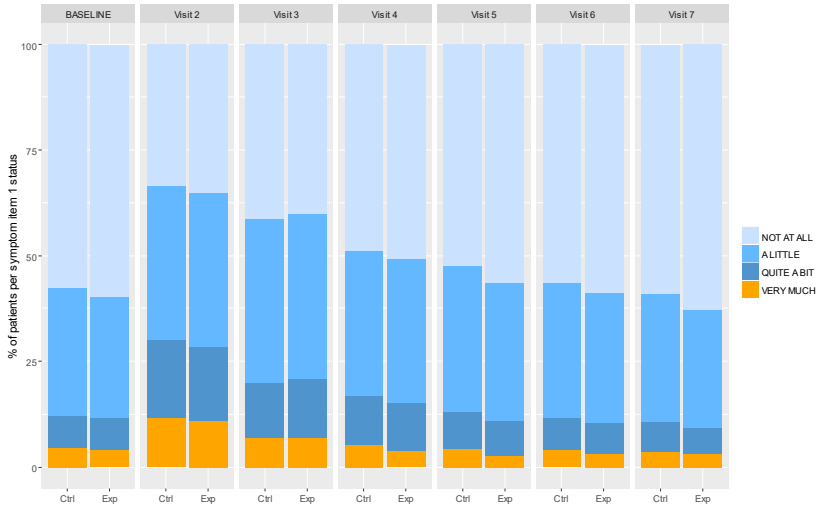
> *"a report assessing the use of patient experience data in regulatory decision making, in particular with respect to the review of patient experience data and information on patient-focused drug development tools as part of applications."*

FDA Standard Information Request for PRO data

Includes:

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





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Review Strategy

- Which instruments are being used? Concepts proximal to disease?
- Are PRO endpoints in the statistical hierarchy?
- What confounders could limit interpretability of results?
- How much data is missing?
- Is the assessment timing reasonable given the drug(s) being tested?
- Can conclusion be made based on the strength of results?
- What are the implications for patients, caregivers and practitioners?
- What is the best way to share PRO data (results) with the public?

Slide courtesy of Dr. Vishal Bhatnagar

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Example of an FDA Review

- **FDA Approval Summary: Pertuzumab for Adjuvant Treatment of HER2-Positive Early Breast Cancer**
  - Three PRO instruments: EORTC-QLQ-C30, EORTC-QLQ-BR23 and EQ-5D
  - The FDA review process for this information is evolving, but this is an example where the PRO data were carefully reviewed and included in the benefit:risk assessment

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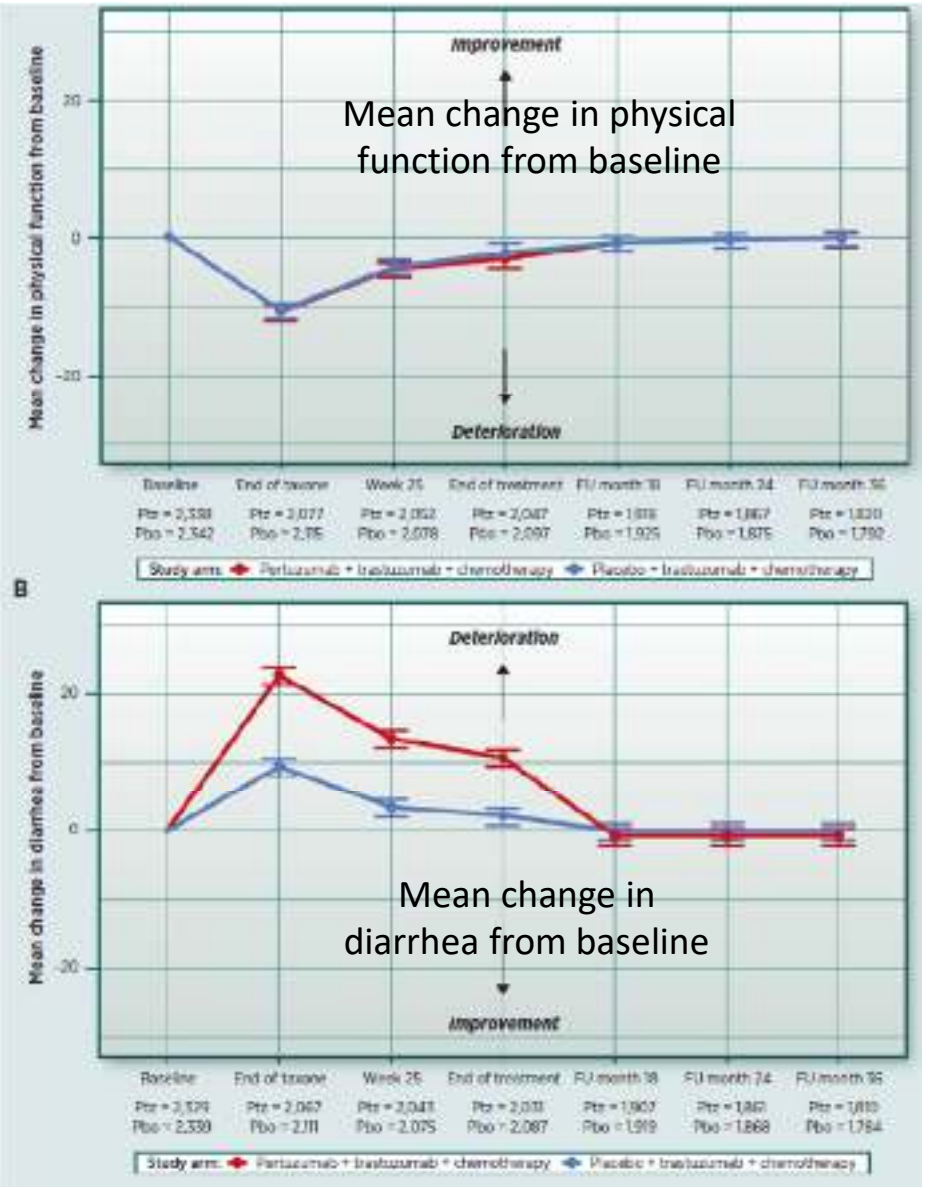
FDA Approval Summary: Pertuzumab

Similar physical function when looking at mean change from baseline

Claims of “no meaningful difference” that are not based on formal non-inferiority designs are problematic

Larger signals seen with single item symptoms



Howie, Lynn J., et al. 2019. *Clinical Cancer Research* 25.10

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COAs in Cancer Clinical Trials Workshop

Workshop Objectives

- Explore the use of ePRO in learning healthcare systems
- Review the ICH-E9-R1 structured "estimand" framework as a guide to link research objectives to suitable trial design, COA tools and endpoints to maximize the utility and interpretability of physical function assessments
- Obtain feedback on several cases of physical function research objectives and their impact on trial design and endpoint construction
- Generalize learnings to the broader FDA patient-focused drug development effort

July 12 -> registration either for in person or webinar https://www.fda.gov/drugs/news-events-human-drugs/fda-asco-public-workshop-2019-clinical-outcome-assessments-cancer-clinical-trials

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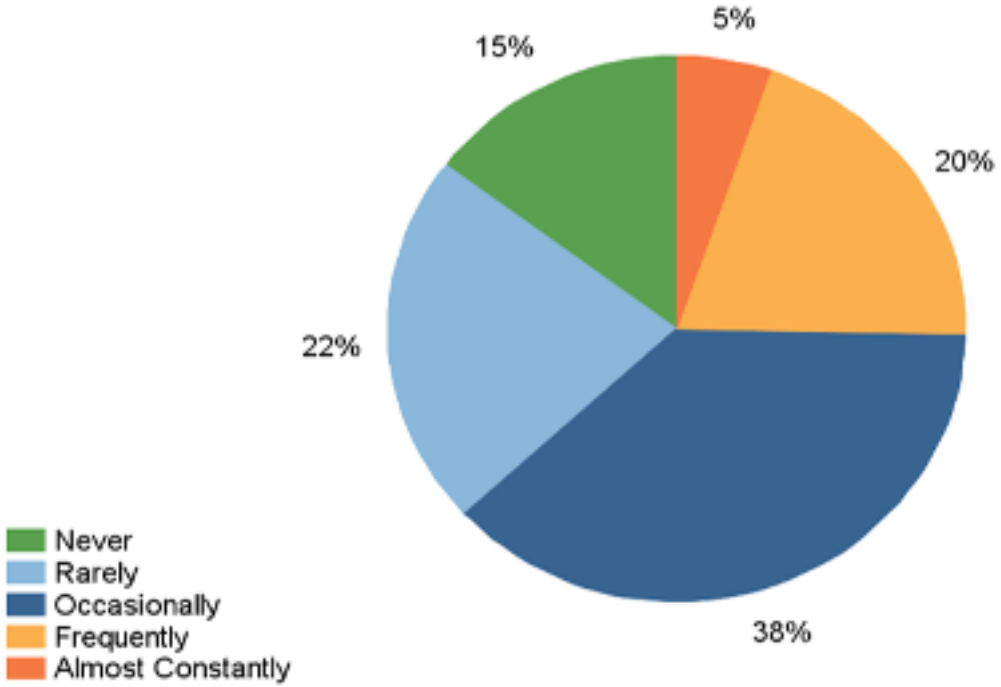
Pilot Project Patient Voice

Aim: *Adhere to the spirit of the 21st Century Cures mandate by exploring the possibility of creating a web-based public source of patient experience data that is accessible to patients, caregivers, and providers*

- Plan to align with the PRO IR from previous slide
- Plan to start with reporting symptomatic AEs only

Limitations: Project Patient Voice is intended as one of many tools for patients to use when discussing a drug with their physician. Do not rely on PatientVoice alone to make decisions about medical care. Do not use Patient Voice to substitute for advice from your health care professional. Conclusions about patient experiences with side-effects may be limited because the complete drug side-effect profile may not have been captured by the patient-reported survey.

Worst Loose or Watery Stool Score While on Therapy



Worst Nausea Score: This was calculated by finding the worst severity rating score a patient reported any time while the patient was taking

Worst Adjusted Nausea Score: This was calculated by finding only severity responses that were worse than the patients score before they

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Core PRO Consideration Across Advanced Cancer Trials

- Concentrate on core outcomes of physical function, symptomatic adverse events, overall side effect bother, disease symptoms
- Assess frequently early and then less frequently late
- Create a clear endpoint and analysis and put it in the statistical hierarchy if you want an efficacy claim

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