Geriatric Oncology Aims For Clinical Trials

When it comes to cancer care, the elderly often get short shrift. Deemed too frail to handle the side effects from many cancer drugs, the elderly are poorly represented in clinical trials. Scarc e trial data have left physicians unsure of how to best treat the aged—so to be safe, physicians may undertreat.

The tide has started to shift, however. Studies increasingly challenge the notion that the elderly are too weak to handle traditional therapy. Over the past 5 years, research has shown that many elderly patients can tolerate the same treatment regimens administered to younger patients—but physicians must choose carefully. Some elderly patients sail through cancer treatment, whereas others suffer severely from side effects.

“It’s not chronological age that determines success,” said Ted Trimble, M.D., head of gynecologic cancer therapeutics at the National Cancer Institute in Bethesda, Md. “It’s the severity of comorbidities.”

But without evidence, selecting patients has been difficult. To boost research, in 2003 the NCI teamed up with the National Institute on Aging and other branches of the National Institutes of Health to launch a 5-year $25 million initiative. The agencies funded eight research institutions to study factors that affect cancer outcomes in the elderly. The large, collaborative, NIH-funded cancer groups in the United States such as Cancer and Leukemia Group B and Eastern Cooperative Oncology Group have also prioritized geriatric oncology in recent years. Organizations such as the American Society of Clinical Oncology have also started to fund fellowships in geriatric oncology.

Although focused attention has generated more data, experts agree that much work remains to be done. Clinical trial design remains too conservative; no one has yet established standard methods to recruit more elderly patients with additional diseases and disabilities into clinical trials. And without greater efforts to educate physicians and patients, research won’t have an impact on clinical care.

The Age-old Problem

People over age 65 are the fastest growing segment of the U.S. population, with those over 85 leading the way. Seniors also make up a large chunk of cancer patients. The latest NC1 Surveillance, Epidemiology, and End Results (SEER) program data, for example, show that 40% of breast cancer patients are over age 65. The median age at diagnosis for colon and rectal cancer is 72 years.

But even though cancer largely affects people over 65, age can preclude certain therapies. In 2001, Deborah Schrag reported in JNCI (vol. 93, no. 11, pp. 850–7) that older patients were much less likely to receive adjuvant chemotherapy after surgery to treat stage III colon cancer. Yet many might benefit from therapy. In a review this year in the Journal of Clinical Oncology, Daniel Sargent found that the 493 patients older than 70 out of 3,700 who received FOLFOX chemotherapy lived just as long and experienced no greater toxicity than their younger peers.

Reviews of the literature turn up similar trends in breast and late-stage ovarian cancer therapies, said Stuart Lichtman, M.D., head of the geriatric clinical program at Memorial Sloan-Kettering Cancer Center in New York.

“What’s happened over the past 15 years is that our perception of what is old has changed,” Lichtman said. “Today’s older generation is much healthier and more active than in previous years,” he explained, “yet society has treated the elderly poorly even when curative therapy exists.”

That false perception has also contributed to the few elderly people participating in clinical trials. A 2004 study published in the Journal of Clinical Oncology found that even though 35% of all cancer patients are over 75, they constitute only 10% of cancer clinical trial patients.

Elderly patients may be so poorly represented because most have an average of three additional diseases, said Martine Extermann, M.D., an attending physician in the senior adult oncology program at H. Lee Moffitt Cancer Center and Research Institute in Tampa, Fla. The additional illnesses may complicate treatment decisions and management. Consequently, most researchers choose to exclude such patients. The result is data that aren’t applicable to most elderly patients.

“There is clearly a very healthy subgroup of the elderly that can take standard therapy,” said Extermann. “But there is a whole group of patients that we do not see in regular clinical trials. We need to design studies for these patients. Otherwise treatment winds up being totally empirical.”

Solution: More Elderly in Trials

To boost participation of the elderly, Extermann offered the following guidelines: First scientists must design more innovative studies. Second, they should include tools such as geriatric assessment questionnaires that determine a patient’s general health and degree of...
disability. And third, researchers should conduct elderly-specific trials when appropriate.

To address the first point, Extermann is exploring a new trial design that uses a system of progressively increasing inclusion criteria. The trial would specify incremental steps, at which point researchers would stop and assess how well elderly patients tolerate the therapy. If everything ran smoothly, then the patients would continue. If the patients did not tolerate the therapy well, they would continue to participate, although at lower drug doses. Extermann is presently discussing the trial design with review boards.

Geriatric assessments should also be a crucial aspect of any cancer clinical trial, experts said. Research suggests that levels of dementia, functional status, and number and severity of additional ailments are associated with how well patients tolerate treatment and their long-term survival. Consequently, such evaluations can guide physicians when deciding how to treat elderly patients. However, these evaluations are presently not conducted during any clinical trials. The Cancer and Leukemia Group B is working to shorten and streamline a model geriatric questionnaire that could be used by physicians or nurses during clinical trials and later for clinical practice.

Finally, researchers often complain that not enough elderly patients volunteer for clinical trials. But a large study carried out last year by the North Central Cancer Treatment Group showed that when researchers restricted trials to elderly people, they garnered greater numbers of volunteers. The study pooled data from studies of non–small-cell lung cancer patients with incurable cancer and found that when researchers restricted clinical trial enrollment to patients older than 65, 17% of patients were older than 80 compared with unrestricted trials, in which only 3% of patients were older than 80. The study also found that elderly patients in the group’s elderly-specific trials suffered fewer severe adverse events than patients in traditional trials.

Forging collaborations with advocacy groups such as the American Association of Retired Persons can also boost trial participant numbers. AARP has collaborated with NIH-funded researchers on several studies and helped recruit volunteers from the group’s member pool. In fact, it was through collaboration with AARP that NIH was able to recruit as many as 550,000 volunteers between 50 and 70 years old for a prospective diet and health study, results from which were published in the New England
Journal of Medicine in August, said Albert Hollenbeck, Ph.D., senior research advisor at AARP.

“But we shouldn’t do elderly-specific studies just for the sake of doing elderly-specific studies,” Extermann said. Instead, she advocates conducting focused research on seniors in situations where standard treatment is toxic and physicians would like to know whether older people would do just as well with lower doses or alternative therapy. People over 60 with leukemia, for example, don’t benefit from cytarabine at high doses but many patients with leukemia are in that age group. Consequently, studies that examine leukemia therapies in the elderly would clearly help provide better treatment.

Adjuvant therapies are another area where elderly-specific studies might be appropriate. A study published in Journal of Clinical Oncology in July, for example, examined elderly patients with B-cell lymphoma who took the drug rituximab in addition to standard therapy. Their median age was 69. Researchers found that patients on the combined therapy remained disease free for significantly longer, showing that elderly patients can tolerate combined therapies as well as younger patients can. There are also several current studies focusing on adjuvant therapy to treat breast cancer in older women.

For these measures to have substantial impact, professional organizations and advocacy groups should educate physicians and patients of the need, experts said. “Doctors should know that patients can be referred to clinical trials even though they are not in outstanding shape,” Extermann said. Patients should also know that regardless of their age, they might qualify to participate.

In 2002 a group of oncologists including Lodovico Balducci, M.D., at the University of South Florida, and Lichtman formed the Geriatric Oncology Consortium. Its mission: to provide resources and education for community-based geriatric oncology research and to address the “urgent” need to study cancer of the aging. The work of such professional organizations is crucial, said Trimble, because it’s the only way to ensure that once the research is available, elderly people get treated appropriately.

“As the population ages, geriatric oncology is not going to remain an obscure thing,” Lichtman said. “This is going to be mainstream oncology.”

—Gunjan Sinha