Treatment of locally advanced breast cancer

As the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer points out,[1] locally advanced breast cancer comprises a heterogeneous group of breast tumours. Because of the complex needs of these patients, including the requirement for combined-modality treatment, we have established a specialized clinic for the treatment of women with locally advanced breast cancer at the Toronto–Sunnybrook Regional Cancer Centre, the first and largest of its kind to provide appropriate interdisciplinary care[2] for this group of patients.

We would like to add a few points to the analysis presented by the Steering Committee. The recently published guideline[1] discusses only the role of chemotherapy in the neoadjuvant setting. Currently, however, neoadjuvant hormonal therapy with third-generation aromatase inhibitors is gaining importance in this population, especially for an elderly, postmenopausal woman whose breast cancer is positive for estrogen receptor or progesterone receptor. The importance of neoadjuvant therapy with aromatase inhibitors and the superiority of these agents over tamoxifen in this setting has been demonstrated in 2 randomized trials.[3,4]

The authors discuss the evolving role of aromatase inhibitors in the adjuvant setting,[5] but other recent studies have shown the benefit of these drugs after tamoxifen.[6,7] The rapidly accumulating evidence in favour of aromatase inhibitors necessitates frequent updating of guidelines with respect to adjuvant hormonal therapy.

Taxane therapy should now be considered the standard of care. The authors mention the results of 2 large trials[8,9] that clearly showed a substantial improvement in the pathologic response among patients receiving taxanes in addition to anthracyclines. Recent presentation of longer follow-up to one of these studies[10] provides more evidence of improvement in survival with the addition of taxane chemotherapy.

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We would like to raise another issue related to adjuvant chemotherapy for the treatment of women with locally advanced breast cancer.[1] For adjuvant therapy of patients with node-positive, operable breast cancer, cross-trial comparison over similar follow-up periods has indicated a greater risk of acute leukemia with more anthracyclines and alkylators. Specifically, among patients treated with 4 cycles of adriamycin and cyclophosphamide (AC) followed by 4 cycles of paclitaxel, the incidence of acute leukemia ranged from 0.25% over a 69-month follow-up period[2] to 0.18% over a 36-month follow-up period.[3] For regimes of 6 cycles of anthracyclines and alkylating agents, the risk of acute leukemia was much greater: 1.42% over 59 months with cyclophosphamide, epirubicin and fluorouracil (CEF)[4] and 1.17% over 48 months with epirubicin and cyclophosphamide.[5] Even as therapy with AC followed by paclitaxel is being compared with a CEF regimen in the randomized phase III MA.21 trial (being conducted by the Clinical Trials Group of the National Cancer Institute of Canada), this side effect profile should not be ignored in discussions of adjuvant chemotherapy.

Given these data, the use of taxanes should be covered in clinical guideline development.

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