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[Three of the authors respond:]

As Sunil Verma and associates note, evidence is rapidly accumulating that aromatase inhibitors offer advantages over tamoxifen in terms of efficacy and toxicity.[1-3] However, none of these studies has shown an overall survival advantage. At the time our guidelines[4] were submitted, there had not yet been a change in treatment policy incorporating these agents. Although the cited studies did not specifically include patients with locally advanced breast cancer, it is reasonable to extrapolate findings from trials in the setting of early breast cancer to the setting of locally advanced breast cancer.

Two randomized studies have used neoadjuvant aromatase inhibitors in postmenopausal patients with operable tumours. After 4 months, the complete response rate, on the basis of pathological evidence, was only 1%.[5,6] However, for patients with inoperable disease who are not eligible for chemotherapy, we would not recommend an aromatase inhibitor alone outside of a clinical trial. Combined-modality therapy with locoregional irradiation and a systemic hormonal manoeuvre would still be the standard of care.

The incorporation of taxanes into adjuvant therapy is also evolving rapidly.[7] The update on the Aberdeen trial[8] was presented after our manuscript was submitted. Although only 97 patients were randomized, the Aberdeen study is important because it included only patients with locally advanced breast cancer and because it showed a significant survival benefit for patients who responded to cyclophosphamide, vincristine, doxorubicin and prednisone (CVAP) (4 cycles) and were subsequently switched to docetaxel (4 cycles) instead of receiving 4 more cycles of CVAP. If this survival advantage is confirmed by the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-27 study,[7] there will be further compelling evidence for a taxane-based approach. Another recently presented study demonstrated a survival advantage of adjuvant docetaxel, adriamycin and 5-fluoruracil over 5-fluorouracil, adriamycin and cyclophosphamide.[9] However, to date, no taxane-based regimen has shown superiority over an adequately dosed anthracycline-based regimen using oral cyclophosphamide, such as CEF (oral cyclophosphamide with intravenous epirubicin and 5-fluorouracil).[10] This is one question being addressed by the randomized trial MA.21 of the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG).

We agree with Deepu Mirchandani and colleagues that the risk of leukemia should be discussed with any patient undergoing anthracycline-based chemotherapy. The NCIC CTG recently analyzed the risk of leukemia in 4 trials of adjuvant chemotherapy.[11] The conditional probability of myeloid and lymphoid leukemia was 1.7% for epirubicin-containing regimens and 1.3% for AC. In a series of trials conducted by the NSABP, the rate of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) with standard-dose AC was 0.21%.[12] Paclitaxel does not appear to increase this risk. In a recent study there were 8 cases (0.5%) of MDS or AML among 1580 patients treated with AC and the same number in 1590 patients treated with AC and paclitaxel.[13] The leukemia risk for docetaxel-based regimens has not yet been reported.[7] Although treatment-related leukemia risk is an important issue for patients with early breast cancer and a good overall prognosis, patients with a high competing risk of death from breast cancer do not have the same risk of this complication. This point was exemplified by a randomized trial comparing CEF with intensified epirubicin and cyclophosphamide in patients with locally advanced breast cancer.[14] In that trial, there were no reported cases of MDS or AML in the 224 patients who received CEF.

Joe Pater addresses the difficulty of writing guidelines when the sand is shifting with respect to inclusion criteria. We agree that those with isolated supraclavicular involvement (N3c disease) should be treated as having inoperable locally advanced disease. There is some rationale for including patients with clinically apparent internal mammary node (N3b) disease in that category as well. Patients who are found to have extensive lymph node involvement (more than 10) postoperatively should be treated with adjuvant and not primary chemotherapy.

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Correction

Because of an error during editing, incorrect information appeared in Table 1 of a recent article about the career choices of new medical students by Bruce Wright and associates.[1] The number of male students at the University of Alberta was 67 (58%), rather than the number reported in the table. The corrected table appears in Table 3.

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Table 3: Student characteristics by university and year of entry; no. (and %) of students*

Characteristics	U of C 2001 *n = 93*†	UBC 2001 *n = 100*†‡	U of C 2002 *n = 95*†	UBC 2002 *n = 114*‡	U of A 2002 *n = 117*‡	Total *n = 519*
Male	42 (45)	43 (43)	41 (43)	50 (44)	67 (58)	243 (47)
Female	51 (55)	56 (56)	54 (57)	63 (56)	49 (42)	273 (53)
Mean age, yr	24.9	24.3	24.1	24.6	23.1	24.2
Population of community where high school was completed						
< 50 000	24 (26)	23 (23)	21 (22)	33 (29)	22 (19)	123 (24)
50 000–99 999	9 (10)	15 (15)	5 (5)	23 (20)	21 (18)	73 (14)
100 000–500 000	13 (14)	16 (16)	11 (12)	18 (16)	8 (7)	66 (13)
> 500 000	46 (49)	45 (45)	57 (60)	40 (35)	66 (56)	254 (49)

Notes: U of C = University of Calgary, UBC = University of British Columbia, U of A = University of Alberta.
*Unless otherwise indicated.
†1 student did not indicate population of the community where high school was completed.
‡1 student did not indicate gender.