CYCLICAL COMBINATION CHEMOTHERAPY IN ADVANCED BREAST CANCER

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Cyclical combination chemotherapy (CCC) is well established in certain late malignancies where it produces impressive results. It is now becoming recognized in advanced breast cancer. The results in 100 women treated by a 4-drug regimen comprising cyclophosphamide (Endoxana), 5-fluorouracil, methotrexate, and vincristine are presented. A 77% objective remission was encountered, 66% of the patients continuing in control at 12 months. To place these results in perspective they have been compared with other patients treated by the first author. Of 102 treated by hypophysectomy, 52% responded, while of 154 treated with norethisterone acetate (NEA) 33.8% responded.

Chemotherapy clearly is a superior procedure overall, but it is recognized that certain clinicopathological characteristics are associated with response to endocrine treatment. By making use of these it is possible to distinguish certain high-response groups and it might be that in certain of these endocrine treatment produced results as good as if not superior to chemotherapy. To formulate a treatment policy relating these two therapeutic principles requires investigation of this aspect.

The predominant pattern of disease recurrence. The local variety shows a high response rate to NEA and CCC with a poorer outcome from hypophysectomy. Osseous disease shows a good response to hypophysectomy and chemotherapy but does badly with NEA. Visceral disease does poorly both with NEA and hypophysectomy. While the incidence of response is somewhat lower with chemotherapy, it is still much higher than that obtained with either endocrine procedure.

The disease-free interval. When this is less than 2 years endocrine results are poor. Chemotherapy shows no such differentiation.

The age of the patient at treatment. Women under the age of 55 do poorly with endocrine procedures. The results of chemotherapy show no such influence.

When factors are classed simply as favourable or unfavourable the optimum situation with NEA and hypophysectomy, where all factors are favourable, gives response rates in the 90% plus range. Conversely, where all factors are unfavourable the response rates lie between 0 and 8%. For chemotherapy the figure ranges from 87% where all factors are favourable to 58% where all are unfavourable.

It would appear that chemotherapy is superior to endocrine measures in almost all situations evaluated. It is concluded that with the exception of NEA in the most favourable condition—that is, slowly evolving local disease in older women—there now remains little part for conventional endocrine therapy.

Implications may extend into the field of so-called early breast cancer. It is pointed out that most women with this disease ultimately die from distant metastases, commonly in bone. Generally, these become apparent despite successful eradication of local disease. Assuming that these metastases have origin-
ated from the primary growth, which is no longer present, it would seem that their dissemination must have occurred before its diagnosis. Their non-diagnosis at that time is related to the diagnostic shortcomings of standard radiological techniques. It is a medical maxim to treat recognized disease at the earliest possible opportunity and accordingly efforts should be made to combat these micrometastases ab initio. In the past no successful treatment has been available but now with the impact of chemotherapy in advanced disease its use at an earlier stage can be considered. Plans for such a collaborative project are being developed. It is, however, necessary to improve the safety and convenience of treatment. Accordingly a trial of androgens is being performed to determine whether they protect against bone marrow toxicity. Results to date are inconclusive apart from a suggestion that platelet counts seem better maintained. Sufficient justification to continue the trial has been obtained.

Results from a prospective trial of trifluoperazine (Stelazine) as a routine prophylactic antiemetic will soon be published.

To shorten the CCC treatment course a prospective clinical trial comparing a short one-day treatment with the conventional 5-day regimen* is under way. This co-operative venture, involving London, Cambridge, Dublin, and Belfast, has been established under the auspices of the CRC National Breast Cancer Trial. It would be premature to discuss the results, which will form the subject of a future communication.

References

1. Edelstyn, G A, and MacRae, K D (1973) British Journal of Cancer, 28, 459.
2. Edelstyn, G A, Gleadhill, C A, and Lyons, A R (1968) Clinical Radiology, 19, 426.
3. Edelstyn, G A (1973) Cancer, 32, 1317.

*The regimen used has been modified as follows: cyclophosphamide 300 mg on Days 1 and 5; 5-fluorouracil 500 mg on Days 1–5; vincristine 1 mg on Days 2 and 5; methotrexate 20 mg on Days 1 and 4.

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