Overturning Barriers Will Take Heavy Lifting

By Harvey Jay Cohen, MD

The great bulk of our knowledge relating to the appropriate therapy for cancer has come from well-conducted clinical trials. However, participants in clinical trials represent a relatively small proportion of the overall patient population with cancer, and this proportion is even smaller for elderly patients. In recent years there have been calls to attempt to increase the enrollment of elderly patients onto clinical trials. Reasons for failure to enroll such patients might include factors relating to the cancer treatment protocols themselves, such as eligibility requirements; excluding patients with comorbid conditions; patient-related issues, which might include logistic issues, as well as attitudinal issues; and physician-related issues, which may also include logistical and attitudinal components.

The article by Dr Steiner and colleagues¹ in this issue of the *Journal of Oncology Practice* attempts to shed light on one particular aspect of this problem; that is, barriers to enrollment of elderly patients in early-phase cancer trials. Patients at private medical oncology practices affiliated with their academic institutions, and who had received prior chemotherapy, were asked about the barriers to enrolling onto a subsequent clinical trial. Patient-related barriers noted included logistic factors such as driving distance or time demands, concerns about being treated at a university center and of losing continuity with their primary oncologist. It is of note that the relationship with their primary oncologist was of very high importance to this group of patients. The authors suggest that potential strategies to overcome these barriers might include providing more information about trials to the community oncologists as well as the prospective enrollees, and creating more supportive systems to help patients navigate the complex terrain leading to a clinical trial. These are logical and reasonable suggestions.

However, there are a number of other considerations that should be taken into account. First, this is a somewhat restricted group of cancer patients: they already have a relationship with an oncologist. Thus, rather than necessarily trying to navigate a pathway to a university center for a clinical trial, one might consider mechanisms to facilitate the ability of the primary oncologist to deliver such a trial via a network approach. Moreover, many cancer patients may never even be referred to an oncologist; thus there may a knowledge gap that needs to be filled not only for oncologists but for primary care physicians as well.

It is of interest that in the study conducted by Kemeny et al,² wherein, of patients specifically eligible for a breast cancer

clinical trial, older patients were 50% less likely to be offered such a trial than were younger ones. This despite the fact that of those offered a trial, there was no difference in participation between younger and older patients. Thus, it would appear that in many instances older patients are as likely to accept enrollment in a clinical trial if offered, but that the fault lies with the physician who fails to offer the option of enrollment. This raises the issue of physician-related barriers as well as patient-related barriers. In that regard, in a survey of oncologists' perceptions of barriers to accrual of older patients to trials, the physicians were often concerned with issues not specifically seen as issues by the older patients.³ These included the potential presence of comorbid conditions aside from those excluded by the protocol, even though it was not clear that such existed, anticipating that older patients would have difficulty understanding the requirements of a clinical trial, and the logistics and time involved in enrolling older patients onto clinical trials.

The findings in the article by Steiner et al, as well as in previous work,⁴ are consistent with the general notion that to older patients the quality of life may be at least as important as duration of life. In that regard, another potential mechanism for enhancing enrollment, and one certainly consistent with the overall goals of oncology, would be to seek treatments that have a higher therapeutic-to-toxicity ratio. A number of new therapies have appeared that have better toxicity profiles for the traditionally troublesome toxicities such as hematopoietic suppression. However, in many cases, new toxicities, which may be particularly difficult for the elderly (such as hypertension and thrombosis) have appeared and must temper our enthusiasm for this approach. Nevertheless, the search for agents with more benign toxicity profiles should be a high priority. In addition, trials designed specifically for elderly patients, or at least block-stratified by age, might improve accrual of older subjects.

Steiner et al have suggested the need for education, in this case of patients, but also of physicians, in overcoming some of the knowledge and logistic barriers, and thus improving enrollment. However, herein lies the heavy lifting. Educational approaches such as these are not easy, and in prior work have been found to be both difficult to administer and of limited benefit. For example, in a Cancer and Leukemia Group B randomized controlled trial of an educational intervention, including seminars, educational materials, lists of available protocols, and monthly e-mail and mail reminders for 1 year, there was no improvement in the accrual of older patients to clinical trials during 2 years after the intervention.⁴ It is likely that a much more intensive

educational intervention would be needed to affect such change.

The lifting may be heavy, but it can be shared if the medical community at large, the oncology community, and patient advocacy groups band together to address this important issue.

Harvey Jay Cohen, MD, is Walter Kempner Professor and Chair of the Department of Medicine, and Director of the Center for the Study of Aging and Human Development at Duke University Medical Center, Durham, North Carolina.

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