National Cancer Institute

Division of Cancer Control and Population Sciences

http://cancercontrol.cancer.gov

Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)

Background

The NCI's Common Terminology Criteria for Adverse Events (CTCAE; http://ctep.cancer.gov/reporting/ctc.html) is a longstanding empirically developed "dictionary" or lexicon, designed for use in clinical trials to aid clinicians in detecting and documenting an array of adverse events (AEs) commonly encountered in oncology. An AE is 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 either unexpected or expected.

An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses of treatment efficacy and tolerability. Each AE is typically graded on a scale of 1 (mild) to 5 (death related to AE), though a grade 5 is not relevant for some AEs, such as hair loss or skin itching. The reporting requirements for AEs are generally protocol-specific and may be divided into two types. The first is the protocol-specific AEs to be addressed at designated evaluation intervals. The second is the pertinent positive clinical signs, symptoms, and laboratory results obtained as part of routine care of patients. The CTCAE is maintained by the NCI's Cancer Therapy Evaluation Program (CTEP). The CTCAE is currently in its fourth version.

There is growing awareness that collecting symptom data directly from patients using patient-reported outcome (PRO) tools can improve the accuracy and efficiency of symptomatic AE data collection. This is based on findings from multiple studies[1-11] demonstrating that physicians and nurses underestimate symptom onset, frequency, and severity in comparison with patient ratings. For example, in a study of men with prostate cancer enrolled in a Phase II clinical trial, physician reporting was neither sensitive nor specific in detecting common chemotherapy symptomatic adverse effects[5].

In the field of pain management, it has long been recognized that only the patient can accurately report the onset, severity and duration of pain and its impact upon function. This principle extends to other symptoms, such as fatigue, erectile dysfunction, and xerostomia (dry mouth), which can be found in the CTCAE. The other advantages of a PRO complement to the CTCAE are discussed in an article by Trotti et al [8].

Overview of the PRO-CTCAE

The NCI's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) system provides a web-based platform to collect patient reports of symptoms they are experiencing while undergoing treatment, for the purpose of enhancing adverse event (AE) reporting http://outcomes.cancer.gov/tools/pro-ctcae.html). To date, 81 symptoms of the CTCAE (version 4) have been identified as amenable to patient reporting. These symptoms have been converted to patient terms (e.g., CTCAE term "myalgia" converted to "aching muscles").

For symptoms such as fatigue and pain, the PRO-CTCAE system asks patients for information about symptom frequency, severity, and interference with usual activities. For other symptoms (e.g., rash), questions focus on the presence or absence of the concern. These items have undergone extensive qualitative review among experts and patients. The PRO-CTCAE electronic system provides an interface for patients, investigators, and clinicians in a secure web-based platform. This work is supported under a contract with Memorial Sloan-Kettering Cancer Center (Principal Investigator: Ethan Basch, MD).

Objectives and Next Steps

The overall goal of the PRO-CTCAE initiative is to employ rigorous scientific methods to create a system for patient self-reporting of adverse symptoms in cancer trials that is widely accepted and used, generates useful data for investigators, regulators, clinicians and patients, and is compatible with existing adverse event reporting systems. In total, there are 126 questions that assess different attributes (e.g.,

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presence, frequency, severity, interference) of 81 symptoms that are represented in both the CTCAE (version 4) and Medical Dictionary for Regulatory Activities (MedDRA) adverse event lexicons. Using cognitive testing, these 126 questions have been extensively evaluated by cancer patients, and found to be comprehensible and to measure the symptom of interest. An electronic system provides a mechanism for scheduled periodic surveillance and collection of patient-reported symptom data, using the web or a touch-tone telephone. Usability testing is ongoing.

Next steps in the project include analysis of the data from validation testing in a large cancer cohort, translation to Spanish, German, Chinese, and Japanese, feasibility testing of the PRO-CTCAE system in two cooperative group treatment trials, and a study comparing alternate models to integrate patient and clinician reporting of AE data for toxicity grading, dose modifications, and cancer care improvement. In the future, it is hoped that the PRO-CTCAE will be used in many clinical trials, allowing patient-centered information about the effectiveness of new treatments to be systematically gathered.

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