Management of Cancer in the Elderly: An Essential Need for More Clinically Relevant Data

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One of the most serious recognized deficiencies in the cancer clinical trials paradigm, particularly within studies designed to achieve regulatory approval of new antineoplastic pharmaceutical agents, is the distressing but often rather ‘routine’ exclusion of the more elderly patient population. This concern is magnified by the observation that cancer is largely (although certainly not exclusively) associated with the aging process, with the recognized risk of malignant disease (both for an individual and for the entire population) increasing with age.

Optimal management of cancer in the very elderly can be quite problematic and often due simply to a profound lack of objective data in this large and growing population of patients. For example, if a new antineoplastic agent or novel combination chemotherapy is reported in the peer-reviewed literature to be effective in patients with a particular tumor type, but the median age of the patients treated on the phase-3 randomized trial demonstrating this outcome was more than 20 years younger than the patient in the oncologist’s office today to discuss disease management, how should these data be appropriately utilized to inform the decision-making process?

Should the treatment regimen be modified (likely a dose reduction) in some manner due to the ‘physiologic age’ of this patient and concerns for the presence of inad-

equate renal function or a known history of mild cardiac dysfunction or peripheral arterial disease? Or should the regimen simply not be administered to the elderly patient due to the unknown risks versus the benefits in this population?

It is also reasonable, in the absence of specific attention to the elderly, to inquire if we even know how the oncology community (outside the narrow confines of a clinical trial) actually manages this patient population. For example, do such patients undergo the same surgery suggested as being beneficial in trials that have focused on the younger patient population? Is potentially moderately toxic ‘adjuvant therapy’ to be recommended for patients where the risk-to-benefit ratio might be different from that identified in evidence-based trials that included a limited (and likely inadequate) proportion of patients defined as being ‘elderly’?

In this issue of *Oncology*, two papers appear that directly address the concerns highlighted in this commentary. The manuscript by Palaia et al. [1] explores the issue of the administration of cytotoxic chemotherapy in patients with gynecologic malignancies (ovarian, endometrial or cervical) who are ‘very elderly’ (≥ 75 years of age). In this retrospective analysis ($n = 49$) approximately one half of the population initially received full-dose cytotox-

ic therapy. Sixty percent of the entire group was able to complete the planned number of treatment cycles. Delays were rather frequently encountered, but there was only one treatment-related death despite the fact that clinically relevant comorbidity was common in this group. The investigators concluded that this elderly patient population with gynecologic cancers could indeed successfully and safely receive antineoplastic therapy demonstrated to be of clinical value.

The second paper involves a retrospective review of a relatively large single institution experience ($n = 444$) with the primary management of malignant melanoma [2]. The investigators identified age to be an important factor for the administration of adjuvant chemotherapy, with a much lower rate of such therapy in the more elderly population (≥ 71 years of age). In addition, the elderly population experienced a greater risk of recurrence, despite the fact that they appeared to undergo similar primary surgical management. Whether the negative impact of age on recurrence is secondary to biological factors or the use of adjuvant treatments, or both, is a relevant clinical question worthy of further investigation.

Finally, it is important to acknowledge that far greater efforts must be undertaken within the clinical cancer research community to define optimal management of cancer in the elderly. It has long been recognized that it would be highly inappropriate to simply state a particular cancer in children should be managed in the same manner as it would be in adults. It is therefore fair to conclude that a similar statement can be made for 75-, 80- or even 85-year-old cancer patients compared to individuals who are 20 or 30 years younger and who comprise the large majority of participants in the clinical trials that define the 'standard-of-care' in a particular clinical setting.

References

- 1 Palaia I, Loprete E, Musella A, Marchetti C, Di Donato V, Bellati F, Benedetti Panici P: Chemotherapy in elderly patients with gynecological cancer. *Oncology* 2013;85:168–172.
- 2 Fleming NH, Tian J, Vega-Saenz de Miera E, Gold H, Darvishian F, Pavlick AC, Berman RS, Shapiro RL, Polsky D, Osman I: Impact of age on management of primary melanoma patients. *Oncology* 2013;85:173–181.