

Pain palliation measurement in cancer clinical trials: the US Food and Drug Administration perspective.

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Abstract

BACKGROUND:

Pain palliation resulting from antitumor therapy provides direct evidence of treatment benefit when combined with evidence of antitumor activity. The US Food and Drug Administration (FDA) previously issued guidance regarding the use of patient-reported outcome (PRO) measures to support labeling claims. The purpose of this article is to identify common challenges and key design strategies when measuring pain palliation in antitumor therapy clinical trials that are consistent with PRO Guidance principles.

METHODS:

Antitumor clinical protocols submitted to the FDA between 1995 and 2012 that included pain palliation as a primary or secondary endpoint were reviewed. Challenges in critical trial design components were identified. Design strategies consistent with PRO Guidance principles are proposed.

RESULTS:

The challenges identified were measurement of pain intensity and analgesic use, enrollment eligibility criteria, data collection methods, responder definitions, missing data, and blinding. Strategies included the use of well-defined, reliable, PRO assessments of pain intensity and analgesics; ensuring that enrollment criteria define patients with clinically significant pain attributable to cancer on an optimal analgesic regimen; defining responders using both pain and analgesic use criteria; incorporating an analysis of tumor response to support evidence of pain response; and minimizing missing data and inadvertent unblinding.

CONCLUSIONS:

Improvement in cancer-related pain resulting from antitumor therapy is an important treatment benefit that can support drug approval and labeling claims when adequately measured if study results demonstrate statistically and clinically significant findings. Sponsors are encouraged to discuss pain palliation assessment methods with the FDA early in and throughout product development.