Novel Endpoints: A Regulatory Perspective

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Elektra J. Papadopoulous, MD, MPH
Clinical Outcome Assessments Staff
Office of New Drugs
Center for Drug Evaluation and Research, FDA
Disclaimer

- Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position.
Clinical Outcome Assessments Staff

• Mission:
  – Integrating the patient voice into drug development through clinical outcome assessment (COA) endpoints that are meaningful to patients, valid, reliable and responsive to treatment

• What we do:
  – Promote innovative, science-based review of COA development, validation, interpretation and communication of COA endpoints throughout the drug development life-cycle
  – Engage with internal and external stakeholders to advance good scientific COA standards and policy development
  – Address unmet medical needs by managing and leading the CDER’s Drug Development Tool Clinical Outcome Assessment Qualification Program
Patient-Focused Outcomes

Those outcomes important to patients’ survival, function, or feelings as identified or affirmed by patients themselves, or judged to be in patients’ best interest by providers and caregivers when patients cannot report for themselves

Donald L. Patrick, Ph.D., MSPH
May 20, 2013
Clinical Benefit

- A *positive clinically meaningful effect* of an intervention, i.e., a positive effect on how an individual *feels, functions, or survives*
  - How long a patient lives
  - How a patient feels or functions in daily life

- **Clinical outcome**: An outcome that describes or reflects how an individual feels, functions or survives
  - Assessed using clinical outcome assessments (COAs)
Highlights of 21st Century Cures and PDUFA VI

• 21st Century Cures and PDUFA VI increasingly places FDA as an active participant in drug development, broadening our traditional regulatory role

• Requires expanded efforts to enhance drug development
  – Patient-focused drug development: collect / analyze patient experience, to use in designing drug development programs (endpoints), and in regulatory decision making (endpoints and risk/benefit considerations)
  – Novel, innovative trial designs: use of complex adaptive and other novel trial designs – and how such clinical trials can be used to satisfy the substantial evidence standard
  – Real world evidence: using data regarding use or potential benefits and risks of a drug derived from sources other than randomized clinical trials – in support of new indications and post-approval study requirements
  – Drug development tools: biomarkers and COAs
Electronic capture of PRO data (ePRO) is also becoming standard, providing a rich pipeline of structured clinical data.

Mobile wearable technologies can complement traditional PRO surveys by generating objective, continuous activity and physiologic data.

Obtaining reliable wearable device data on activity level, coupled with direct patient report on their ability to carry out important day to day activities, can provide information on physical function that is directly relevant and important.

https://www.fda.gov/NewsEvents/Newsroom/FDAVoices/ucm619119.htm
How do we measure how patients feel and function?

**Traditional Approaches**

- Pain score 0–10 numerical rating
- Images of nurses and patients

**Novel Approaches**

- Images of wearables and virtual reality equipment
Some potential impacts of endpoints collected via remote data capture

- Enhancement of endpoints that matter to patients in daily life (e.g., information of patients’ experiences between clinic visits)
- Reduced participation burden/fewer barriers to clinical trial participation (e.g., travel)
- Larger, more inclusive, and more generalizable trials

Adapted from: Clinical Trials Transformation Initiative’s Mobile Clinical Trials – Novel Endpoints Project
Digital health technology tools: Regulatory considerations for clinical outcome assessment

• Evidentiary considerations--broadly similar to other types of outcome measures
  – Is the assessment is **well-defined** and **reliable**?
  – Does the endpoint score represents something meaningful to patients?
  – How much within-patient change in score/variable makes a difference in patients’ lives?

• For continuous monitoring, defining meaningful endpoints can be challenging given the potential for large amounts of data
Some pathways for FDA engagement: Clinical Outcome Assessments

1. IND/NDA/BLA Pathway
   - **Within an individual drug development program**
   - Investigational New Drug (IND) submissions to FDA
   - Potential to result in *labeling* claims

2. DDT COA Qualification Pathway
   - **Outside of an individual drug development program**
   - Development of novel COAs for use in multiple drug development programs addressing unmet measurement needs
   - Potential to result in *qualification* of COA

3. Critical Path Innovation Meetings Pathway
   - **Outside of an individual drug development program**
   - Potential for *general CDER advice* on specific methodology or technology (e.g., PRO instrument) in its early stages of development
   - Meetings are *informal, non-binding* discussions
Novel endpoint development in dermatology example: Alopecia areata

- COA Qualification—ongoing instrument development effort
  - PRO—“patient-reported symptoms and impacts of alopecia areata”

- FDA public meeting for patients and caregivers (Sept 11, 2017)
  - Meeting report “Voice of the Patient” issued March 2018

- Critical Path Innovation Meetings
  - Development of a Patient Reported Outcome Instrument for Alopecia Areata (April 2017)
  - Clinical Assessment Tools for Alopecia Areata (Dec 2017)
COA Staff

• **Associate Director:**
  Elektra Papadopoulos, MD, MPH

• **Regulatory Project Manager:**
  • Kim Chiu, PharmD
  • Kristina Luong, PharmD

• **DDT Qualification Scientific Coordinator:**
  – Michelle Campbell, PhD

• **Team Lead**
  – Selena Daniels, PharmD, MS
  – Wen-Hung Chen, PhD
  – Sarrit Kovacs, PhD

• **Reviewers:**
  – Michelle Campbell, PhD
  – Yasmin Choudhry, MD
  – Ebony Dashiell-Aje, PhD
  – Onyekachukwu Illoh, OD, MPH
  – Julia Ju, PharmD, PhD
  – Susan Pretko, PharmD, MPH

• **ORISE Fellow:**
  – Prima Ghafoori, PharmD
  – Yujin Chung, PharmD
For more information

• Clinical Outcome Assessment Qualification Program Webpage:

• Critical Path Innovation Meetings (CPIM):

• BEST (Biomarkers, EndpointS, and other Tools) Resource
  https://www.ncbi.nlm.nih.gov/books/NBK338448/

• CDER: Patient-focused drug development webpage:
Thank you!