Electronic Capture of PROs in NCI Clinical Trials

Lori Minasian, MD, FACP
Deputy Director,
Division of Cancer Prevention, NCI

Vision for PROs in NCI Clinical Trials

- Incorporate patient reported information into the study design to identify safe and effective interventions to treat, prevent and control cancer.
  - Improve our ability to identify tolerable regimens

- Improve operational efficiency for the collection of PROs for investigators and site staff
  - Streamline data collection and analysis with integration of PROs into the existing electronic data collection

- Improve the feasibility and usability of PRO collection to enhance patient participation
PRO Definitions

- **HRQOL** (Health Related Quality of Life)
  - A multi-dimensional concept that includes domains related to physical, mental, emotional and social functioning.
  - Purpose of measuring HRQOL is to determine the impact of the illness and its treatment on the well-being of the person.
    - The aggregate effect

- **PROs (Patient Reported Outcomes)**
  - Any report of the status of a patient’s health condition directly from the patient.
    - Focus on specific construct (symptom or function or other)
      - Diary of hot flashes, dietary intake, or physical activity
      - Response to specific question(s) related to pain or function, etc

HRQoL/PRO Should Inform the Primary Study Question

- What part of the patient experience helps understand the benefit/risk for this study?
  - *Functional outcomes, symptom burden, or overall HRQOL*

- Data collected needs to reflect the clinical issue
  - *Time points for collection correspond to delivery of intervention and expected responses*
  - *Disease outcomes are correlated with the PRO information*

- Analysis plan for the HRQoL/PRO is in the statistical section with methods and sample size
  - *Summary score for HRQoL*
  - *Symptom score or summary score for PRO*
What HRQOL or PRO Tools Are Used in NCI Clinical Trials

- NCTN, NCORP have collected PROs for decades
  - Using valid, reproducible, & reliable HRQOL Tools
  - Usually compare aggregate effects between arms of study
  - FACT (General, Disease Specific, Toxicity) commonly used
  - EORTC Tools (QLQ C-30, EQ-5D)

- NIH Developed PROMIS
  - Item Bank of Questions where the answers have been “normed” across different populations.
    - Across disease areas, including some site specific cancers

- NCI Developed PRO-CTCAE

NCI’s PRO-CTCAE Tool

- PRO-CTCAE is designed for patient reporting of symptomatic adverse events

- PRO-CTCAE is an item bank of questions
  - Derived from the CTCAE adverse event items
  - Complimentary to CTCAE (and to be used with)

- Incorporate into study design for patient reporting in similar timeframes for clinician reporting

- PRO-CTCAE is ONLY for descriptive reporting
  - Framework for including PRO-CTCAE is AE reporting
  - Not ready for clinical and protocol specific decision-making based upon individual PRO-CTCAE scores
Incorporation of PROs for NCTN, NCORP and ETCTN

<table>
<thead>
<tr>
<th>NCTN/NCORP</th>
<th>ETCTN</th>
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<tr>
<td>Incorporation of PROs</td>
<td>Long history of incorporating HRQoL into randomized trials</td>
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<tr>
<td>Availability of PROs</td>
<td>HRQoL and PRO instruments curated into caDSR</td>
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<tr>
<td></td>
<td>Pre-populated RAVE CRFs</td>
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<tr>
<td></td>
<td>Standard PROs have been verified for electronic capture</td>
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<tr>
<td>Inclusion of PROs</td>
<td>Review PROs in NCTN and NCORP trials for RAVE CRFs</td>
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<td>Confirm electronic capture is equivalent</td>
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Collection Methods for PROs

- **Paper and pencil**
  - Long history of paper booklet collection

- **Telephone**
  - Some Groups have central telephone collections
  - IVRS useful

- **Electronic**
  - Industry using electronic direct patient capture methods
  - Increasingly being used, often with device provided by study

- RTOG has used VisionTree for electronic data collection (a few trials)
- ACRIN has used EASEEPRO for ePRO collection for COMET
- Alliance has begun work with Medidata ePRO

*Understanding the need for equitable selection of patients

*Flexibility for Multiple Modalities is key*
Patient Cloud ePRO Overview

- What is Patient Cloud ePRO?
  - A mobile app that collects patient responses to questionnaires / diaries and transfers data to the Medidata Clinical Cloud
  - Set-up and execution with intuitive role-based user interface
    - (patients do need email address)

- Fully integrated with Rave EDC to leverage the entire Medidata platform
- Available for Android and iOS mobile devices

List of Instruments

- Global Health
- HAD-G
- BS-QOL
- SCL-90-R
- Short Form-36 (SF-36®)
- Upper G Symptoms

Patient Questionnaire

1. Which of the following symptoms are you currently experiencing? (Select all that apply)?
   - Nausea
   - Vomiting
   - Abdominal Cramping
   - Sweating
   - Blurry Vision
   - Headache
   - None of these apply.

PRO-CTCAE

Indicate to what extent you feel this way right now, that is, at the present moment.

1. Interested
   - Very Slightly or Not at All
   - A Little
   - Moderately
   - Quite a Bit
   - Extremely

Register

Forgot Password?

About
NCI's ePRO Working Group

- Working Group Discussion Items
  - Workflows
    - Transition from use of Paper Source Documentation to ePRO.
    - Define a process to record patients not filling out forms.
    - Establish protocol template language for the inclusion of ePRO.
    - Establish informed consent template language for the use of ePRO.

- Implementation Pilot
  - Anticipate 10-15 trials for NCTN and NCORP
  - Anticipate 4-5 trials for ETCTN

Data Standards for Electronic Collection of PROs

- Create a list of business needs/requirements for stakeholders on the inclusion of PROs.
  - Data Management Centers
  - Accrual Sites and staff
  - Patients

- Evaluate the logistical features and operational aspects to inform the “business rules”

- Unique to collect data directly from patients into database without any filtering
  - Compliance Monitoring for Quality Assurance
  - Privacy Issues
  - Consideration for monitoring patients response
Addressing Regulatory Issues of PROs in NCI clinical trials

- NCI and FDA have regular meetings exploring issues regarding PROs in cancer clinical trials
  - Data standards meetings,

- Integrate regulatory requirements unique to electronic collection of information from patients
  - Real time review of symptom severity
  - Bring your own device (BYOD)
  - Mixed modalities and quality control

FDA, NCI and OHRP staff met in April 2017 to discuss the issue of patient reported “severe” findings

- Most patients on cancer clinical trials are followed closely
- Real-time monitoring?
  - Not currently done with HRQOL and other PROs
  - Usually reviewed and reported after trial completion
  - Results not provided for individuals, but rather in aggregate
  - Disclosure for patients as a reminder to “need to contact your provider”
    - Acceptable

- Bring your own device
  - NCI provides an opportunity to evaluate
ePRO and the NCI CIRB

- Already some trials sent to CIRB with electronic data capture of PROs
  - Phase 3 trials from NRG using VisionTree (appendix for e-collection)
  - COMET, the PRO correlative study exploring patients’ understanding of tumor profiling is using a different platform for electronic collection

- One concern is the handling of “severe” reports
  - Real-time monitoring?
    - Not now
  - Disclosure for patients “need to contact your provider”
    - Acceptable

Summary

- Electronic collection of patient-reported outcomes is becoming increasingly common
  - NCI has invested in the electronic Patient Cloud within Medidata RAVE
  - Platform consistent with the established electronic data collection for the networks within the NCI’s shared infrastructure for clinical trials.

- Active ongoing work to understand the workflow process currently
  - Determine the requirements for ePRO
  - Facilitate the collection of PROs across all the Networks within the clinical trials “shared infrastructure”

- Understand the unique issues with data collected directly from patients and going into the database