

December 2003.

## **Cancer Clinical Trials and the Elderly: Searching for Certainty**

*Jeannette Y. Wick, RPh, MBA, and Guido R. Zanni, PhD*

Clinical trials evaluate the safety and effectiveness of new drugs, procedures, or products used to treat, diagnose, or prevent diseases. In cancer trials, end points most often involve improved survival, longer disease-free states, or better quality of life or functioning.

This we know with certainty: 57% of cancers and 71% of cancer-related deaths occur in people considered elderly (Figures 1 and 2),<sup>1</sup> and, physiologically, elders differ significantly from their younger counterparts. Organ decline is common, as are coexisting medical morbidity and polypharmacy. Despite these facts, elderly people are usually inadequately represented in the very clinical trials that might provide evidence about the best way to treat their cancers. Sometimes their exclusion is by design; elders' comorbidities muddy protocol design and ultimate findings. At other times, their exclusion stems from clinicians' failure to inform elders about clinical trials and encourage their participation.

Much remains uncertain: We suspect that elderly cancer patients experience more adverse events from chemotherapy and the newer biologics, and that clinicians may need to lower doses or treat cancers less aggressively, especially in the oldest of the old. In addition, cancer may manifest differently in older individuals (Table),<sup>2</sup> and study of older people who survive the longest may offer clues about survivorship. Finally, the definitions of "old" or "elderly" are fluid. Age 65 seems quite young in a society where longevity keeps increasing.

### **Making It Easier to Participate in Clinical Trials**

To encourage elders to volunteer as research subjects, investigators are taking steps to eliminate participation obstacles. Unless exclusion of elders is explicitly needed, age alone should not limit participation. Investigators must defend exclusion of subjects older than age 60. Some trials are designed specifically with older adults in mind. Much cancer research is coordinated by cooperative groups (organizations that continually generate and conduct new clinical trials consistent with national priorities for cancer treatment research), and many of these now address underrepresentation of elders in trials. The Cancer and Leukemia Group B cooperative group, for example, completed a study of women with breast cancer who were older than 70 years to determine if the addition of radiation therapy (RT) to tamoxifen would improve survival. Their results: Use of RT does not extend survival, but it may lengthen disease-free periods.<sup>3</sup>

The Geriatric Oncology Consortium (GOC), a multidisciplinary organization of cancer clinicians and oncology practices, is also working to improve clinical trial availability. The GOC conducts research and educational programs specifically targeting the elderly cancer population.

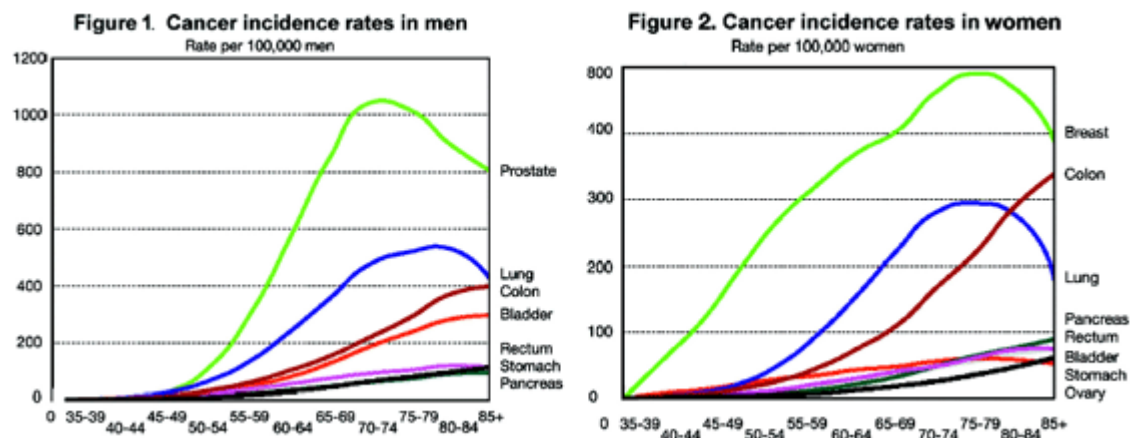
At the local level, the best way to boost enrollment is to introduce the subject of potential trial participation early in the diagnostic process. Kemeny et al found that older patients were less likely to be offered a clinical trial, but when the offer was made, a full 50% of older patients volunteered, compared with 56% of younger patients.<sup>4</sup> When offering a clinical trial, clinicians should emphasize the benefits.

### **Clinical Trial Benefits**

Clinical trials offer several potential benefits to the elderly participant. First, participants in clinical care generally receive exceptional, state-of-the-art care, care that often surpasses that offered in usual settings. Researchers have access to many of the newest innovations and the best diagnostics and treatments. Additionally, clinical trial staff members are prepared to answer every question via the informed consent process and can offer comprehensive information. As in other areas of medicine, the majority of cancer treatment is provided in ambulatory settings, and, increasingly, its focus is on sustaining quality of life or functioning once tumor burden has been reduced or eliminated.

### Barriers to Participation

With benefits like these, enrollment in clinical studies should be brisk. Unfortunately, many barriers interfere. Older adults, many of whom are familiar with World War II's horrendous experiments and the Tuskegee Syphilis Study (in which 399 African American men were not treated for syphilis so that researchers could see its natural history),<sup>5</sup> may have low trust levels or dislike the randomization process used in many studies. They may fear randomization to a "no treatment" arm. Additionally, they may have concerns about the cost of care, be apprehensive about research, or find regular visits to the research facility or trialspecific requirements inconvenient (eg, tissue or blood sample, surveys). Increasingly, potential participants cite transportation as an issue.



### What Pharmacists Should Counsel

Today, human rights protections are in place to ensure, especially when the diagnosis is cancer, that standard treatments are not withheld, and placebo is never used in lieu of effective treatment. Concerning cost, Medicare pays for routine patient care costs and costs due to medical complications associated with participation in clinical trials; the drug or biologic under study is generally provided free of charge by the study's sponsor. Participants' apprehension should be allayed by good communication, and most research sites use a standard, easy-to-read informed consent document. The National Institute of Health's Web site ([www.lhncbc.nlm.nih.gov/clin/forum.html](http://www.lhncbc.nlm.nih.gov/clin/forum.html)) explains the clinical trial process to patients. Recently, some research sites have video-recorded informed consent information so patients can take it home, viewing it at their leisure or with people important to them. Visit frequency is explained early in the process, and requirements that would be unnecessary if the patient chose usual care are explained in detail. Finally, many sites now arrange transportation for older patients.

### Finding a Trial

The National Cancer Institute's Cancer Information Center (located at <http://cis.nci.nih.gov/> or by phone at 1-800-4-cancer) helps potential participants identify appropriate trials. Its ClinicalTrials.gov ([www.clinicaltrials.gov/](http://www.clinicaltrials.gov/)) is a search engine designed to link patients with appropriate trials. Two nongovernment sites, Veritas Medicine ([www.veritasmedicine.com](http://www.veritasmedicine.com)) and Acurian ([www.acurian.com](http://www.acurian.com)), are also userfriendly ways to locate trials, not just for cancer, but for any condition.

#### Table

Some Cancers Manifest Differently in the Elderly
Cancers that are more indolent (slow to progress)
<ul style="list-style-type: none"><li>• Breast cancer</li><li>• Non-small-cell lung cancer</li></ul>
Cancers that have a shorter remission duration
<ul style="list-style-type: none"><li>• Non-Hodgkin's lymphoma</li><li>• Ovarian cancer</li></ul>
Cancers resistant to induction therapy
<ul style="list-style-type: none"><li>• Acute myelogenous leukemia</li></ul>
<small>Source: Reprinted, with permission, from Boccia RV. The older patient with cancer. Presented at Advancing Cancer Care in the Elderly, Geriatric Oncology Consortium, Washington, DC, September 19, 2003.</small>

#### Summary

To date, many noble volunteers who have participated in clinical trials have helped us learn. Some findings have refuted common beliefs. We now know that some cancers that occur in elders can be treated as aggressively as in younger populations, thus improving outcome. Radiation has been identified as a viable alternative to chemotherapy, and, for some drugs, elders' adverse-event profiles have been delineated - leading to better supportive care strategies. Pharmacists who understand the clinical trials process can help elders find exceptional care while contributing to the advancement of science.