Further Thoughts on Adjuvant Treatment for Older Breast Cancer Patients

March 01, 2008
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The adjuvant treatment of breast cancer is facing a challenging phase due to the increasing knowledge of breast cancer biology and consequent need to personalize treatments. Medical oncologists are asked to practice evidence-based medicine, but their approach is often based on results of trials conducted in extremely heterogeneous populations. On the other hand, provocative data that take into account the biologic heterogeneity of breast cancer are coming from retrospective analyses and therefore considered mainly hypothesis-generating and not adequate to affect clinical practice.

Challenges are even more evident when dealing with the adjuvant treatment of elderly breast cancer patients, given the need to consider additional variables related to patients themselves. The elderly represent a varied population; it is extremely important to properly define the functional reserve ultimately responsible for treatment efficacy (ie, in elderly patients, the treatment effect may not be observed due to competing causes of death) and treatment tolerability.

The need to face this double heterogeneity (tumor and patient) together with the paucity of data coming from adjuvant trials focused on elderly patients are responsible for a great number of unanswered questions accurately raised by Dr. Downey. Only properly conducted clinical trials will be able to correctly answer these questions. In the meantime, guidelines based on an extensive review of the available data have been published to help clinicians manage elderly breast cancer patients in their daily practice.[1]

Among the topics reviewed by Dr. Downey, we would like to comment on the following issues.

Endocrine Therapy

We agree that the benefits of aromatase inhibitors (AIs) seem to be equivalent in older and younger women. However, detailed information on older women entered in the adjuvant trials of AIs are needed to know whether general considerations about the role of these agents in the adjuvant setting can be transferred to the unfit elderly and the oldest old. While we wait for the results of ongoing trials to clarify the optimal duration and sequence for the use of AIs, some practical recommendations can be made, based on available data.[2]

Upfront AIs should be considered for patients at risk of early relapse (ie, patients with at least four positive nodes) and/or large tumors. Tamoxifen remains a valuable option for early breast cancers at low risk of relapse (ie, grade 1 tumors < 1 cm, with a low proliferative index). Patients falling between these two categories might be good candidates for sequential treatment. An extended adjuvant treatment might be proposed to healthy elderly women with high-risk breast cancer after completing 5 years of adjuvant tamoxifen. Careful evaluation of concomitant comorbidities and the different spectrum of toxicity of tamoxifen vs aromatase inhibitors (cardiovascular events, lipid metabolism, preexistent osteoporosis, cognitive functions) must also be taken into account when recommending adjuvant endocrine therapy in the elderly population.

Chemotherapy
Despite the paucity of data from randomized trials or meta-analyses investigating the role of adjuvant chemotherapy in elderly patients, the general consensus is that fit elderly women with endocrine-resistant breast cancer should be offered adjuvant chemotherapy. Much less clear is the role of adjuvant chemotherapy in patients with estrogen receptor (ER)- and/or progesterone receptor (PR)-positive breast cancer.

Dr. Downey’s conclusions are that “elderly women with high-risk ER-positive breast cancer who are otherwise healthy should still be considered candidates for chemotherapy.” We believe that it is important to better define the concept of high risk in this context, as related to the need for chemotherapy. Nodal status is considered one of the most important prognostic factors in breast cancer, with node-positive patients at high risk of tumor relapse. Mounting evidence suggests that the benefit from adjuvant chemotherapy is independent of nodal status but related to the biologic characteristics of the tumor.

Very recently, Dr. Kathy Albain presented data suggesting the predictive value of the 21-gene recurrence score (RS) assay in patients with node-positive breast cancer.[4] RS was calculated for postmenopausal patients with ER-positive, node-positive breast cancer randomized to receive tamoxifen or six cycles of anthracycline-based chemotherapy plus tamoxifen, in The Breast Cancer Intergroup of North America 0100 trial. The additive benefit of chemotherapy observed in the clinical trial was seen in patients with a high RS, whereas no benefit was apparent in patients with a low RS, and no statistical benefit was observed in patients with an intermediate RS. These data reproduce what was already observed in applying the 21-gene RS assay to node-negative patients entered in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B20 trial.[5] Of note, Dr. Albain also showed that for patients with a high-risk RS, chemotherapy was beneficial regardless of age.

In clinical practice, the joint evaluation by an experienced pathologist of traditional markers such as Ki67, ER and PR level of expression, HER2, nuclear grade, and vascular invasion could help in identifying patients with an uncertain level of endocrine sensitivity who could have additive benefit from chemotherapy.

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References: References

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