

Do Clinical Trials Belong in Clinical Guidelines?

NCCN guidelines are notable for their comprehensive, maybe even exhaustive, nature. The goal of the guidelines is to create a template for most conceivable common clinical circumstances. Some nodal points in the guidelines are supported by high-quality evidence from randomized clinical trials. Others are supported by lesser data, expert opinion, or, in certain instances, the best guess of clinical experts. A great strength of the guidelines is that they patch together these decision points; those reinforced by strong ropes of data and those held by more tenuous lines of judgment.

Such thoroughness is very useful in clinical practice, both in high-volume clinical situations in which clinicians are often quite experienced, and arguably even more so in low-volume clinical circumstances, that are often unfamiliar to practicing oncologists, who refer to guidelines for real guidance. This thoroughness creates somewhat of an illusion, however, that NCCN guidelines panel members always know the right thing to do next, that little uncertainty exists, or that things couldn't be done better.

This is rarely the case in oncology, of course, which is why clinical trials are needed. NCCN guidelines always recommend consideration of clinical trials. In fact, the introduction to all the disease-based guidelines states:

The NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Although these sentiments are widely accepted throughout the NCCN and larger oncology community, participation rates in clinical trials remain dismal. In the United States, fewer than 5% of patients with cancer participate in prospective clinical studies. Slightly higher percentages may be observed at academic cancer centers, although often these are phase I or II trials that are not likely to define standards of care. Poor rates of participation in clinical trials are unquestionably slowing the rate of progress in oncology care.

As an example of what a more concerted effort can accomplish, consider the ABCSG-12 trial, the plenary talk at ASCO 2008, and a subsequent paper in the *New England Journal of Medicine*. This randomized, prospective phase III trial was open to premenopausal women with hormone receptor–positive breast cancer. Based on simple assumptions about the prevalence of breast cancer in Austria, it is likely that more than 30% of all eligible patients in that nation participated in this trial. That is how plenary talks arise!

Why are rates of participation in clinical trials so low? This is a multifactorial problem with many contributors, including lack of interest by oncologists or patients, limited access to clinical trials, excessive bureaucratic demands on clinical trials, inadequate financial support for clinical research, barriers to access to centers with clinical studies, and cultural biases regarding investigational approaches to treatment. Strong scholarship is beginning to yield insights into the factors that preclude greater clinical trial participation, and hopefully these observations will help change policies and attitudes and thereby reinforce the successes of clinical trials in oncology.

However, a simple observation, which can be modified, is that clinicians don't try hard enough to put patients onto clinical studies; they don't invest enough effort to have access to well-crafted, important clinical studies, and don't have enough motivation to more strongly encourage patients to participate. This is hubris. Clinicians should not be so satisfied with the current approaches to cancer treatment. Guidelines and practices must try harder to acknowledge important ongoing clinical studies and steer appropriate patients toward them. Next year's patients with newly diagnosed cancer will be thankful.



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