EXECUTIVE SUMMARY
Symptom Management and Quality of Life Steering Committee
Clinical Trials Planning Meeting
Building Bridges: the Identification of Core Symptoms and Health-Related Quality of Life Domains for use in Cancer Research
September 22-23, 2011

Meeting Co-chairs: Deborah Watkins-Bruner, Ph.D., R.N. and Bryce Reeve, Ph.D.
SxQOL SC Co-chairs: Michael Fisch, M.D., M.P.H. and Deborah Watkins-Bruner, Ph.D., R.N.

Introduction

The National Cancer Institute (NCI) Symptom Management & Quality of Life Steering Committee (SxQOL SC) convened a Clinical Trials Planning Meeting for identifying core symptoms and domains for use in cancer clinical trials on September 22-23, 2011 in Washington, DC.

The objectives and goals of the meeting were to:

1) Identify a standard core set of patient-reported symptoms and/or health-related quality of life (HRQOL) domains to be assessed in clinical trials with cancer patients. Selected symptom and HRQOL domains should be ones that are commonly experienced across cancers and are helpful to inform clinical research findings and policy decisions.

2) Identify a core set of symptoms and/or HRQOL domains that should be assessed in clinical trials that include patients with either a head and neck cancer, prostate cancer, or gynecological cancer.

3) Identify patient-reported questionnaires that are appropriate to capture relevant symptoms and HRQOL domains selected in objectives 1 and 2.

Meeting attendees included SxQOL SC members, clinicians, clinical trials experts, biostatisticians, translational scientists, health-related quality of life scientists, patient advocates, and NCI staff.

Background

In 2001, the NCI created the Cancer Outcomes Measurement Working Group (COMWG)[1] consisting of 35 experts convened to examine the state of the science and identify future priorities for outcomes assessment in cancer research. After an extensive review of the cancer outcomes research field over the previous two decades, the COMWG found that assessing health-related quality of life (HRQOL) and symptom burden is feasible using questionnaires that meet established criteria for reliability and validity.[2]

Building on the COMWG findings, the NCI sponsored an international conference in 2006 entitled, "*Patient-Reported Outcomes Assessment in Cancer Trials (PROACT): Evaluating and Enhancing the Payoff to Decision Making*." The meeting resulted in a 2007 JCO monograph[3] which identified significant issues and challenges for the incorporation of patient-reported outcomes (PROs: includes HRQOL and symptom burden) in cooperative group trials. Among them was the recognition of the potential for patient-reported symptoms to enhance adverse event monitoring in cancer trials.

Both the COMWG and PROACT reported that a key impediment to move the field forward was a lack of universally recognized standard set of PRO domains to routinely be collected in cancer trials. Clinical trial investigators struggle with the task of knowing what domains to measure in their study that would inform the understanding of the safety and efficacy of the intervention under investigation. The literature is vast on this topic, yet there lacks one source where consensus has been reached on the key PRO domains. As a result, investigators may drop consideration of a PRO endpoint or spend significant time up front to review the literature, consult with co-investigators, and agree on measured endpoints. Further, there lacks consistency from one study to the next on what PRO endpoints are measured which reduces our ability to compare or combine results across trials. Thus, identification of a core set of PRO domains has multiple advantages:

1) Enables clinical trial investigators to come to one source to know what HRQOL and symptom domains to include in their study. This source document will list which domains need to be assessed by cancer type and/or treatment mode and associated questionnaires that measure the domain.

2) Allows researchers and funding agencies to identify domains that lack good quality measures or identify existing questionnaires that require more validation evidence for use in clinical trials. This will lead to a research agenda for measures development and validation in NCI-sponsored trials.

3) Identifies a core set of data elements that will facilitate comparison and combination of data across research studies around the world. This is in line with bio-informatics database initiatives to identify common data elements for meta-analysis types of studies.

Consensus and Recommendations

There was general enthusiasm for identifying a core set of symptoms to be assessed in all studies along with other disease/ site specific symptoms. However, there were a number of caveats identified related to the purpose, screening, efficacy, and timing of assessments. Researchers currently do not have a good way to look across various studies, and compare and follow patients over time. The assessment of these core patient-reported symptoms would not be mandated nor

replace any other hypothesis driven assessment. Limitations acknowledged were that there remains a need for a thorough, systematic review on functional status and quality of life before specific recommendations could be made on these patient reported outcomes.

Proposed core set of symptoms to assess in all cancer trials:

Due to concern for patient burden, core symptoms have been separated into first and second tier symptoms. First tier symptoms are those highly recommended to be assessed in all cancer patients regardless of disease site, stage, or treatment modality. The second tier symptoms are recommended for assessment if other hypothesis-driven, site, stage or modality specific patient reported outcomes would not overwhelm subjects or be likely to increase lack of compliance.

Proposed core set of *first tier symptoms*. Insomnia/ Sleep Disturbance, Pain (general), Fatigue, Nausea, Depressed mood/ sad feelings, Anorexia/ decreased appetite, Anxiety, Concentration Problems

Proposed core set of *second tier* symptoms: Dyspnea/ shortness of breath, Vomiting, Neuropathy/ Numbness or tingling in hands or feet, Diarrhea

Issues to consider with use of the proposed core set of symptoms for all cancers include:

- The need to consider spectrum (local, advanced, metastatic) of the disease and treatment intention (curative, palliative, adjunctive) as the core set of symptoms may differ
- The need for the symptoms to be benchmarked in context of population norms, when in the course of treatment/ follow-up these symptoms are assessed, and the question of why symptoms should be monitored if it will not change treatment.
- Consideration of latent variables not identified
- How the tier may change based upon patient attribution

Proposed core set of symptoms to assess in three site specific cancer trials: In addition to the core set of symptoms recommended above, it is recognized that there are common disease site-specific symptoms that should be assessed across site-specific trials. The conference had time and resources to make recommendations for patient self-reported symptoms in three common disease sites: prostate, head and neck, and ovarian cancers.

Recommendations for PROs to collect in prostate cancer trials

Localized prostate cancer: urinary incontinence (how much control, how often leak, how much leak), urinary obstruction/irritation (burning, slow flow, night-time urination, frequency), bowel/rectal symptoms (diarrhea, urgency, blood, cramping, pain), sexual dysfunction (erections, orgasm, desire), hormonal symptoms (hot flashes, breast tenderness, weight change)

Advanced prostate cancer: pain (intensity, interfering with daily activities), energy/vitality (fatigue), emotional well-being (feeling depressed, nervous, trouble sleeping), physical capacity (ability for work, physical activities, ADLs)

Other important measures: regret, satisfaction with care, anxiety about disease

Recommendations for PROs to collect in head and neck cancer trials

Swallowing, pain/oral, skin changes, dry mouth, dental health, opening mouth/trismus, taste, excess/thick mucus/saliva, shoulder disability/motion, social functioning, and functional status.

Recommendations for PROs to collect in ovarian cancer trials

Abdominal core (abdominal pain, appetite loss, bloating, constipation, cramping, indigestion, nausea, vomiting, weight gain or loss), Neuropathy, Fear of recurrence or death, Sexual function, Overall quality of life

This Executive Summary presents the consensus arising from the CTPM. These recommendations are not meant to address all clinical contexts, but rather represent priorities for publicly funded clinical research.

Anticipated Action(s)

- Publish white papers (4) related to recommendations for all cancers, prostate cancer, head and neck cancer, and ovarian cancer
- Present findings at national meetings
- Disseminate recommendations to treatment trialists (i.e., NCI Disease-Specific Steering Committees, Task Forces and NCI Cancer Clinical Trial Cooperative Groups)
- Work with the Cooperative Groups to determine feasibility of incorporating core sets of symptoms

References

1. http://outcomes.cancer.gov/areas/assessment/comwg.html
2. Joseph Lipscomb, ed., Carolyn C. Gotay, ed., Claire Snyder, ed. *Outcomes Assessment in Cancer: Measures, Methods and Applications*. Cambridge, England: Cambridge University Press, 2004.
3. *Journal of Clinical Oncology*, Vol 25, No 32 (November 10), 2007

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AGENDA

NCI Symptom Management & Quality of Life Steering Committee
Clinical Trials Planning Meeting on
Building Bridges: the Identification of Core Symptoms and Health-Related Quality of Life Domains for use in Cancer Research
September 22-23, 2011

Hyatt Regency Washington on Capitol Hill
Capitol Room
400 New Jersey Avenue, NW
Washington, DC 20001

Meeting Goals:

1) Identify a standard core set of patient-reported symptoms and/or health-related quality of life (HRQOL) domains to be assessed in clinical trials with cancer patients. Selected symptom and HRQOL domains should be ones that are commonly experienced across cancers and are helpful to inform clinical research findings and policy decisions.

2) Identify a core set of symptoms and/or HRQOL domains that should be assessed in clinical trials that include patients with either a head and neck cancer, prostate cancer, or gynecological cancer.

3) Identify patient-reported questionnaires that are appropriate to capture relevant symptoms and HRQOL domains selected in goals 1 and 2.

Session Topic	Presenter	Time
Sept. 22, 2011 (Thursday)		
Registration and Dinner		5:30 pm
Welcome and Introductions	Deborah Bruner, Bryce Reeve	6:00 pm
Charge from cancer survivor	Mary Lou Smith	6:10 pm
NCI: Perspective on Patient Reported Outcomes in Cancer Clinical Trials	Lori Minasian	6:20 pm
Goals and Limitations of Selection of a Core Set of PROs for Cancer Clinical Trials	Deborah Bruner	6:30 pm

Meaningful Use of Patient-Reported Data in Cancer Treatment Trials: Balancing Decision Making Utility, Measurement Standards, and Response Burden	Bryce Reeve	6:40 pm
All Cancers: Identifying Core Symptoms and HRQOL Domains		
Common and Prevalent Symptoms Reported by Cancer Patients	Amylou Dueck	6:50 pm
Patient-Reported Outcomes for Adverse Event Reporting	Ethan Basch	7:10 pm
From Screening to Efficacy Endpoints	David Cella	7:25 pm
All Cancers Core Set Recommendations	Carolyn Reilly	7:40 pm
Panel Members Introduction and Charge for Panel Discussion	Deborah Bruner	7:50 pm
Panel Discussion	Ethan Basch Deborah Bruner David Cella Corneel Coens Amylou Dueck Lori Minasian Sandra Mitchell Carolyn Reilly Mary Lou Smith	7:55 pm
Panel Wrap-up	Deborah Bruner	8:55 pm
Adjourn		9:00 pm
Sept 23, 2011 (Friday)		
Welcome, Summary of Day 1, Overview of Day 2	Deborah Bruner, Bryce Reeve	8:00 am
Prostate Cancer		
Prostate Cancer Survivor Perspective	Richard J. Vetter	8:10 am
Prostate Cancer Use of Patient Reported Outcomes in a Clinical Trial	Himu Lukka	8:20 am
Prostate Cancer PRO Expert Perspective	Ronald Chen	8:40 am
Prostate Cancer Core Set Recommendations	Howard Sandler	9:00 am
Panel Members Introduction and Charge for Panel Discussion	Howard Sandler	9:10 am
Panel Discussion	Neil Aaronson Peter Chang Ronald Chen	9:15 am

	Himu Lukka Howard Sandler Richard J. Vetter	
Panel Wrap-up	Howard Sandler	10:15 am
Break		10:20 am
Head and Neck Cancer		
Head and Neck Cancer Survivor Perspective	Pat Gavin	10:30 am
Head and Neck Cancer - Treatment and Toxicity	Drew Ridge	10:40 am
Patient Reported Outcomes: Clinical Trials Issues in Head and Neck Cancer	Barbara Murphy	11:00 am
What can PROs Teach Us?	Avi Eisbruch	11:20 am
Head and Neck Cancer Core Set Recommendations	Bhishamjit Chera	11:40 am
Panel Members Introduction and Charge for Panel Discussion	Ben Movsas	11:50 am
Panel Discussion	Bhishamjit Chera Avi Eisbruch Pat Gavin Ben Movsas Barbara Murphy Drew Ridge	11:35 am
Panel Wrap-up	Ben Movsas	12:35 pm
Working Lunch		12:40 pm
Ovarian Cancer		
Measuring Miracles: Reflections of an Ovarian Cancer Survivor	Meg Gaines	1:10 pm
How and *Why* PROs inform GOG 252: A Phase III Trial of Bevacizumab with Intravenous versus Intraperitoneal Chemotherapy	Lari Wenzel Steve Plaxe	1:20 pm
Priority Symptoms and QOL Domains for Women with Recurrent Ovarian Cancer based on data from GOG 259: The WRITE Symptoms Study	Heidi Donovan	1:40 pm
Ovarian Cancer Core Set Recommendations	Lari Wenzel	2:00 pm
Panel Members Introduction and Charge for Panel Discussion	Lari Wenzel	2:10 pm
Panel Discussion	David Cella Heidi Donovan Kristine Donovan Meg Gaines Richard Penson	2:15 pm

	Steve Plaxe Vivian vonGruenigen Lari Wenzel	
Panel Wrap-up	Lari Wenzel	3:15 pm
Meeting Wrap-up		3:20 pm
Adjourn		4:00 pm

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