Toxicity was acceptable and roughly comparable to 5-FU/FA regimens in conventional doses, but high-dose 5-FU was associated with uncommon side-effects, such as hand–foot syndrome, cardiotoxicity and neurotoxicity. Further desirable study of this regimen will undoubtedly be hampered by its enormous cost, notably in view of the fact that, so far, with regard to survival, 5-FU/FA regimens are not superior to 5-FU alone [7].

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Phase II Study of 4-Epirubicin, Etoposide and Cisplatin as Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer

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MOST PATIENTS with locally advanced breast cancer (LABC) stage III disease, including patients with resectable and "inoperable" tumours will develop distant metastasis [1]. The 5-year disease-free survival (DFS) for stage IIIB without systemic treatment is about 10%. Combined modality therapy has been, therefore, the standard of care for these patients [1, 2], and involves the administration of neoadjuvant chemotherapy [2, 3]. Despite objective responses higher than 70%, only about 30% of stage IIIB patients are alive and disease-free at 5 years [2, 3].

In an attempt to improve treatment results, we have used a combination of 4-epirubicin (4-EPI), etoposide (E) and cisplatin (P), EEP, as a neoadjuvant treatment for non-inflammatory LABC. 4-EPI is active in breast cancer [4, 5] with less toxicity than doxorubicin [4, 5]. The combination of E and P is also active in previously treated and untreated patients [6–8].

From September 1989 to August 1992, 27 patients were treated with 4-EPI 50 mg/m^2 intravenously (i.v.) day 1, E 80 mg/m^2 i.v. days 1–3, and P 20 mg/m^2 i.v. days 1–3 every 3 weeks, followed by local therapy (mastectomy ± radiotherapy) and adjuvant therapy with FEC (5-fluorouracil, 4-EPI and CTX) or CMF. The number of cycles of FEC or CMF was managed to complete 10 cycles of chemotherapy, considering the cycles of EEP administered previously.

The patients were aged 33–63 years (median 42); 6 had stage IIIA disease and 21 stage IIIB; 19 were premenopausal and 8 post-menopausal; the median tumour size was 12 cm (range 7–24) with 24 tumours ≥ 10 cm. All 27 patients had 0–1 performance status.

The median number of cycles of EEP was four (range two to eight). 26 patients were evaluable for response and 1 was excluded (FEC substituted EEP after the second cycle, due to toxicity).

Pathological complete remission (pCR) was obtained in 11.5% (3/26) of patients, 85% (22/26) achieving a partial remission (PR). 20 patients (74%) received local therapy. At 48 months, 43% of the patients are projected to be alive, with a median follow-up of 20 months (range 11–48). The actuarial DFS at 42 months is 22%. 9 patients (33%) are still alive with no evidence of disease. 2 patients of 17 (12%) had locoregional recurrence, 8 had locoregional and distant metastasis (47%) and 7 (41%) had distant metastasis only. Most patients developed nausea and vomiting (grade II 16 patients, grade III 9 patients). There were five episodes of fever with leucopenia.

Hortobagyi and colleagues using FAC in 174 patients with LABC, observed an objective response in 87.4% with CR in 16.7% and PR in 70.7%. The 5-year overall survival was 84% for IIIA and 44% for IIIB. DFS was 84% for stage IIIA and 33% for IIIB. Only 22% of the patients had tumours larger than 9 cm [2, 3].

Most of our patients had tumours larger than 10 cm. Despite a high response rate, CR and long-term results were not better than standard systemic therapy.

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