Electronic Capture of PROs in NCI Clinical Trials

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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

	NCTN/NCORP	ETCTN
Incorporation of PROs	Long history of incorporating HRQoL into randomized trials	Limited to no history of incorporating any PROs in early phase trials
Availability of PROs	HRQoL and PRO instruments curated into caDSR Pre-populated RAVE CRFs Standard PROs have been verified for electronic capture	Interest from investigators to incorporate PROs PRO-CTCAE for symptomatic AEs
Inclusion of PROs	Review PROs in NCTN and NCORP trials for RAVE CRFs Confirm electronic capture is equivalent	Identify ETCTN trials to incorporate PRO-CTCAE Create RAVE Global PRO-CTCAE Library Development of data standards for PRO-CTCAE ongoing with FDA

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

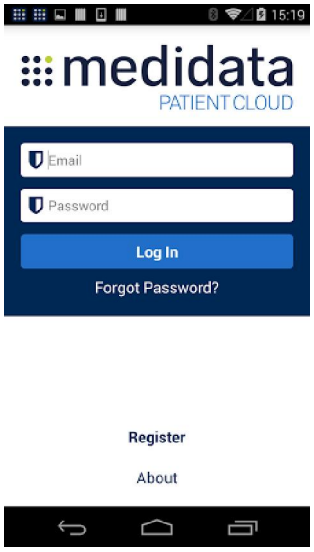
  - RTOG has used VisionTree for electronic data collection (a few trials)
  - ACRIN has used EASEEPRO for ePRO collection for COMET
  - Alliance has begun work with Medidata ePRO

Understanding the need for equitable selection of patients

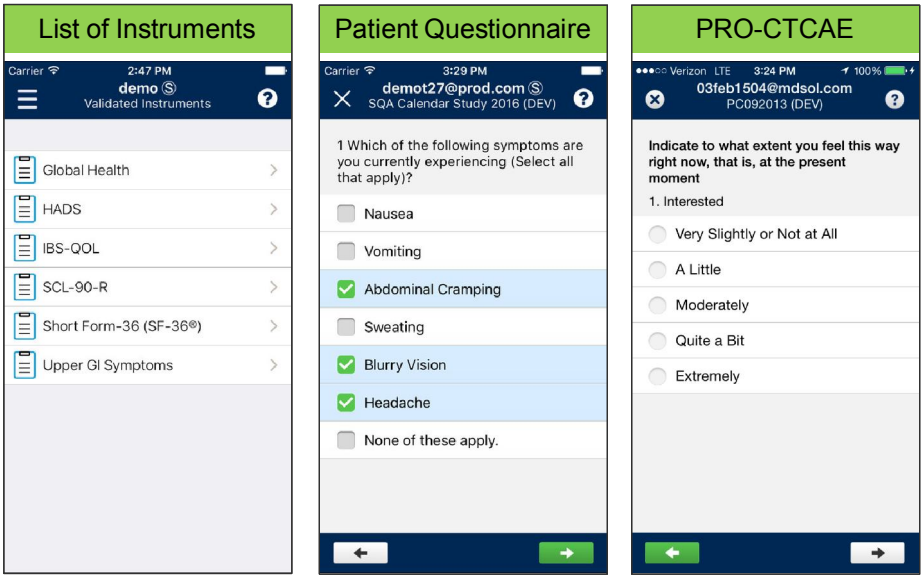
Flexibility for Multiple Modalities is key

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



Patient Cloud ePRO Overview



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

Addressing Regulatory Issues of PROs in NCI clinical trials

- 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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