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 tumors ($p < 0.05$). 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.

79 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/peri-menopausal 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.]

80 POSTER

First interim results of an ongoing study comparing the GNRH-agonist leuprorelinacetate 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 leuprorelinacetate 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 (N_{1-9}), E_3-receptor-positive patients.

Parameter	CMF, n = 75	LAD 3 M, n = 77
Age, years (Mean ± SD)	42.3 ± 3.5	40.4 ± 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.

81 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 innoculation 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 mm^2. 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.

82 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 = 0.0.03/0.02), 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.