Supporting Quality and Patient Safety in Cancer Clinical Trials

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Adverse event (AE) reporting is a critical component of all cancer clinical trials, and the National Cancer Institute’s Common Terminology Criteria for Adverse Events™ (CTCAE) is the primary system used by clinicians to describe the severity of AEs. The National Cancer Institute’s Patient-Reported Outcomes version of the CTCAE (PRO-CTCAE) assesses patient self-reports of symptoms using a Web-based system that can be incorporated into all cancer clinical trials. Oncology clinical trial nurses are responsible for the protection and safety of patients enrolled in cancer trials and, therefore, should develop an understanding of PRO-CTCAE.

The National Cancer Institute’s Community Cancer Centers Pilot (NCCCP) was launched in 2007 and targeted an estimated 85% of patients with cancer receiving care in the communities where they reside (National Cancer Institute [NCI], 2010b). The NCCCP is a partnership between the NCI and a network of community hospital cancer centers in rural, suburban, and urban areas in the United States. The mission of the NCCCP is to “enhance cancer care at community hospitals, and to create a platform to support basic, clinical, and population-based research” (NCI, 2010b, p. 1).

The original network consisted of 16 sites; however, funds from the American Recovery and Reinvestment Act permitted network expansion to 30 sites in 22 states (NCI, 2010b) (see Figure 1). NCCCP sites are engaged with academic centers in studying ways to improve the quality and safety of cancer care, including adverse event (AE) reporting in cancer clinical trials.

One such initiative is the validation study of the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events™ (PRO-CTCAE). NCCCP sites are participating in research assessing the psychometric properties of the PRO-CTCAE (NCI, 2009). The PRO-CTCAE includes a Web-based questionnaire composed of 81 symptoms from the CTCAE identified by NCI as significant and adaptable to patient self-reporting (NCI, 2010c).

Participants can answer as many as 126 questions that assess for the presence, frequency, severity of symptoms, and symptom interference with the individual’s activities of daily living (NCI, 2010c). Patient-reported symptoms are transmitted via the secure Web-based platform to the oncology research team. A patient’s comprehension of the questions, in addition to the accuracy and efficiency of patient-reported outcomes, will then be assessed (A.C. Dueck, personal communication, January 4, 2011).

The goal of the PRO-CTCAE project is to use the system in all cancer clinical trials (NCI, 2010c). This validation study is being conducted at NCI-designated comprehensive cancer centers and NCCCP sites throughout the United States (see Figure 2). Patients are eligible if they have a diagnosis of cancer and are receiving chemotherapy, biologic therapy, molecularly targeted agents, or radiation therapy. About 900 patients will be enrolled nationally at participating institutions (A.C. Dueck, personal communication, January 4, 2011).

Adverse Events

Oncology clinical trial nurses are responsible for the protection and safety of patients enrolled in cancer trials and for AE reporting, and should develop an understanding of PRO-CTCAE prior to testing in the cooperative group clinical trial setting (Daugherty, Leos, Schmieder, Weiss, & Good, 2010). AEs are defined by NCI as “any unfavorable sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or intervention that may or may not be considered related to the medical treatment or intervention under investigation; the AE may be unexpected or expected” (NCI, 2010c, p. 1).

AEs are graded on a scale from 1 (mild) to 5 (death related to AE) and are captured during specific intervals and during routine care (NCI, 2010c). The CTCAE is supported by NCI’s Cancer Therapy Evaluation Program and has been the primary system used by oncology research clinicians to describe the severity of AEs in cancer clinical trials (Trotti, Colevas, & Good, 2009).
Sester, & Basch, 2007). NCI originally designed the Common Toxicity Criteria (CTC) for use in the clinical trial setting by both public (cooperative groups) and private sponsors (pharmaceutical and medical device corporations), but the system also is used in the clinical setting to support treatment decisions, symptom management, and medication administration (Trotti et al., 2007).

**Patient-Reported Outcomes**

PROs are defined as “any aspect of an individual’s health status that comes directly from the individual, without modification or interpretation by another observer” (Lipscomb et al., 2007, p. 5134). PROs have become the desired mechanism to capture symptom data in trials and facilitate the assessment of study treatment benefits (Trotti et al., 2007, p. 5122). PROs, derived from health-related quality-of-life tools, have been noted to allow for more disease-specific symptom assessment and, in 2006, the NCI Patient-Reported Outcomes Assessment in Cancer Trials conference established that “the patient’s own account should be considered the gold standard” (Trotti et al., 2007, p. 5124). Patient self-reporting systems may improve the accuracy of AE data capture and subsequent follow-up.

**Development**

NCI awarded a contract to Memorial Sloan-Kettering Cancer Center (MSKCC) in New York, NY, to develop the PRO-CTCAE based on work reported in Basch et al. (2007). Researchers at MSKCC evaluated monitoring long-term toxicities in patients undergoing chemotherapy treatment via electronic PROs. Patients with lung cancer (N = 107) accessed the Symptom-Tracking and Reporting (STAR) online system to report their treatment side effects from both the clinic and home (Basch et al., 2007). Clinician notifications (N = 179) were generated by the STAR system for grade 3 (severe) or grade 4 (disabling) AEs. These notifications were provided to the patient, and an e-mail message was sent directly to the designated nurse. Pain, shortness of breath, and anorexia were the most common alerts (Basch et al., 2007). The majority (90%) of patient participants rated satisfaction with the system, and 77% thought the system improved the quality of their patient-clinician discussions (Basch et al., 2007).

This study also included a survey of nurse perceptions related to the STAR system. Survey results reflected that 100% of respondents (N = 7) believed the STAR system aided in patient discussions, treatment decisions, and documentation (Basch et al., 2007). Basch et al. (2007) also noted that all of the nurses had altered their nursing management because of patient-reported information from STAR data, including medication modifications, lifestyle recommendations, and physician consult coordination. The investigators concluded that patient self-reporting online is an appropriate strategy for monitoring toxicities associated with chemotherapy treatment (Basch et al., 2007).

**Quality of Care and Patient Safety**

The oncology research clinician gathers analytic data (i.e., laboratory values), objective data derived from clinical examinations, and subjective data from the symptoms reported by the patient when capturing reportable AEs (Trotti et al., 2007). Clinician capture of subjective data requires multiple steps. First, the patient reports the symptom to the clinician. The clinician then makes an assessment and interprets the symptom. Documentation of the information in the patient’s chart and, in the case of cancer clinical trials, into the research database follows. Issues with the quality of care and patient safety are inherent with this approach to gathering subjective data because multiple steps in information transfer increase the potential for AE reporting errors (Trotti et al., 2007).

Patients report earlier onset, more severity, and longer presence of symptoms when compared to clinicians’ reports of symptoms in the clinical trial setting...
The PRO-CTCAE Web-based system provides a way for patients to self-report their symptoms during treatment and may enhance the accuracy and efficiency of AE detection and data capture (NCI, 2010c). By informing oncology clinicians of patient-reported symptoms in real time, the system has the potential to augment the patient-clinician relationship, allow for prompt mitigation of toxicities, promote timely and accurate interdisciplinary communication, and may ultimately improve the quality and safety of care (Sherman et al., 2009).

Lipscomb et al. (2007) noted the “promising developments in the use of PROs to complement clinician-reported drug toxicity in clinical trials” (p. 5138). One example of a drug-related patient-reportable side effect is nausea. Patients and their families rate the experiences of nausea and vomiting as one of the most distressing side effects of cancer treatment, and NCI reports that clinicians may be underestimating this side effect (NCI, 2010a, 2010c). Patients enrolled into the PRO-CTCAE study will be able to indicate the presence of nausea, the frequency (i.e., never, rarely, occasionally, frequently, and almost constantly), the severity (i.e., mild, moderate, severe, and very severe), and how much the nausea interferes with their daily activities (i.e., not at all, a little bit, somewhat, quite a bit, and very much). Inadequately managed nausea can result in anorexia, self-care impairments, increased healthcare use, and treatment discontinuations.

**Conclusion**

Patient safety can be enhanced using PRO tools that provide for accurate and consistent monitoring, which can then prompt earlier identification and management of AEs. Oncology nurses routinely gather patient-reported outcomes in all practice settings. A consistent systematic way of assessing side effects, such as a PRO system that includes the patient’s perception, would support this level of care. As with any new system, challenges exist for implementation and adherence. AEs experienced by the patient can be complex, and developing a standard system of reporting can be complicated (Trotti et al., 2007). Nurses should consider the patient’s level of computer literacy, access to computers, and willingness to use the system. In addition, PROs are related to quantifiable items and do not necessarily discriminate the psychosocial and emotional influences experienced by the patient. The nurse must consider this when developing the plan of care.

Oncology nurses are responsible for the safety and well-being of patients. PROs provide a new opportunity for oncology nurses to capture information in an accurate and efficient manner and provide for early detection and treatment of toxicities. Oncology nurses may have the opportunity to use this tool at the completion of the NCI’s PRO-CTCAE validation study.

In conclusion, the objective of the PRO-CTCAE project is to incorporate this system into all cancer clinical trials and, eventually, into routine clinical care (Trotti et al., 2007). Understanding the rationale for the PRO-CTCAE system will enable oncology nurses to more readily apply this tool to future clinical practice. This or other similar systems may then become a standard for quality cancer care.

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**References**


