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Letter to the Editor

Estrogen Receptor Status of Advanced Breast Cancer Immediately Before Chemotherapy does not Predict for Response

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There is disagreement on whether estrogen receptor content (ER) influences the response of advanced breast cancer to chemotherapy [1, 5, 8, 11]. A previous retrospective study from this unit showed no effect of ER status on frequency of response to chemotherapy [11]. As most reports have utilized ER measurements made some time before chemotherapy and changes in ER status may occur, especially after antiestrogen or ablative hormone therapy [9], we instituted a prospective study to determine whether receptor status immediately before commencement of chemotherapy influences response rates.

All patients with progressive locally advanced or disseminated breast cancer about to start chemotherapy for the first time and with tissue available for biopsy were eligible for inclusion in this study. Patients with visceral disease only, those in whom biopsy of an accessible lesion would mean loss of sole measurable disease, and those in whom histological examination of adjacent tissue did not show malignancy were excluded. Because of the long half-life of the antiestrogen tamoxifen, especially after continuous administration [2], and because its presence could induce false-negative ER determinations [7], this agent was stopped at least 4 weeks before biopsy in all cases.

Chemotherapy was administered in the context of several clinical trials, and included

a) Adriamycin 70 mg/m^2 IV (60 mg/m^2 for patients older than 60), ± vincristine 1.4 mg/m^2 IV (maximum 2 mg) at 3-weekly intervals for eight cycles, followed by cyclophosphamide 100 mg/m^2 PO (maximum 150 mg) on days 1–14, methotrexate 30 mg/m^2 IV (maximum 50 mg) on days 1 and 8 (20 mg/m^2 for patients older than 60), and 5-fluorouracil 600 mg/m^2 IV (maximum 1 g) on days 1 and 8 (400 mg/m^2 for patients older than 60) of a 4-week cycle, continuing until relapse;

b) Cyclophosphamide, methotrexate, and 5-fluorouracil as above;

c) Adriamycin 40 mg/m^2 IV every 3 weeks for 12 cycles + mitomycin C 10 mg/m^2 IV every 3 weeks to relapse (AM);

d) Mitoxantrone 12 mg/m^2 IV every 3 weeks to relapse.

Before commencing cytotoxic chemotherapy, all patients had evidence of progressive disease. They were assessed clinically, measurements being taken of all visible and palpable lesions, with color photography of visible lesions. A bone survey (isotopic), with radiographs of areas of increased uptake, chest radiograph, and biochemical screen (including liver function tests) were performed in all cases, and liver scans when indicated. The patients were assessed periodically at either 3- or 4-weekly intervals, according to the chemotherapy schedule given. Response was assessed by UICC criteria [3], and response duration and survival estimated by the log-rank method [10].

Estrogen receptor (ER) analysis was carried out by the method of King et al. [6]. An ER value of < 5 fmole cytosol protein/mg was defined as negative (ER-), and any value greater than this was regarded as positive (ER+).

Thirty-five patients were entered into this study, 22 with ER+ tumors and 13 with ER− tumors. Patients in the two groups were similar in age, stage of disease at diagnosis, sites of involvement and disease-free interval. Twenty-one patients with ER+ tumors had prior endocrine therapy, as against ten with ER− tumors. Twenty-nine patients (18 ER+, 11 ER−) had adriamycin-containing regimens. There were 13 responses (59%) to chemotherapy in patients with ER+ tumors (3 CR, 10 PR), and seven (54%) responses in patients with ER− tumors (all PR). Median response duration was longer in patients with ER+ tumors (31 weeks) than in patients with ER− tumors (17 weeks), but this was not significant. Survival from start of chemotherapy was similar in the two groups.

These results confirm those of neither Lippman et al. [8] nor Kiang et al. [5], but show that in our practice, response to cytotoxic chemotherapy is the same for ER+ and ER− tumors. In addition, this lack of a relationship between ER status and response to cytotoxic chemotherapy is demonstrated whether assay for ER is done on tumor biopsied immediately before chemotherapy, as in this report, or there is intervening hormonal therapy, as in our previous study [11].

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