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Research Priorities in Geriatric Oncology: Addressing the Needs of an Aging Population

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The number of older adults with cancer is rising, and the United States population is aging. In 2011, the “baby boom” generation began turning 65, and the U.S. population aged 65 and older is expected to double by 2030. Because cancer is a disease associated with aging, this trend is anticipated to increase the incidence of cancer among older adults by 67%.¹ Despite this, enrollment in cancer clinical trials favors a younger population,^{2–4} and few trials specifically focus on the unique issues that affect older patients. Consequently, little evidence-based data are available on the care of the growing number of older adults with cancer. To bridge this gap, a U13 conference grant, “Geriatric Oncology Research to Improve Clinical Care,” brought together multidisciplinary investigators from geriatrics and oncology to identify the areas of highest research priorities in cancer and aging. The first U13 Conference, “Biological, Clinical, and Psychosocial Correlates at the Interface of Aging and Cancer Research,” established a collaboration among the Cancer and Aging Research Group (CARG), the National Institute of Aging, and the National Cancer Institute. The first conference was designed to identify research goals and factors that would help shape geriatric oncology research. As part of this conference, participants with expertise in cancer and aging were asked to list the 5 most important areas of research in oncology/hematology and geriatrics. Here, we review their responses and the rationale for these research directions.

Cancer Therapeutics in the Oldest Adults (Ages 75 and Older)

Among FDA-approved treatments for cancer, only 9% of patients enrolled in registration trials were 75 years or older, whereas 31% of patients with cancer are within that age group.³ Therefore, clinicians have inadequate data on which to base drug dosing or anticipate therapeutic side effects for almost a third of patients with cancer. Furthermore, aging is associated with a steady decline in physiologic function, and several studies have shown that older age is a risk factor for chemotherapy toxicity.^{5,6} Although the rationale for studying treatments specifically in this population is well established,⁷ the mechanism for doing so is not in place. Ideally, for cancers predominantly associated with aging, the FDA should mandate that studies include older adults, to inform the geriatric usage section of package inserts. This would ultimately ensure adequate research for cancer therapeutics used in older adults.

Cancer Therapeutics in Frail/Vulnerable Individuals (Independent of Age)

Patients of any age with a poor performance status are often excluded from cancer clinical trials. Furthermore, comorbid conditions are common exclusion criteria. However, the interaction among cancer, treatments, and comorbidities pose significant treatment and survivorship issues for older adults and their treating clinicians. Even in a relatively younger

population (ages 65 and older), factors other than age often identify which patients are at risk for chemotherapy toxicity, and these factors have proven to be better predictors than conventionally used oncology performance status measures.^{6,8} Specific studies of treatment algorithms are needed for patients who would otherwise be considered ineligible or unfit for most current treatment protocols.

Development of a Geriatric Assessment Tool

Wide heterogeneity characterizes the aging process. Factors other than, or in addition to, chronologic age can determine an older adult's "functional age." Geriatric assessment includes evaluating independent predictors of morbidity and mortality in older adults, such as functional status, comorbid medical conditions, psychological state, cognitive function, nutritional status, and social support. Geriatric assessment can predict the risk of toxicity, and these assessment tools are increasingly included in cooperative group trials.^{6,8,9} The next generation of studies must identify interventions that can decrease the risk of toxicity as well as improve or maintain function and quality of life in older adults with cancer.

Development of Geriatric-Specific Outcomes

The typical primary and secondary outcomes in cancer clinical trials are progression-free and overall survival. Although these are important to an older population, additional outcomes, such as impact of therapy or disease on function, cognition, and the ability to live independently, are of similar importance. The need for functional assistance is a predictor of distress for older adults with cancer and their caregivers.¹⁰ Furthermore, an economic and psychological toll is associated with functional dependence in an aging society, particularly because most care-giving is "informally" provided by friends and family. Better understanding of geriatric-specific outcomes would help clinicians and patients weigh the full risks and benefits of treatment, and help patients and families prepare for the functional impact of cancer or cancer therapy.

Clarifying the Relationship of Cancer Biology and Aging

Cancer and aging are integrally related; however, the biologic underpinnings of this relationship need greater clarity. Furthermore, a tumor that develops in an aging person may be biologically quite different from that in a younger individual. For example, in breast cancer, the proportion of hormone receptor–positive tumors increase with increasing patient age.¹¹ With acute myelogenous leukemia, older patients often have more aggressive cancers, which are less likely to respond to standard therapies.¹² An understanding of how cancer biology changes across the aging spectrum would provide insight into novel therapeutic targets, as well as opportunities for cancer prevention. Ultimately, this will require correlative science conducted with samples from the tumor, the host, and controls without cancer.

Conclusions

To accomplish these goals, a multifaceted approach is urgently needed. The U.S. cooperative group setting provides an existing mechanism and infrastructure for high-quality geriatric oncology research that can ultimately be practice-changing. Partnering with community oncology sites is essential to include the vast majority of older adults being treated outside universities and cancer centers. Expertise in cancer and aging on NCI steering committees would further ensure that geriatric-specific questions are identified and included in clinical trials. More NIH program announcements specifically targeting older patients with cancer are needed to develop this research. Consortia of investigators with expertise in cancer and aging must conduct studies that fall outside the traditional purview

of cooperative group studies. Partnerships among researchers, patient advocates, and lawmakers are needed to change the legal requirements for cancer therapy approval to ensure that adequate numbers of older patients are included in trials. Together, these mechanisms could bridge many of the gaps in our knowledge, ultimately providing evidence-based medicine that will improve care of older adults with cancer.

Biography

Dr. Arti Hurria is a geriatrician and oncologist. She completed a geriatric fellowship at Harvard, followed by a hematology-oncology fellowship at Memorial Sloan-Kettering Cancer Center. In 2006, Dr. Hurria joined the City of Hope as Director of the Cancer and Aging Research Program. She is vice chair of the Alliance Cancer in the Elderly Committee and a recipient of the Paul Beeson Career Development Award in Aging Research (K23 AG026749-01), among other awards. She is Editor-in-Chief of the Journal of Geriatric Oncology and chair of the NCCN Senior Adult Oncology Panel and has served as PI on multiple studies to improve clinical care for older adults with cancer.

Supriya Gupta Mohile, MD, is an Associate Professor of Medicine in Hematology/Oncology at the James Wilmot Cancer Center. She is a board-certified geriatrician and oncologist with clinical expertise in treating patients with genitourinary and gastrointestinal cancers. A graduate of Pennsylvania State University, she earned her MD at Thomas Jefferson Medical School. She completed internship, residency, and fellowships in hematology/oncology and geriatrics at University of Chicago Medical Center, where she also earned a master's degree in health outcomes research. She has received an American Society of Clinical Oncology Young Investigator Award and Merit Awards, among others.

William Dale, MD, PhD, is an Associate Professor of Medicine and the Section Chief of Geriatrics and Palliative Medicine at the University of Chicago with a secondary appointment in Hematology/Oncology. He is a board-certified geriatrician with a doctorate in health policy. In 2006, Dr. Dale established, and he now codirects, the Specialized Oncology Care & Research in the Elderly (SOCARE) Clinic at the University of Chicago,

which offers interdisciplinary, individualized, and integrated treatment to older cancer patients.

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