Eur J Cancer, Vol. 28, No. 2/3, p. 317, 1992.
Printed in Great Britain

0964-1947/92 $5.00 + 0.00
Pergamon Press plc

Breast Cancer: Lots of Data, Steady but Slow Clinical Progress

EORTC Breast Cancer Working Conference, 3–6 September 1991, Pauscollege Leuven

BREAST CANCER is probably one of the most typical examples in the field of oncology where the management has switched in less than 2 decades from a very simple, straightforward approach, to a difficult and sophisticated domain.

Not so very long ago, all patients underwent mastectomy and the only pending question was whether postoperative radiotherapy was to be given. Even this last question was usually asked as a "black or white" problem with little discrimination for the different subgroups.

The development towards less aggressive local treatments with breast preservation and of different systemic modalities for advanced disease with also the concept of adjuvant treatments have led to a rapid expansion of the field of scientific topics which are studied in relation to the treatment of breast cancer. These go from the level of molecular biology and biochemistry, amongst other things trying to refine the insights of the biology of the individual tumours and therefore the prognosis of specific patients to which treatment can be tailored, over problems of health resources allotment to be covered in the assessment of effectiveness of screening and cost-benefit ratios of adjuvant treatment, to the specific problems of quality evaluation of the technical aspects of treatment and the assessment of "adequacy" of treatment indications and finally the psychological side effects and possible support of patients.

The rapid accumulation of scientific data in recent years has been fascinating. It is therefore sometimes slightly disappointing to compare the availability of data with the slow accrual of new facts in medical practice. This has to do with the complexity of the chain of events going from diagnosis to final outcome, and to the long time intervals which are necessary to have a final assessment of the impact of new modalities of policies but also to the shortage of structural organisation in clinical research. Still too many data are collected in studies which by their concept are doomed to lack the necessary power to draw any conclusion.

The Breast Cancer Working Conference in Leuven was again a typical mixture of this state of the field. With the active participation of over 700 enthusiastic scientists, very interesting basic data were presented and stimulating discussions were held, including clinical research where progress is however, much slower.

In the present package of papers, there are several "review articles", covering specific aspects, as they were presented during the conference. Also, a number of scientific papers which were presented in the different symposia and proffered paper-sessions have been collected and peer reviewed through the normal channels of the journal.

E. van der Schueren
Universitair Ziekenhuis St Rafael
Capucijnenvoer 33
BG-3000 Leuven
Belgium

Eur J Cancer, Vol. 28, No. 2/3, pp. 317–318, 1992.
Printed in Great Britain

0964-1947/92 $5.00 + 0.00

Ductal Carcinoma *in situ* of the Breast: Do we Still Need Trials?

AT PRESENT there are several national and international trials examining aspects of the management of ductal carcinoma *in situ* (DCIS) of the breast. As more information becomes available, more rapidly, from non-randomised studies, will the trials become redundant? Emphatically no. In this issue Silverstein *et al.* (pp. 630–634) report a series of 227 patients with DCIS, largely diagnosed because of mammographical abnormalities. Their results raise as many questions as they answer.

98 patients (43%) were treated by mastectomy, the main indication being the extent of DCIS, mean pathological diameter of the lesions being 3.7 cm. 1 of these patients developed an invasive relapse. Wide excision and radiotherapy (with or without an interstitial boost) was used in 103 (45%). Average size of lesion was 1.4 cm, and 8 patients relapsed, 5 with DCIS and 3 with invasive disease. Wide excision, without radiotherapy, was used to treat 26 (average size 1 cm) and there were 2 relapses, 1 invasive and 1 non-invasive.

Received and accepted 7 Oct. 1991.

The majority of patients had lesions which could be completely excised and this will be heartening news for the UK trial of screen-detected DCIS [1]. The experience of the EORTC Breast Cancer Cooperative Group in trial 10853 was that only one-third of patients with DCIS were suitable for the trial, which compares wide local excision with wide local excision and external radiotherapy (50 Gy) [2]. The majority of the contributing centres to trial 10853 were treating symptomatic rather than screened women.

Silverstein has shown, as have most other studies that axillary clearance is not required, and that mastectomy reduces the risk of ipsilateral recurrence to almost zero [3–5]. Additionally, even when patients with smaller lesions are selected for breast conservation there will be an increased risk of recurrence of DCIS or progression to invasive disease. Whether this can be altered by radiotherapy still remains unanswered.

Large well-controlled trials will be needed to determine this. EORTC trial 10853 is still open, and has to date accrued 276 cases. Eligible patients will have had DCIS completely excised (confirmed after pathological examination of inked edges). No axillary dissection is performed and no radiation boost is given to the biopsy site. Getting more surgeons and their patients to participate in this trial will enable sub-group analysis to be conducted of the various histological variants of DCIS. Then, perhaps, the effect of radiotherapy on DCIS will become apparent.

I.S. Fentiman
ICRF Clinical Oncology Unit
Guy's Hospital
London, SE1 9RT U.K.

1. Fentiman IS. Treatment of screen-detected ductal carcinoma *in situ*: a silver lining within a grey cloud? *Br J Cancer* 1990, **61**, 795–796.
2. Fentiman IS, Julien J-P, van Dongen JA, *et al.* Reasons for non-entry of patients with DCIS of the breast into a randomised trial (EORTC 10853). *Eur J Cancer* 1991, **27**, 450–452.
3. Von Rueden DG, Wilson RE. Intraductal carcinoma of the breast. *Surg Gynecol Obstet* 1984, **158**, 105–111.
4. Fentiman IS, Fagg N, Millis RR, *et al. In situ* ductal carcinoma of the breast: implications of disease pattern and treatment. *Eur J Surg Oncol* 1986, **12**, 261–266.
5. Rosen PP, Senie R, Schottenfeld D, *et al.* Non-invasive breast carcinomas. Frequency of unsuspected invasion and implications for treatment. *Ann Surg* 1979, **18**, 377–387.

Eur J Cancer, Vol. 28, No. 2/3, pp. 318–321, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00
Pergamon Press plc

Papers

Tamoxifen Up-regulates c-*erb*B-2 Expression in Oestrogen-responsive Breast Cancer Cells *in vitro*

Susanna Antoniotti, Piera Maggiora, Claudio Dati and Michele De Bortoli

Expression of the c-*erb*B-2 proto-oncogene is inhibited by oestrogens in oestrogen-responsive human breast cancer cells, at both mRNA and protein level. Here we report that, where the regulation of c-*erb*B-2 is concerned, tamoxifen displays a full anti-oestrogenic activity, enhancing the expression of c-*erb*B-2 in oestrogen receptor-positive cells cultured with untreated fetal calf serum or reversing the inhibitory effect of added oestrogens. Meanwhile, tamoxifen strongly inhibited cell growth. Tamoxifen was inactive on both c-*erb*B-2 expression and growth of oestrogen receptor-negative cells. These results may have important implications to explain occasional failure of tamoxifen therapy in oestrogen receptor-positive breast cancers.
Eur J Cancer, Vol. 28, No. 2/3, pp. 318–321, 1992.

INTRODUCTION

THE c-*erb*B-2 proto-oncogene (also called HER2/*neu*) encodes a 185 kD transmembrane tyrosine kinase (p185) [1], sharing a 50% homology with the epidermal growth factor receptor [2]. c-*erb*B-2 is frequently amplified in a variety of human adenocarcinomas and the resulting p185 overexpression is thought to confer a particular aggressiveness to the tumour. Human breast cancer has been extensively investigated and c-*erb*B-2 amplification and overexpression shown to be associated with early relapse and death [3, 4].

Work from our and other laboratories has demonstrated that the expression of c-*erb*B-2 in mammary cells is subjected to hormonal regulation [5, 6]. In particular, we have recently shown that oestrogens specifically inhibit c-*erb*B-2 expression in breast cancer cells [5]. Oestrogen receptor positive (ER+) breast cancers are commonly treated with endocrine therapies, mainly by the use of anti-oestrogenic drugs such as tamoxifen, which shows clear antimitogenic properties on oestrogen-dependent cells.

Therefore, we have investigated the effect of tamoxifen on c-