

disease (n = 49), normal premenopausal (at 8 equal intervals across the menstrual cycle) (n = 8) and postmenopausal women (n = 28). Levels were measured by radio-immunoassay.

Results: pTSP in women with EBC (median 461, IQR = 346–844) was elevated when compared to women following surgery (median = 227, IQR = 177–270) ($p < 0.001$), and normal controls (median = 225, IQR = 188–260). Women with EBC who had nodal metastases (n = 22) had higher levels of TSP (median 509, IQR = 411–997) than women who were node negative (median = 297, IQR = 225–401) (n = 31) ($p < 0.05$). pTSP in women with high grade tumours (n = 36) was raised when compared to grade 1 tumours ($p < 0.05$). pTSP levels in women with ABC (median 588, IQR = 401–904) were higher than women with no evidence of recurrent disease ($p < 0.001$) and normal controls ($p < 0.001$).

Conclusion: Plasma thrombospondin levels are a marker of metastatic disease in EBC and ABC and may be useful in assessing response to chemotherapy.

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POSTER

The 'ZEBRA' study: An open randomised trial of 'Zoladex' vs CMF as adjuvant therapy in the management of node positive stage II breast cancer in pre/perimenopausal women aged 50 years or less

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To evaluate long-term use of Zoladex (Z), an LHRH agonist, as an adjuvant treatment for breast cancer in pre/perimenopausal women, this study was designed using cytotoxic chemotherapy, the current systemic adjuvant treatment of choice, as a comparator. Recruitment started in 1990 and closed in December 1996. 1640 patients from 102 centres in Europe, Australia and Argentina, were randomised to Z (2 years therapy – 3.6 mg s/c depot every 28 days) or CMF (cyclophosphamide, methotrexate, 5-fluorouracil; 6 cycles; 4 weekly). The aims are to compare disease-free survival, overall survival, safety, adverse reactions and quality of life. As a sub-protocol (n = 187), the effect of treatment on Bone Mineral Density was assessed. Oestrogen receptor status is currently negative for approx. 20% – review ongoing. Data collection is continuing but preliminary review of demographic data shows: breast conserving surgery was carried out in 47% patients, mastectomy in 53% and radiotherapy was given in 69%. 70% of the patients had 1–3 positive nodes and 47% had a tumour size ≤ 2 cm. Demographic and pre-treatment characteristics were comparable in the two arms. First analyses are planned to be reported mid-1999.

[Zoladex (goserelin) is a trademark property of Zeneca Limited.]

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POSTER

First interim results of an ongoing study comparing the GNRH-agonist leuporelinacetate and CMF as adjuvant treatment in premenopausal breast cancer

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Purpose: Chemotherapy is considered the best option in daily practice for adjuvant treatment of node-positive premenopausal breast cancer patients. Irreversible hormonal ablation by bilateral oophorectomy is an alternative which is not acceptable for the majority of patients. The ongoing TABLE Study compares a standard CMF-polychemotherapy with two years of treatment with the GNRHa leuporelinacetate 3-month-depot (LAD 3 M) in terms of efficacy, safety and endocrinological effects.

Methods: Prospective, randomized, open multicentre clinical phase III trial, for node positive (N₁₋₃), E₃-receptor-positive patients.

Parameter	CMF, n = 75	LAD 3 M, n = 77
Age, years (Mean \pm SD)	42.3 \pm 3.5	40.4 \pm 4.3
T ₁ /T ₂ /T ₃ (%)	42/28/30	44/25/31
N ₁₋₃ /N ₄₉ (%)	55/45	52/48
ER+/PR+ (%)	96/63	97/69
Safety	CMF, N = 213	LAD 3 M, n = 207
Serious Adverse Drug Reactions (ADR, n)	5	0
Withdrawals due to ADRs	3	2

Results: Since 1995 420/600 patients have been already enrolled. The baseline parameters and the first safety results of 152 patients analyzed are presented in the table.

Almost all patients treated with LAD 3 M showed a sustained suppression of oestradiol levels beyond castration range (≤ 30 pg/ml). In contrast, most of the patients treated with CMF have signs of residual ovarian activity or nearly normal oestradiol levels after cessation of the chemotherapy.

Conclusions: LAD 3 M and CMF have different safety profiles and lead to distinct endocrine situations. A long-term follow-up is necessary to assess the impact of the two treatment regimens on recurrence rates and time to tumor progression. In addition the tolerability of LAD 3 M and CMF will be important issues which could have a major impact on patients' acceptance and quality of life.

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POSTER

Effect of dietary GLA +/- tamoxifen on growth and ER in a human breast cancer xenograft model

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Purpose: Gamma Linolenic Acid (GLA) has been identified to possess a number of selective anti-tumour properties including modulation of steroid receptor structure and function. The present study has investigated the effect of dietary GLA on the growth rate and oestrogen receptor (ER) expression of ER+ve human breast cancer in a rodent xenograft model.

Methods: Experimental diets A, B, C, D were commenced after subcutaneous inoculation of 40 female nude mice with the MCF-7 BIM cell line (Group A = control diet; B = GLA supplement; C = control diet + s.c. tamoxifen pellet; D = GLA + tamoxifen pellet; 10 mice/group). The mice were terminated when tumour cross-sectional area reached 250 mm². ER H-score was assessed from immunohistochemical assay of frozen tumour samples.

Results: All mice remained healthy on the diets. Groups C and D had significantly slower tumour growth ($p = .0002$, $p = .0006$) with similar trend in B ($p = .065$) compared to control group A. ER was significantly reduced in all groups compared to A ($p = .00001$ overall) with group D displaying greater degree of reduction than with either therapy alone (B vs D $p = .0002$; C vs D $p = .0002$).

Conclusions: This xenograft model has demonstrated GLA to have a modulatory effect on expression of ER and suggests this may be a mechanism by which GLA inhibits ER +ve breast cancer growth. The effects of GLA on ER function and the possibility of synergistic action with tamoxifen via down-regulation of ER require further investigation.

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POSTER

Prognostic value of cathepsin D expression and association with histomorphological subtypes in breast cancer

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Purpose: Additional prognostic factors are of great importance in breast cancer patients in order to tailor adjuvant therapy. The present study investigates the prognostic value of invasive ductal carcinomas of the breast.

Methods: Cathepsin D expression was detected immunohistochemically in 103 breast cancer patients stage pT1/2. We assessed the association between cathepsin D expression and histomorphological tumour subtypes (invasive ductal carcinoma with extensive intraductal component, multifocal tumour). Cathepsin D expression was examined at two cut-off levels (positive/high immunostaining score) and separately identified within the epithelial and stromal component of all tumours.

Results: Epithelial expression was detected in 32/20 patients (31.1%/19.4%). Stromal component expressed cathepsin D in 35/19 cases (34%/18.4%). Epithelial cathepsin D expression was associated with stage ($P = 0.02/0.02$) and nuclear grade ($P = 0.03/0.02$), but not with lymph node or oestrogen receptor status. Epithelial cathepsin D expression showed significant prognostic value for overall survival (log-rank $P = 0.003/0.01$) and recurrence-free interval (log-rank $P = 0.04/0.02$). Cathepsin D expression in stromal cells was associated with neither established prognostic factors nor survival. Multivariate analysis revealed that cathepsin D expression failed to be an independent predictor of patient's outcome. Cathepsin D expression shows no significant association with histomorphological subtypes of breast cancer.

Conclusion: Our study supports the prognostic impact of immunohistochemical detected cathepsin D expression in the epithelial component of breast cancer.

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POSTER

A phase II study of a potent and selective aromatase inhibitor, anastrozole (ZD-1033), in Japanese postmenopausal women with advanced/recurrent breast cancer

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Purpose: This trial was conducted using two dose levels of 'Arimidex' (anastrozole) (0.5 mg or 1 mg once-daily), the aim being to determine the dose of anastrozole (ZD 1033) to be used in randomised comparative trials involving Japanese women.

Methods: The trial design was randomised, open-label, parallel-group. Patients were required to be postmenopausal with advanced/recurrent breast cancer. The primary endpoints were objective response and tolerability, with secondary endpoints including oestradiol (E2) measurements, and cortisol and aldosterone assessments.

Results: 73 postmenopausal patients entered the trial, 36 patients in the 0.5 mg group and 34 patients in the 1 mg group were eligible. Response rates (CR/PR) were 27.8% in the 0.5 mg group and 38.2% in the 1 mg group (n.s). Plasma E2 was significantly reduced from baseline with both doses of anastrozole (82% suppression with 0.5 mg and 81% with 1 mg being the maximum seen over the 12 week assessment period). There was no evidence of an effect upon adrenal steroidogenesis. Both doses of anastrozole were well tolerated (no toxicity's > grade 2), with no significant differences between the groups.

Conclusion: Based on the objective response data and oestradiol measurements, and since increased toxicity was not observed with the higher dose, anastrozole 1 mg was selected for further study in randomised comparative studies.

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POSTER

The increasing of effect after discontinuation of the treatment with Taxotere in patients with breast cancer

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Purpose: 39 patients with morphologically proven advanced breast cancer were treated with taxotere. Taxotere was administered in dose 100 mg/m² every 3 weeks. As a premedication we used medrol instead dexametason.

Methods: 33 pts have received previously chemotherapy: neoadjuvant – 5 pts (2 – FAC, 3 – CMF), adjuvant – 23 pts (16 – CMF, 7 pts with anthracyclines), chemotherapy for advanced breast cancer had 18 pts (17 pts with anthracyclines, 1 pt – CMF).

Results: The results of treatment were the following: overall response was 20/39 (51.3%), CR – 3/39 (7.7%), PR – 17/39 (43.6%), SD – 7/39 (17.9%), PD – 12/39 (30.8%). 35% of pts achieved response after 3 cycles, and 100% – after 6 cycles.

Median survival overall group is 19.7 mo. One year survival is 82% of pts. The increasing of effect, that we observed in 6 pts after the stop of the treatment during follow up: in all 6 pts – after 3 mo, in 2 pts – after 6 mo. 1 pt achieved CR 3 mo later after treatment break. The duration of response was: PR from 9 to 25 mo, CR – 5 mo.

Conclusion: Taxotere appears to be one of the most effective cytostatic agent against advanced breast cancer, and the effect can be increase after stop treatment. We consider the mechanism of this effect should be explain.

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POSTER

Intratumoral focused chemotherapy with cisplatin/epinephrine injectable gel for palliative treatment of metastatic breast cancer

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Purpose: In a phase III study we are evaluating the safety and effi-

cacy of intratumoral chemotherapy with cisplatin/epinephrine injectable gel (CDDP/epi gel) for local treatment of solid tumors of various histologies. The delivery system provides high tumor drug concentrations for extended periods.

Methods: Two identical, open-label studies enrolled patients with solid tumors who had failed previous therapy. CDDP/epi injectable gel was administered intratumorally (2 mg CDDP/cm³ tumor) weekly for 6 weeks, or until objective complete response of all target tumors. Patients were then followed for 4 weeks. Evaluations included palliation or prevention of tumor-related symptoms for the most troublesome tumor (MTT), tumor response for the MTT and responses of all treated tumors (tumor response: ≥50% tumor volume decrease sustained ≥28 days), and adverse events.

Results: 30 patients with metastatic breast cancer represented the largest group of cancers treated in the ongoing study with 94 evaluable tumors (1–7 tumors/patient) treated to date. Total patient cumulative dose of 1 to 215 mg CDDP (median 27.4 mg) was administered in 1–6 intratumoral injections of CDDP/epi gel. Preliminary results show 6 of 30 (20%) patients had response of the MTT, and 11 of 30 (37%) patients had response of one or more tumors. Overall, 19/94 (20%) of all treated tumors had objective tumor responses. Treatment goals reflected the desire to improve function or disease management (wound care, pain control, tumor invasion). Ten of 30 patients (33%) attained the physician-selected primary treatment goal. Treatment with CDDP/epi gel was generally well-tolerated. Common toxicities (e.g., vomiting and nausea) of intravenous cisplatin were less frequent and easily managed with CDDP/epi gel.

Conclusion: Local tumor control with CDDP/epi gel provides a new therapeutic tool for management of solid tumors as a single modality and holds promise for use in combination with standard therapies.

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POSTER

EORTC-IBBC (Investigational Drug Branch for Breast Cancer): Seven years of active European collaboration

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IBBC is a subgroup of the EORTC-Breast Group. The goals and a summary of the trials run till 1995 have been published recently (EJC 33: 1173, 1997). The following table summarizes the ongoing studies. More data from these studies will be presented at the conference.

Drugs	No. of pts Expected/entered	Comments
Doxo vs Doxo + CPA + Taxol	260/165	In collaboration with EORTC-ECSCG (phase III).
Caelyx	32/14	6 week schedule (phase I-II).
Docetaxel + Amifostine	21/18	Accrual at 70 mg/m ² is ongoing. Feasible. Toxicity of Docetaxel is less than expected!
Liarozole	116/110	Antitumor activity was seen. Significant GI and skin toxicity observed.
Exemestane vs Tamoxifen	100/39	First-line therapy (phase II).
Epirubicin (bolus) + CPA (bolus) + 5 FU (CI)	25/0 (feasibility)	Locally advanced disease. Escalating doses of Epirubicin.
Gemcitabine + 5 FU (CI)	15/0 (feasibility)	2 nd or 3 rd line therapy.

In parallel, the role of the MUGA scan in monitoring cardiac function, the pharmacokinetics of Docetaxel (± Amifostine) and Caelyx and the effects of Exemestane on the lipid profile and coagulation tests are under investigation.

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POSTER

Topical use of Miltex® in patients with breast cancer's cutaneous manifestations

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Purpose: In patients with breast cancer's cutaneous manifestations first-line treatment includes local management (surgical and/or radiotherapeutical). Also hormonal therapy and chemotherapy may be useful under certain clinical conditions. If traditional therapy is ineffective or impossible new