Patient-Reported Outcomes and Quality of Life Committee

Goals

Quality of Life (QOL) research in NCCTG was officially established in September 1999 and was renamed as the Patient-Reported Outcome and Quality of Life Committee (PROQOL Committee) in 2007. The primary goal of the PROQOL group is to assess relevant QOL endpoints that have tangible outcomes for cancer patients and clinical practice. We will continue to follow our three guiding principles of facilitating the implementation of QOL in treatment trials as appropriate, developing new methodology to increase the precision and efficiency of QOL assessment, and carry out QOL-directed protocols where indicated to complement the treatment trial research portfolio.

As a result of the successful NCI site visit in July 2006, the PROQOL Committee was approved as a Discipline-oriented Scientific Committee with six years of funding. Research for the present grant cycle includes three major themes:

**Theme 1: Genetics and QOL:** The first paper was published on Twin Research and Human Genetics to describe the establishment of the GENEQOL Consortium to investigate the genetic disposition of Patient-Reported Quality-of-Life Outcomes. It was a collaborative work with the University of Amsterdam/Karolinska Instutite from the international and interdisciplinary consortium, the GENEQOL Consortium held in Feb. 2009. Five primary patient reported quality-of-life outcomes have been identified as initial targets: negative psychological affect, positive psychological affect, self-rated physical health, pain, and fatigue. A new concept has been submitted for the GI Correlative Science Committee on an exploratory analysis of N9741 in searching for genetic predictors of chemotherapy toxicity, efficacy, and quality of life outcomes. This study contains two aims looking to assess genetic variation and association with various clinical outcomes in the study N9741. The first aim is to look at genetic variants associated with the pharmacogenomics of 5-FU, while the second aim looks as assessing association of genetic variants with quality of life (QOL) outcomes. A new concept was approved allowing Dr. Gen Shinozaki of the Department of Psychiatry at Mayo to use the data from N9741 to explore linkage between a set of genetic markers that have preliminary indication of a relationship with mood disruption. Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation (ALTTO) trial opened in May 2007 and is projected to accrue 8000 patient worldwide. This trial is for adjuvant therapy in patients with HER2 positive breast cancer. A quality of life (QOL) substudy is available to patients and includes the LASA6, single-item measures of fatigue, rash, and diarrhea, and the FACT-B assessed at five time points. Planned analyses include comparison of arms as well as association between genetic markers and QOL. Concepts are also under development in the neuro, lung, and surgical committees with embedded QOL and genetic components. Dr. Sloan will be presenting a special session in 2009 Annual Conference of International Society for Quality of Life Research (ISOQOL) in October in New Orleans, Louisiana. Series of manuscripts will be published in QOL Research.

**Theme 2: Improve the clinical trial patient experience:** PRO-CTCAE Items are newly developed and are being assessed in a diverse patient population, which represents the spectrum of disease burden and symptoms in cancer care. A study is being developed to provide
supportive data for the psychometric integrity of the PROCTCAE items, and will also provide insights towards possible modifications of individual items. At the conclusion of the proposed study, the PRO-CTCAE will be ready for broad implementation in NCCTG cancer treatment and control trials. N0392, the Was It Worth It protocol, is accruing, intending to gather data on patient’s assessment of their clinical trial experience to inform and improve clinical trial design. 2008 ASCO abstracts were presented to report on analyses indicating better ways to assess pain, peripheral neuropathy, and osteoporosis. A concept has been written and submitted to analyze reasons why patients do not complete or return QOL booklets, with the purpose to determine areas where we can improve practice to ensure compliance.

**Theme 3: Value-added of PRO assessments:** Real-time, self-reported QOL assessment is a uniquely different approach to incorporating QOL assessments in oncology practice. This approach includes the use of real-time QOL assessments and feedback, the use of normative data based triggers for poor QOL, and the use of NCCN distress practice guidelines for initiating clinician-based interventions. A study is being designed to test whether the provision of real-time, self-reported QOL data during the course of radiotherapy will improve patient-reported QOL. The focus of this protocol will be in two areas: one related to the patient perspective of care: 1) to obtain estimates for effect sizes on differences in key QOL domains between patients receiving realtime QOL data and those not receiving QOL data; and 2) to obtain preliminary estimates of differences in patient satisfaction between patients receiving real-time QOL data and those not receiving QOL data; the other related to the clinician perspective of care: 1) to evaluate clinician attitudes towards the incorporation of real-time QOL data into oncology patient management; 2) to evaluate the use of a set of clinical pathways for the incorporation of real-time QOL data into oncology patient management; 3) to evaluate the potential impact on the quality of the patient-physician relationship with real-time use of QOL data compared to interactions where QOL data are not used (physician assessment); and 4) to obtain preliminary estimates of whether the real-time use of QOL data in a radiation oncology practice significantly increases the duration of the weekly on treatment visit.

**Protocols and Studies**

Since 1995, there have been 185 studies using Mayo Clinic Rochester as a data center with a QOL component, 81 of which are NCCTG. The Uniscale, LASA, SDS, and FACT/FACIT continue to be the most commonly used QOL tools. We have 6 NCCTG studies in development with QOL components: cancer control (1), CNS (3), and Lung (2). As of 08/20/2009 there are 15 studies with QOL components that are open to accrual: cancer control (3), breast (1), CNS (4), gastrointestinal (2), GYN (1), head/neck (1), lung (2), multiple (1) and the Was It Worth It (N0392) study. There are 60 closed protocols: breast (6), CNS (1), GI (14), GU (3), GYN (2), hematology (1), lung (5), other (1), multiple (3) and cancer control (24). Twenty of the studies have published manuscripts. Two have submitted manuscripts and seven have manuscripts accepted but not yet published. The remaining closed studies are in some stage of manuscript completion.

**Liaisons**

Clinical liaisons continue to provide support and facilitate interaction between the NCCTG QOL
committee and tumor group committees. The liaisons are: Yolada Garces (Lung), Axel Grothey, Joleen Turja (Colorectal), Paul Brown (Neuro-Oncology), Michele Halyard (Breast), Susan McClement (nursing), and Tait Shanafelt (Hematology). Memberships with questions or ideas regarding tumor-specific QOL should feel free to contact these colleagues. The 2009 retreat will be held via teleconference in April.

Grant Activities

Submitted in February 2009 was the Patient Reported Outcome Measurement Information System (PROMIS) grant. Reviewers comments are being responded to in consideration of funding. This grant requests funding for the Mayo Clinic to serve as a research site for a broad-based national and international network to validate the PROMIS domains in the context of clinical studies and to develop the PROMIS system to facilitate adoption by clinical researchers. The Mayo Clinic PROMIS Research Network (MCPRN) will be in collaboration with member sites of the North Central Cancer Treatment Group, Memorial-Sloan-Kettering Cancer Center, M.D. Anderson Cancer Center, the Australia Clinical trials network, and the Canadian Clinical Trials Network to allow for rapid accrual and the rapid exploration of application questions for PROMIS products to compare relative efficiencies for differences in modalities, (paper/pencil vs. laptop vs. hand held tablet), disclosure status (e.g., results disclosed to physician or not), and racial differences (minority versus not). Specific analytical aims include testing the relative performance psychometrics of the PROMIS tools and the new PRO-CTC measures versus simple single-item numerical analogues, exploration of patient satisfaction and distress, and determining the prognostic nature of PROMIS products for overall survival, disease-free survival and time to progression.

The T32 training grant submitted by Drs. Sargent and Sloan submitted in January is being resubmitted. A score was given to the grant but it was not funded. The intent of the grant is to establish a postdoctoral program in clinical trial design and PRO research. If successful, this will provide a pool of young postdoctoral candidates from whom the NCCTG can capitalize in building new studies and exploring research aims.

Neither of the two challenge grants submitted for the recent NIH stimulus package competition was funded. However both grants have been incorporated into subsequent grant application. The first grant, with Dr. Sloan as PI, will follow up on our research relating genetics to PRO variables in trial N9741. The first aim will be to perform an analysis of genes linked to PROs in previous studies, including fatigue and other symptoms (depressed mood, insomnia, anorexia, overall outlook) as well as overall quality of life. The second aim proposes to perform a Genome-Wide Association Study (GWAS) to assess which other genes might correlate with severity of symptoms (fatigue, outlook, total symptom burden) and overall quality of life. The third aim is to study the genes associated with symptom severity in relation to Time to Progression and Overall Survival. The second will extend Dr. Halyard's real-time pilot protocol into three NCCTG sites.

Other Activities

The PROQOL team presented 4 abstracts to ASCO 2009. They are:
1. Assessing simple measures of patient-reported fatigue for oncology clinical trials: a pooled analysis of 3,915 patients. Accepted as a poster.
2. Baseline quality of life as a prognostic factor for overall survival in lung cancer patients. Accepted for publication. Accepted for publication.
3. Association between lung cancer survival and pessimistic explanatory style. Accepted as a poster discussion.
4. Longitudinal assessment of cognitive impairment among lung cancer survivors. Accepted as a poster.

Other manuscripts in development discuss the impact on study results of various imputation techniques, the results of the Control Preference Scale (CPS) in regard to the patient characteristics, the results of the CPS in regard to different health care systems, the incidence of sleep problems (N0493), the relationship between CTCAE and PRO outcomes (N0591), the relationship between QOL and survival (N9741), the QOL of lung cancer patients, and the QOL difference in minority patients (N0691). Other meta-analyses include the assessment of peripheral neuropathy and the exploration of the Skindex-16 assessment tool.

The QOL web site, https://ncctg.mayo.edu/ncctg/group/qol.html, continues to be a complimentary resource. This web site contains instruments, references, and meeting minutes. Members are encouraged to visit the site for updates on particular studies or to gather resource information on QOL measures, papers, and activities. A bibliography, scoring keys and validity/reliability paragraphs are also available.

Published Manuscripts and Abstracts (2009)


- Pilot study of Panax quinquefolius (American ginseng) to improve cancer-related fatigue: a randomized, double-blind, dose-finding evaluation: NCCTG trial N03CA. Support Care Cancer 2009 May 06. [Epub ahead of print]


• Quality of life after breast cancer surgery: What have we learned and where should we go next? J Surg Oncol 2009 Jun 1; 99(7):447-55.


• A patient-level pooled analysis of the prognostic significance of baseline fatigue for overall survival (OS) among 3,915 patients participating in 43 North Central Cancer Treatment Group (NCCTG) and Mayo Clinic Cancer Center (MC) oncology clinical trials. J Clin Oncol 2009

• Relationship of sensory symptoms and motor function in patients with chemotherapy-induced peripheral neuropathy (CIPN) utilizing the EORTC QLQ CIPN20: NCCTG study N06CA. J Clin Oncol 2009

• Evaluation of the effect of intravenous calcium and magnesium (CaMg) on placebo-controlled phase III trial. Journal of Clinical Oncology 2009 May 20


• Assessing simple measures of patient-reported (PR) fatigue for oncology clinical trials: A pooled analysis of 3,915 patients. Journal of Clinical Oncology 2009 May 20
• Association between lung cancer survival and pessimistic explanatory style. Journal of Clinical Oncology 2009 May 20

• Baseline quality of life as a prognostic factor for overall survival in lung cancer patients. Journal of Clinical Oncology 2009 May 20

Members are encouraged to share feedback on the studies that follow this summary and the research efforts initiated. Please contact Dr. Jeff Sloan, 507-284-9985 or email at jsloan@mayo.edu for questions, input or feedback on the PROQOL research program.
Multiple

N0392 Assessment of Patient Satisfaction with Participation in Phase II/IIINC-CTG Clinical Trials
**Purpose of Study:**

1) The primary research hypothesis will be to examine whether patient quality of life (QOL) needs are being met throughout the course of the trial. Specifically, determining if the patients thought participation in the clinical trial was worthwhile.

**Study Chairs:** Jeff A. Sloan Ph.D.  
**QC Specialist:** Carol A. Leonard  
**Statistician:** Pamela J. Atherton M.S.  
**Nurse Resource:**

**Status:** 06/07/2006 Activated  
**Projected Number of Patients:** 3870  
**Excluded:** None  
**Final Accrual:** NA  
**Stratification Factors:** None  
**Schema:** Register  
CPS + WIWI assessment

**Treating Schedule:**
No treatment information

**Study Design:** Patients enrolled to designated NCCTG phase II or III treatment trials will be asked to complete QOL assessments upon study enrollment, after the first cycle of treatment (or 1 month) and at the end of treatment (or 1 year). This will allow us to evaluate patient perceptions of their experience in NCCTG clinical trials.

**Accrual:** As of 08/04/2009, 150 patients have been enrolled. There have been no cancels or ineligibles.

**Patient Characteristics:** Patient characteristics are listed in the Baseline Characteristics Table.

**Adverse Events:** Are not collected for this trial. Adverse events are being collected for the parent trial(s).

**Study Status:** Study is continuing as per protocol.
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## Characteristics

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### Race

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- Black or African American: 3
- American Indian or Alaska Native: 1
- Unknown: Patient unsure: 2

### Study Phase

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- III: 6