Update on Clinical Trials Planning Meeting from November 2011

Building Bridges: Identification of Core Symptoms and Health-Related Quality of Life Domains for Use in Cancer Clinical Trials

Recommendations and Implementation

Chairs: Bryce Reeve, Deborah Watkins-Brunner
DCP: Lori Minasian, Ann O’Mara
DCCPS: Sandra Mitchell
DCTD: Andrea Denicoff
Background
HRQOL in Cancer Clinical Trials

- Inclusion of HRQOL Endpoints Provide Valuable Information
  - Treatment, Prevention, Cancer Control Trials with HRQOL

- However:
  - HRQOL Results Inconsistently Published with Treatment Data
    - Often Published Later in Different Journals
  - HRQOL is Not Fully Integrated into Analysis of Toxicity or Efficacy Assessment
    - DSMC example
    - NCIC analysis
      - (Au, Expert Reviews 2010)
PRO ≠ QOL ≠ HRQOL

Patient Reported Outcomes = Anything Reported by the Patient

Quality of Life = Related to Any Aspect of Life

Health-Related Quality of Life (HRQOL)

Evaluation of impact of illness or treatment on physical, emotional, & social aspects of QOL
Greater Emphasis on PROs in Research

- **Food and Drug Administration (FDA):**
  - Guidance on Use of PROs as Endpoints in Trials
  - PRO Instrument Qualification in Drug Development
  - Patient Centered Drug Development Program (2013)

- **Center for Medical Technology Policy:**
  - PRO Effectiveness Guidance

- **Patient-Centered Outcomes Research Institute (PCORI):**
  - Puts Patients in the Center of Health Research
  - Requires Patient Input/Engagement in the Research

- **National Quality Forum (NQF):**
  - Methodological Issues for PROs in Outcomes of Care
PRO Activities Across NCI Clinical Trials

- **CCCT** - Coordination of Scientific SC and CTPMs
- **DCP** - Lead Division for SxQOL SC;
  - Primary reviewers of PRO/HRQOL endpoints in trials
  - Collaborator in PRO-CTCAE development
- **DCTD** - Lead Division for Disease SCs;
  - Secondary reviewers of PRO/HRQOL in treatment
  - Collaborator in PRO-CTCAE development
- **DCCPS** - Lead Division for health outcome measurement in cancer,
  - PRO-CTCAE (NCI) and PROMIS (NIH)
- **CBITT** - Lead for Common Data Elements (CDEs) & PROs
  - Collaborator in development of PRO-CTCAE system
  - Working Group Forming for CDEs of PROs, HRQOL instruments
PRO Endpoints in Cancer Clinical Trials

**Challenges:**
- Ensure the Hypothesis-driven Inclusion of PROs
  - Clinical Context, PRO Expertise, Statistical Analysis
- Optimize Study Efficiency
  - Keep Patient Burden Low
  - Keep Staff (at Site & Stats Centers) Burden Low
  - Facilitate Common Data Elements

**Opportunities:**
- Permit Cross Trial Comparison of Pt Symptom Response
  - Facilitate Comparative Effectiveness Research
- Provide Symptom Data from Patient Perspective for Improved Patient & Clinician Decision-Making
PRO Endpoints in Cancer Clinical Trials

Solution:
- Standardized, Systematic, Finite Core Set of PRO Domains
  - General Set
  - Disease Set and (Intervention Specific Set)
  - Permit Better Discrimination of Treatment Effect & Toxicity
Objectives for Clinical Trials Planning Mtg

- Identify Core Set of PRO Domains to be used in cancer clinical trials irrespective of disease
- Identify Core Set of PRO Domains to be used for three specific cancer types.
Methods
Overview of the Methods

- Systematic literature review¹
- Primary data sources
  - NCI CDUS and AdEERS data
  - EORTC QLQ-C30 Reference Values Dataset²
  - PRO-CTCAE Validation Study Data
  - Functional Assessment of Cancer (FACT) Data Set³
  - Symptom Outcomes and Practice Patterns (SOAPP) study⁴
- Multi-stakeholder meeting (Fall 2011)
- Expert Panel for Synthesis and Refinement
- Methods can be applied to achieve scientific consensus on core PRO domains for other disease sites

¹ Reilly CM, Bruner DW, Mitchell SA, et al. Support Care Cancer 2013; Epub Ahead of Print; PMID: 23314601
Criteria for Selection of Core PRO Domains

- Listed in the Top 10 Symptoms of at least 2 Datasets
  - Literature Review
  - Prevalence and/or Severity
- Present Across Diverse Cancer Populations
- Measurable from the Patient Perspective
- Endorsed by Participants at CTPM/Stakeholder Meeting
Rationale for Three Specific Disease Sites

- Multiple Treatment Modalities
- Significant Treatment Related Morbidities
- Some Crossover or Similarities Between the Disease Sites for the Treatment-Related Morbidities

- Head and Neck Cancer
- Prostate Cancer
- Ovarian Cancer
Evidence-Based Process for Selecting Core Domains

- Literature Review
- Secondary Data Analysis
- Items Proposed
- Items Refined Through Expert Consensus and Additional Criteria including Responsiveness to Change as a result of treatment efficacy or toxicity
Outcome

- Recommended Core Set of Limited PRO Domains for Collection Across all Clinical Trials which Utilize a PRO

- Recommended Disease Core Set of Site Specific Symptoms and/or HRQOL Domains for Head and Neck Cancer, Prostate Cancer and Ovarian Cancer
Recommended Core Sets, Not Tools

Standard core set of patient-reported symptoms recommended to consider to use across trials

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Disease Core Sets/Domains

- **Ovarian Cancer**: abdominal core, neuropathy, fear of recurrence, sexual function, overall HRQOL
- **Prostate Cancer**: urinary incontinence, urinary obstruction, bowel function, sexual dysfunction, hormonal symptoms
- **Head & Neck Cancer**: swallowing, oral pain, dry mouth, dental health, taste, opening mouth, shoulder function, social function
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## Coverage by Instrument of the Core Symptom Domains

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Actions

- Recommend the Core Domains
  - Nested Sets, (General, Disease Area, Study Specific)
- Continue to Emphasize the Importance of Hypothesis-Driven Inclusion of PROs
  - Appropriate Analysis of PROs Data
- No Recommendation for Specific Assessment Tools

Next Steps:
- Publish
- Work with Steering Committees & Cooperative Groups
- Steering Committee Chairs Conf Call on March 22, 2013
Example of Clinical Utility for Incorporation of PRO Information
Examples of Utility of PROs

- GOG 172 (Ovarian Cancer Treatment Trial)
  - Abdominal discomfort (pain, cramping) exists before intervention, exacerbated by IP chemo before resolving

- Ruxolitinib FDA approval in Myelofibrosis included PROs
  - Primary Endpoint Spleen Reduction
  - Co-primary Endpoint Symptom Reduction (6 items)
    - Night Sweats, Itchiness, Abdominal Discomfort, Fullness, Pain Under ribs, Bone Pain
CTAC Input

- Proceed with Implementation of Recommended PRO Core and Disease Specific Domains

Questions:
- Consideration Beyond for NCTN Network Group Trials
  - Cancer Center Studies?
  - Limit to Network Groups?
- Issues or Special Considerations with Implementation?