A second problem, related to the discrepancy between clinical and pathological complete remission, is the localisation of the prechemotherapy site of the tumour in a case of clinical complete remission (CR). Patient 4 had obtained a clinical CR and underwent lumpectomy after ultrasound localisation of a doubtful remaining lesion. In the margin of the lump, a very small amount of viable IDC was found, and more IDC in the mastectomy specimen.

The third problem was a major discrepancy between the clinical and pathological response. 3 patients (5–7) had a small lesion after induction chemotherapy. In 2 patients, a lumpectomy and in 1 patient a mastectomy was performed, which were irradical because of the presence of multifocal tumour rests. In all patients, invasive lobular carcinoma (ILC) was found, which is known for its multicentric diffuse growth pattern [10, 11].

Although there have been reports on the discrepancy between clinical and pathological evaluations of response after induction chemotherapy in breast cancer [1, 12], our experience indicates a cautious approach should be taken in the use of chemotherapy to induce "lumpectability", and it is recommended that the response is verified pathologically, especially in patients with CIS and/or ILC.

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Sequential Chemotherapy, Beta Interferon, Retinoids and Tamoxifen in the Treatment of Metastatic Breast Cancer. A Pilot Study

F. Recchia, S. Rea, G. Corrao, A. Fingerhut and L. Frati

CHEMOTHERAPY (CT) for metastatic breast cancer remains palliative, and no clear therapeutic strategy has yet been established for responders with subclinical minimal residual disease. *In vitro* studies have shown that interferons (IFN) and retinoids inhibit the growth of oestrogen receptor positive (ER+) and negative (ER−) breast cancer cell lines [1, 2], and sensitise them to the antiproliferative action of anti-oestrogens through the enhancement of oestrogen receptors [3–6].

This rationale led us to undertake a phase II pilot study to explore the attractive working hypothesis of administering two non-cross-resistant CT regimens, followed by maintenance therapy, with β-IFN, retinoids and tamoxifen (TAM) in a group of patients with poor prognosis metastatic breast cancer. Eligibility criteria included pathologically documented measurable or evaluable breast cancer; age <75 years; performance status <3; no anthracycline chemotherapy; recovery from previous radiotherapy and/or CT with WBC count >3500 mm^3, platelet count >100 000 mm^3; normal kidney and cardiovascular function and written informed consent. Induction CT was 4-epidoxorubicin 60 mg/m^2/day 1, cyclophosphamide 500 mg/m^2/day 1, vincristine 2 mg day 1, 5-fluorouracil 500 mg/m^2 days 1 and 8, prednisone 50 mg days 1–5, and this was repeated every 3 weeks for six courses, followed by mitomycin-c and mitoxantrone 10 mg/m^2, methotrexate 40 mg/m^2 day 1 for two courses every 4 weeks. Maintenance therapy for responders was β-IFN 1 × 10^6 IU/m^2 three times a week, retinyl palmitate 50 000 IU twice daily, TAM 10 mg three times daily, until disease relapse.

Responses and toxicities were categorised according to WHO criteria. 36 patients were enrolled in the trial from January 1987 to January 1992. Median age was 61 years (range 37–74); 4 were premenopausal and 32 postmenopausal. Median disease-free interval was 19 months (range 1–28) for 27 patients, while 9 patients had metastases at the time of diagnosis. All patients had

Correspondence to F. Recchia at Via Rossetti 1, 67056 LUCO DEI MARSI (AQ), Italy.
F. Recchia is at the Division of Internal Medicine (Oncology Unit), Civil Hospital, 67051 Avezzano; S. Rea, A. Fingerhut, F. Recchia and L. Frati are also at "Centro di Riferimento Oncologico Franco-Italiano", Moterotondo, Rome; S. Rea is also at the Surgical Oncology University of L'Aquila; G. Corrao is at the Medical Statistics and Biometry University of L'Aquila; and L. Frati is also at the General Pathology University "La Sapienza", Rome, Italy.
A. Fingerhut was a visiting Professor at the Surgical Oncology University of L'Aquila, Italy.
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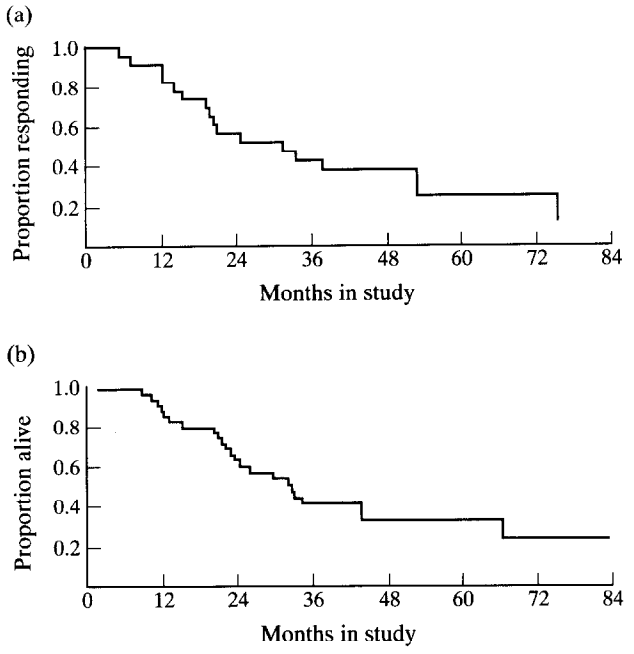

Figure 1. Response duration (a). Overall survival (b).

infiltrating ductal carcinoma. 17 patients had >10 axillary nodes. 21 patients (58%) had received endocrine therapy. 21 patients (58%) had previous cyclophosphamide–methotrexate–5-fluorouracil CT (12 adjuvant and 9 for metastases). 17 patients (47%) had received radiotherapy for palliation. A mean of 7.5 CT courses were administered to each patient. Median follow-up was 33 months.

Toxicity of CT was mainly haematological, with fifteen patients having grades 2–3. 16 patients had grade 2 gastrointestinal toxicity. Toxicity of maintenance therapy was mild, and mainly hepatic.

11 patients had a complete response (CR) (31%), 12 had a partial response (PR) (33%), 7 had stable disease (19%), while 6 had progressive disease (17%) (overall response rate 64%, 95% CI 48–80%). A CR was observed in 3 patients that had a PR to CT alone (two liver and one bone metastases) after 3 months of maintenance therapy. Responses were achieved in bone (8 patients), soft tissue (5 patients) and viscera (10 patients). As of December 1993, 33% of patients were alive, and median response duration and overall survival were 31 (range 5–75) and 32 (range 9–83) months, respectively (Figure 1). 2 patients with cutaneous lesions and PR had an increase of ER tumour content from 60 to 90% and from 40 to 80% of cells during maintenance therapy.

Due to the tumour heterogeneity, CT is capable of eradicating sensitive, actively proliferating cell clones. Disease may relapse in the presence of CT-resistant, slowly proliferating cells (minimal residual disease). Retinoid analogues of vitamin A, such as TAM, enhance the secretion of transforming growth factor-β which inhibits growth of most epithelial cells [7]. Synergism of action has been shown for retinoids and IFN in advanced squamous carcinomas of the skin and the cervix [8, 9]. The action of IFN and retinoids could be synergistic with TAM in inhibiting the regrowth of minimal residual disease. In the present trial, we obtained a 64% response rate and a median response duration and survival of 31 and 32 months, respectively, without affecting quality of life. In conclusion, it is possible to administer CT and immuno-hormonotherapy sequentially with acceptable toxicity, and to prolong response duration.

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Dose Intensification of Carboplatin and Etoposide as First-line Combination Chemotherapy in Small Cell Lung Cancer

P.A. Ellis, D.C. Talbot, K. Priest, A.L. Jones and I.E. Smith

CISPLATIN COMBINED with etoposide (EP) is one of the most effective first-line regimens in small cell lung cancer (SCLC) [1, 2], although the cisplatin component can be associated with significant toxicity [1]. Our group has previously tested the less toxic cisplatin analogue carboplatin [3] in combination with etoposide (CE) in SCLC reporting high response rates [4], results which have been subsequently confirmed by others [5, 6]. In

Correspondence to I.E. Smith.
All authors are at the Royal Marsden Hospital, Sutton, Surrey SM2 5PT, U.K.
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