Best supportive care

Lack of a standardized, detailed definition of best supportive care (BSC) in oncology currently diminishes the meaning of results from clinical trials, and hampers the translation of investigational results to the usual care setting. In a recent issue of Journal of Clinical Oncology, two articles presented studies in which patients with advanced malignancies were randomly assigned to experimental therapy versus BSC. Amado et al1 analyzed KRAS mutation status in metastatic colorectal cancer patients randomly asigned to receive panitumumab versus BSC (original results reported by Van Cutsem et al2). Jassem et al3 compared pemetrexed with BSC in patients with advanced malignant pleural mesothelioma. Van Cutsem et al demonstrated an improvement in progression-free survival and objective response rates with panitumumab compared with BSC; these results were mirrored by Amado et al in their KRAS mutation analysis. Jassem et al demonstrated superior progression-free survival and response rates with pemetrexed over BSC. These reports beg the question, what is BSC? Unless and until we uniformly define this comparator, such studies demonstrating improvement achieved with new antineoplastic agents have not contributed clinically meaningful information.

Though articles typically provide definitions for BSC as a control condition, these definitions seem to be largely determined by convenience and status quo practice. Van Cutsem et al defined BSC as “the best palliative care per investigator excluding antineoplastic agents”;2 Jassem et al defined BSC as “treatment administered with the intent to maximize quality of life without a specific antineoplastic regimen,” which included “antibiotics, analgesics, antiemetics, thoracentesis, pleurodesis, blood transfusions, nutritional support, and focal external-beam radiation for control of pain, cough, dyspnea, or hemoptysis.”3

These studies illustrate a key point in clinical trial design when BSC is used in a control arm: BSC is neither well-defined nor standardized. A 2004 systematic review of trials comparing chemotherapy to BSC in GI cancers revealed that BSC was not consistently defined in the four trials included.4 Three subsequent studies in advanced colorectal cancer have been published with BSC arms.2,5,6 The descriptions of BSC in these trials range from “best palliative care per investigator”;2 to a detailed listing of what might be considered BSC (“analgesics, antibiotics, blood transfusions, corticosteroids, antiemetics, antidiarrheals, or vitamins”).6 The BSC intervention, even when described in detail, is typically left to the discretion of each investigator without explicit guidance for initiation or escalation.

In addition to impairing our ability to ascertain an agent's antineoplastic effect, lack of a standardized BSC definition is particularly problematic in clinical trials evaluating patient-reported outcomes such as health-related quality of life. Health-related quality of life might worsen for patients in a BSC arm in comparison with patients in an antineoplastic therapy arm, but without a standardized BSC definition, we cannot be sure whether nonuniform delivery of BSC could account for these results.

The absence of a clearly articulated BSC definition also challenges clinicians as they attempt to translate trial results to their population in a manner that replicates the experimental setting and thus achieves similar results to those attained in the trial. This is particularly the case for trials in which experimental agents are delivered in conjunction with BSC. Here, an unclear definition of BSC might result in variation in the way that therapy is translated into the usual care setting.

Updated conceptual analysis of BSC in the clinical trial setting is necessary. This analysis—encompassing literature review, guidelines review, and key informant interviews—should culminate in the articulation of a practical, contemporary definition of BSC. The feasibility of BSC thus defined should be assessed first in a single-arm study, and subsequently as part of a randomized study comparing an antineoplastic agent to well-defined BSC.

Patients who enroll onto studies with BSC arms are often nearing the end of life, and have usually experienced a great deal of treatment and treatment-related toxicity. As clinicians, we accept an ethical imperative to treat disease to the best of our ability and also to relieve suffering. A standardized definition of BSC will help ensure that we understand the true potential benefit of antineoplastic therapies, and will ensure that our patients in fact receive the best of what modern supportive care has to offer [1)].

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http://jco.ascopubs.org/content/26/31/5139.full