Generalizability of Cancer Clinical Trial Results

Elting et al.[1] have demonstrated that a number of characteristics differ between patients with cancer who do and do not participate in randomized controlled trials. Many of these characteristics are associated with the likelihood of survival, leading the authors to conclude that the lack of comparability between trial participants and nonparticipants calls into question the generalizability of clinical trial results. They go on to assert that, after initial evaluation of selected patients in randomized trials, large, population-based effectiveness trials of all comers will be needed to provide realistic benefits of treatment in general oncology practice. I disagree with both conclusions.

1. Just because trial participants and nonparticipants differ in certain ways does not mean that the impact of cancer treatment or prevention activities will differ between them. What would call into question the generalizability of the results of a given trial would be either: a) a suggestion that, in 1 or more subgroup(s) of the trial participants, the overall result did not apply (recognizing that many such suggestions turn out to be false positive[2]); or b) specific reasons (eg, genetic, hormonal, metabolic) to believe that some groups of patients ought to be atypical in their response to the therapy. Although exceptions do occur (eg, the apparently greater efficacy of epidermal growth factor receptor tyrosine-kinase inhibitors among Asian patients with lung cancer[3]), generally, the influence of treatment does not differ enough across patient subgroups to bear on the decision whether or not to use that therapy.

2. Once results of initial trials are available in selected patients, equipoise often no longer exists. In such a circumstance, a similar trial based on all comers would not be ethical to undertake.

Elting et al. argue that, because fewer than 5% of patients with cancer participate in randomized controlled trials, the generalizability of the results of those trials is questionable. I suggest that, if the quality of these trials is high, then we should not hesitate to generalize from them—that's how science works!—barring some *specific* reasons to believe that the study participants and patients in question ought to differ in their response to the particular therapy.

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