In this issue of Clinical Cancer Research, Townsley et al. report the toxicities they observed in 401 patients enrolled on 19 phase I and II trials of targeted therapeutic agents as part of the National Cancer Institute's (NCI) early therapeutics development program (1). They compared toxicities between younger patients (≤64 years) and older patients (≥65 years). They saw no significant differences in toxicity between these two groups of patients. They concluded that older patients who are otherwise eligible for phase I/II trials seem to tolerate new biological/targeted therapy as well as younger patients.

Both in research clinical trials and in clinical practice, there needs to be more attention to management of the elderly. The majority of people with cancer are the elderly. Approximately 60% of new cancers and 70% of new cancer deaths occur in individuals older than 65 years of age (2). Yet, clinical trials data show that older patients are significantly underrepresented on cancer clinical trials (3–6). Even more importantly, population-based data suggest that older patients are often undertreated or even untreated (7–14). This is undoubtedly due in part to concerns about poorer tolerance of treatment, including surgery, radiation, and especially chemotherapy, and excess toxicity in older patients.

Townsley et al.'s observations are consistent with earlier reports evaluating toxicities associated with more conventional cytotoxic chemotherapeutic agents. Older patients who are eligible for phase I/II trials or phase III trials seem to tolerate chemotherapeutic agents as well as younger patients or have manageable toxicity (15–18). Because older patients enroll in NCI-sponsored clinical trials at much lower rates than would be expected based on the burden of cancer in the elderly, and because older patients must meet the same eligibility criteria to enroll in NCI trials as younger patients, they are a highly select subset of the general elderly population, sometimes referred to as the “fit elderly.”

What can explain undertreatment of older cancer patients in the United States? In general, insurance status cannot explain fully explain undertreatment because the vast majority of U.S. residents older than age 64 years are eligible for Medicare. Older patients, however, often have inadequate access to optimal cancer care. They are less likely to be referred for treatment at NCI-designated Cancer Centers, for example, which treat ~5% of newly diagnosed cancer patients in the United States (19). Similarly, older patients are less likely to be treated at university teaching hospitals than younger patients are more likely to be treated at community hospitals, which may not have the multidisciplinary services required for optimal cancer care.

Compared with younger patients with cancer, older patients with cancer have less social support (20). They are more likely to have lost a spouse through death or have a spouse with significant morbidities. Their circle of friends and family members who can assist with the exigencies of daily life and cancer care are generally smaller. Older patients with cancer are more frequently burdened with comorbidities than younger patients (21). These comorbidities may preclude cancer treatment altogether, or incline caregivers towards modifications of standard therapy (22).

Do we have an adequate database of information on how best to treat older cancer patients? As mentioned above, many trials have shown that the fit elderly, those who meet standard eligibility criteria, tolerate both standard and experimental regimens as well as younger patients. We have less information, however, on the frail elderly, those with major comorbidities, and those in between, with some degree of comorbidity but reasonable functional status. There are declines in kidney, liver, and bone marrow function with age that may increase the potential toxicity of cancer treatment (23). Although physiologic eligibility requirements for our larger trials have been loosened over the past decade, these changes alone have not increased the numbers of older patients in clinical trials (24).

It may be time to consider specifically targeting an accrual goal for well-characterized older patients to acquire more information on how best to treat patients with comorbidities. We need data from prospective studies, including both cohort and phase II trials, on these groups. Studies involving the frail elderly might be best conducted in centers with expertise both in oncology and gerontology. Recently, the NCI and the National Institute on Aging funded eight centers to collaborate on cross-disciplinary studies on cancers in the elderly. Studies evaluating cancer treatment among older patients with some degree of comorbidity can be conducted through the NCI’s Clinical Trials Cooperative Groups, CCOP Research Bases, NCI-designated Cancer Centers, and university teaching hospitals. It is important to perform a comprehensive geriatric assessment as part of the treatment evaluation for older patients (25). We do need an effective geriatric assessment instrument, which can be used easily in a busy oncology practice, to help oncologists distinguish between the fit elderly, the frail elderly, and those in between. Such an instrument might ideally be used at the time of initial presentation, during treatment, and in follow-up, to optimize cancer care from diagnosis through survivorship.
an instrument will need validation in a variety of clinical settings, and across the broad spectrum of race, ethnicity, and socioeconomic status in the United States.

Even with the gaps in our knowledge of how best to treat cancer in older patients, however, we do have a clear charge. We need to ensure that all patients with cancer, regardless of age, race/ethnicity, gender, or economic status, are offered the best possible therapy, management of symptoms, palliative care, and end-of-life treatment. The study of Townsley et al. contributes to the evidence base that can be used to make research and treatment decisions with the new generation of targeted cancer treatments.

References
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Cancer Treatment and the Older Patient
Edward L. Trimble and Michaele C. Christian


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