The review by Balducci provides an excellent overview of issues regarding the pharmacotherapy of anticancer therapy in older patients. The introduction to geriatrics emphasizes the need to be able to determine the patient's physiologic age.

Evolving Armamentarium

As the armamentarium of anticancer therapies has increased over the past few years, the issues that are presented in this paper will become of increasing importance. This is particularly true because of the increase in the number of oral therapies. Such therapies will increase the concerns surrounding polypharmacy, drug interactions, and costs of therapy. These newer therapies have also changed the focus of dose-limiting and therapy-limiting toxicity. While hematologic toxicity was once the most feared complication of therapy when treating elderly patients, this has been partially obviated by the use of hematopoietic growth factors (ie, filgrastim [Neupogen], pegfilgrastim [Neulasta]). On the other hand, the nonhematologic toxicities of therapy have become increasingly important. Dr. Balducci enumerates these when discussing the newer cancer therapies: Anemia, mucositis, cardiomyopathy, neuropathy, osteoporosis, vascular complications, and cutaneous reactions are emerging as the most significant toxicities. Given the increased comorbidity in older patients, these issues may limit the utility of novel therapies unless such problems are studied in the older patient population. Indeed, since the newer targeted therapies (as well as traditional chemotherapy) will be used primarily in older patients, age-related studies are of particular importance.

Pharmacokinetic Differences

Pharmacokinetics of traditional chemotherapy have been studied in “typical” patients—ie, those who are younger and with no comorbidity. End-organ dysfunction trials have been performed for a number of drugs including irinotecan, paclitaxel, gemcitabine (Gemzar), and pemetrexed (Alimta).[3-6] To date, few studies have shown a difference between “typical” patients and elderly—ie, few age-related changes. When pharmacokinetic differences have been present, they have often not been clinically relevant.[7] Few (if any) studies have looked at changes in pharmacokinetics or toxicity over multiple cycles. Pharmacokinetic studies are difficult to conduct due to the heterogeneity of the older population, which can result in too much variability to be clinically applicable. Differences in clinical toxicity are often the result of drug scheduling, not age. For example, this is the case with fluorouracil (bolus weekly vs bolus monthly vs infusion vs oral) and taxanes (weekly vs every 3 weeks).[8] The nonhematologic dose-limiting toxicity is often not related to significant differences in pharmacokinetics (eg, neuropathy from oxaliplatin); this toxicity may instead be affected by a preexisting comorbidity. Nonchemotherapy options such as targeted therapy and antibodies have lessened the importance of pharmacokinetic differences. However, this will require further study in the older population. As many of these drugs are available in oral formulations, ways of ensuring compliance and adherence will also require evaluation.

Future Studies
Future studies in older patients will need to assess patients in particular subsets, including the healthy, vulnerable, and frail elderly. These patients may be suffering from anemia, hypoalbuminemia, or deficiencies in ADLs and IADLS. They will have multiple comorbidities, will more often be survivors of prior cancers, and will have already been treated with chemotherapy and radiation therapy. Studies will need to emphasize changes in cognition, changes in function with treatment, dependency with treatment, and long-term toxicity. Design issues will need to determine the appropriate endpoint in elderly patients (ie, survival, freedom from disease progression, etc). These traditional endpoints may not be the most appropriate in this population. Maintenance of independence and function may be more practical and meaningful. We will also need to evaluate whether our current toxicity scales are appropriate for the elderly.

**Conclusions**

Society has treated elderly cancer patients poorly, even in cases where curative therapy exists. They undergo less adequate surgery, are less often given chemotherapy, and receive lower doses of chemotherapy, often resulting in poorer outcomes. Studies need to focus on older patients, and these investigations will involve the majority of oncology patients treated in the future. Dr. Balducci’s paper provides the appropriate background for the development of these needed clinical studies. Elderly cancer patients need to be the focus of our endeavors—they deserve nothing less.[9]

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**References:**


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