based on the products of the MUC1 gene. The product of this gene, polymorphic epithelial mucin (PEM), is expressed by normal epithelial cells but is overexpressed and aberrantly glycosylated in tumours. Cellular and humoral responses to PEM have been detected in both breast and ovarian cancer patients, and the cytoxic T cells recognising this antigen are not dependent on presentation by HLA class 1 molecules. Clearly, antigen presentation is of crucial importance, since tumours have not been rejected in cancer patients even though the cancer cells express not only PEM, but also mutated oncogenes, such as TP53, or proto-oncogenes, such as c-*erb* B2. This emphasises the importance of preclinical studies with mouse model for evaluation of vaccine formulations, including the possible use of co-stimulatory molecules, such as B7, and DNA-based vaccines.

Optimisation of existing therapies is still perhaps the most important consideration for clinicians and for patients presenting now with breast cancer. Recent research from Guy's Hospital on the timing of surgery in premenopausal women and its effect on prognosis is described by Fentiman and Gregory. Of patients who underwent tumour excision at the time of unopposed oestrogen (days 3–12), the 10-year survival was 54% compared with 84% for those undergoing surgery at other times of the menstrual cycle. This effect was mostly confined to patients with axillary node involvement, and the data are consistent with tumours being less cohesive under conditions of unopposed oestrogen. There has been controversy concerning this finding, and an overview has been conducted which showed that overall no significant effect was demonstrated, but that the heterogeneity of the results suggest that the positive findings are not the chance result of a normal distribution.

Being able to predict response to therapy is clearly desirable to avoid the considerable side-effects of some drugs if they are likely to be ineffective. Klijn and colleagues comprehensively review the data on prognostic factors and response to both endocrine and cytotoxic therapy. They emphasise that in fact valuable prognostic factors may be worthless in determining response to therapy, and poor prognostic factors may predict response. For example, those tumours expressing c-*erb*B2 are more likely to respond to chemotherapy, unlike those displaying multidrug resistance. In premenopausal women, the primary tumour and metastatic disease may differ in response as a result of the endocrine effects of adjuvant chemotherapy. These biological markers may eventually serve as targets for new biological therapies.

Advanced breast cancer is not curable, and yet the long natural history of the disease means that it is a very common problem, which is discussed by Rubens. Optimal management takes into account not only duration, but also quality of survival. As more patients receive systemic adjuvant therapy, so the response of recurrent disease may be reduced. Bone metastases are a common problem and these can be successfully palliated with both bisphosphonates and beta-emitting radioisotopes, with response being monitored biochemically as well as by imaging.

With breast cancer, our aim is not just to diagnose the disease at an earlier stage and treat optimally with a multidisciplinary approach, but also to identify women at risk so that preventative strategies may be used. Morrow and Jordan review this timely topic, focusing on the use of tamoxifen, in the context of the National Surgical Adjuvant Breast Project trial, which is now running in the U.S.A. They conclude that although tamoxifen is likely to prove safe and effective, there are some unanswered questions with regard to long-term toxicity, and this must be determined by a prospective randomised trial.

In considering the body of breast cancer-related work produced by scientists and clinicians, a survey of which is presented here, it becomes very clear that interaction between the laboratory and the clinic continues to be vital to progress in the development of diagnostic procedures and therapies. Although the clinical relevance of some laboratory research is still a distant prospect, much of this research has reached the stage where its "potential" needs to be tested in clinical practice. The science has advanced tremendously; the challenge remains to make the exciting results coming from the laboratory into a practical benefit for the large number of women who are going to be confronted with the disease. It is our hope that this volume of *Cancer Surveys* takes a small step in the direction of achieving that aim.

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Letters

Combination Chemotherapy With Carboplatin and Etoposide of Brain Metastases From Cancer

A. Santini, P. Malacarne, M. Indelli and A. Maestri

ETOPOSIDE HAS proved useful in the case of small cell lung cancer (SCLC) [1, 2], while carboplatin has been successfully used in head and neck cancer and in ovarian cancer [3]. Platinum derivatives and etoposide have been employed even in the treatment of brain tumours [4]. The association of etoposide and cisplatin, useful in the treatment of many solid tumours, has proven to be highly effective in the management of brain metastases from breast carcinoma [5].

The present study was designed to assess the efficacy of carboplatin and etoposide in brain metastases from solid tumours.

22 consecutive patients (15 males and 7 females, median age 55.7 years, range 40–71) have been studied; 13 patients [10 lung cancers, 3SCLC, 7 non-small cell lung cancer (NSCLC), 3 occult tumours] who had not received any previous chemotherapy, and 9 (4 breast cancers, 4 lung tumours, 2 SCLC, 2 NSCLC, 1 uterus

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Table 1. Response to chemotherapy and survival of all patients

Response	No. of patients (%)	Primary tumours	Duration of response, weeks (median)	Overall survival, weeks (median)
CR	1 (4.54)	SCLC	32	31–88 (46.28)
PR	6 (27.27)	3 SCLC 3 NSCLC	22–31 (25.33)	
NC	3 (13.63)	1 breast 1 NSCLC 1 occult	10–20 (16.33)	10–44 (26.0)
P	11 (50.0)	5 NSCLC 1 SCLC 2 breast 1 uterus 2 occult		2–66 (24.63)
NE	1 (4.54)	breast		

CR, complete remission; PR, partial remission; NC, no change; P, progression; NE, not evaluable.

cancer) who had had previous treatment with one or more different types of chemotherapy. 3 of these patients (2 NSCLC, 1 SCLC) had had previous treatment with platinum derivatives. All the patients under study had cerebral metastases documented by contrast-enhanced brain computed tomography (CT), carried out after the beginning of steroid therapy. All the patients were treated with carboplatin (300 mg/m^2 day 1 every 4 weeks) associated with etoposide (120 mg/m^2 days 1–3 every 4 weeks). Clinical evaluation was carried out before every cycle of chemotherapy, while CT scan was practiced every two cycles. Response to therapy and toxicity were valued in accordance with WHO criteria; overall survival was calculated in weeks from the date of the beginning of chemotherapy. The patients eligible for evaluation were 21 as 1 patient (breast cancer) refused to continue therapy after the first course. Altogether 64 cycles of chemotherapy were administered. Response to chemotherapy, duration of response and survival of all patients are shown in Table 1. Of the 7 patients who responded to treatment, 3 partial response (PR) had had previous chemotherapy: 2 of these (1 NSCLC, 1 SCLC) with platinum derivatives. In 6 cases, the site of progression was the encephalus, sometimes associated with extracranial disease. In 1 case, cutaneous metastases continued development.

Toxicity did not cause delays or reduction of doses. In 3 patients, who had showed WHO grade IV myelotoxicity, treatment was, however, suspended because of progression.

Our data show how the replacement of cisplatin with carboplatin, which is less toxic and certainly more manageable, maintains the same high level of success as the etoposide–cisplatin combination. The best results have, therefore, occurred in the treatment of the tumours which are most sensitive to the combination. In the treatment of brain metastases from lung cancer, the association of carboplatin and etoposide could be a valid alternative to traditional radiotherapy. In fact, as we know, the brain is rarely the sole site of metastases [2], and patients receiving cranial irradiation alone almost always die of extracranial tumour rather than cerebral metastases, therefore a chemotherapy treatment will be necessary.

The chemotherapy, when it is efficacious, can be useful for controlling all the sites of metastases including cerebral lesions. This may be particularly useful when using well tolerated drugs like carboplatin and etoposide.

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Hypersensitivity Reactions to Carboplatin Given to Patients With Relapsed Ovarian Carcinoma

J.S. Morgan, M. Adams and M.D. Mason

ALTHOUGH HYPERSENSITIVITY reactions to cisplatin occur in 1–20% of patients [1], hypersensitivity reactions to carboplatin appear uncommon, occurring in less than 8% of patients [2–5].

We have reviewed the case notes of 180 cases of histologically proven overian carcinoma treated with single-agent intravenous carboplatin at the Velindre Hospital. Overall, 8.7% of patients developed a hypersensitivity reaction. However, of 34 patients given a second and third course of carboplatin on relapse, 15 (44%) developed a hypersensitivity reaction compared to only one reaction seen in 180 patients during their first course of carboplatin ($P<0.01$, Fisher's exact test).

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