O-116. THE ZEBRA STUDY: REVERSIBILITY OF BONE MINERAL DENSITY LOSS IN PRE-/PERIMENOPAUSAL PATIENTS WITH NODE-POSITIVE EARLY BREAST CANCER AFTER TREATMENT WITH ZOLADEX™

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The large (n = 1640), multicentre, randomized ZEBRA (Zoladex™ Early Breast Cancer Research Association) study has previously reported that Zoladex (goserelin; 3.6 mg every 28 days for 2 years) is as effective as cyclophosphamide/methotrexate/5-fluorouracil (CMF; 6 × 28-day cycles) in pre-/perimenopausal patients with oestrogen receptor positive early breast cancer. In a protocolled sub-study, bone mineral density (BMD) of the lumbar spine (L2–L4) and neck of femur were assessed by dual-energy X-ray absorptiometry at baseline then annually for up to 5 years. Patients with a baseline and at least one post-baseline measurement at the same site in a protocolled time window were included in the analysis. In total, 96 selected patients from eight centres (Zoladex, n = 53; CMF, n = 43) were included in the analysis of data to 3 years follow-up. Demographic characteristics were well balanced, as were baseline BMD data. Mean percentage BMD losses for Zoladex and CMF were 8.2 vs 4.5 (p = 0.00008) at 1 year and 10.5 *vs* 6.5 (p = 0.0005) at 2 years for lumbar spine, and 4.5 *vs* 4.4 (p = 0.70) at 1 year and 6.4 *vs* 4.5 (p = 0.04) at 2 years for neck of femur. After 3 years (i.e. 1 year after cessation of Zoladex), based on mean percentage change from baseline, partial recovery of BMD was observed in the Zoladex group, whereas losses persisted in the CMF group overall (lumbar spine: 6.2 with Zoladex [n = 29] *vs* 7.2 with CMF [n = 26], p = 0.26; neck of femur: 3.1 with Zoladex [n = 30] *vs* 4.6 with CMF [n = 26], p = 0.48). As a result, no significant differences in BMD were observed between the two groups at 3 years. All Zoladex patients in the BMD sub-study became amenorrhoeic while receiving treatment compared with 63% of the CMF group at 48 weeks and 69% at 2 years. Menses returned in the majority of Zoladex patients after cessation of therapy, whereas amenorrhoea was permanent in most CMF patients. In the CMF group, based on amenorrhoea status at 48 weeks, mean percentage BMD losses at the lumbar spine were greater for amenorrhoeic than non-amenorrhoeic patients. In summary, ovarian suppression resulting in amenorrhoea was closely related to BMD loss in both groups, with the partial recovery of BMD in the Zoladex group associated with return of ovarian function in the majority of patients. Longer term follow-up, including analysis of data to 5 years follow-up, is planned to determine the degree of potential recovery of BMD with Zoladex and whether there is continuing progressive bone loss with CMF.

O-117. EXPRESSION OF ESTROGEN RECEPTOR β – COMPARISON BETWEEN INVASIVE LOBULAR AND DUCTAL CANCERS OF THE BREAST

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Background: Two estrogen receptors (ER), -α and -β now exist. While it is known that ERα is expressed more frequently in invasive lobular cancer (ILC) than in invasive ductal cancers (IDC), little is known about the expression of the more recently characterised ERβ in ILC. The aim of this study was to compare the protein expression profile of ERβ in ILC and IDC and to correlate this with clinico-pathological features including tumour grade, lymph node status and ERα.

Methods: Immunohistochemical analysis of ERβ was performed on a cohort of 200 invasive breast tumours (110 ductal and 90 lobular). Expression of ERβ within tumour nuclei was compared to adjacent normal breast tissue, which was present in all cases. Results were scored semi-quantitatively by adding the score of the percentage of stained tumour nuclei (0–5) and the intensity of staining (0–3). Tumours with scores of 0–4 were considered as negative while a score of 5–8 was considered positive.

Results: A higher proportion of ILC were ERβ positive (95.5%) as compared to 80% of IDC (P = 0.001, Chi squared test). Loss of expression of ERβ was associated with poorly differentiated (Grade 3) cancers (P = 0.009). A significant correlation was not observed between expression of ERβ and ERα (P = 0.215) and lymph node involvement (P = 0.278).

Discussion: ILC of the breast have distinct clinico-pathological features such as a higher rate of ERα positivity and are more often of a lower Grade (Grade 1/2) as compared to IDC. A higher expression of ERβ in ILC and the correlation of loss of expression of ERβ with high grade tumours suggests that expression of ERβ in breast cancers is a marker of low biological aggressiveness.

O-118. INCIDENCE AND PROGNOSIS IN EARLY-ONSET BREAST CANCER

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The incidence of breast cancer is increasing and disease-specific survival rates are improving in Europe. The aim of this study was to explore if early-onset breast cancer followed the same trends and further to investigate how prognosis could best be assessed. Age-adjusted incidence and death rate for the 5,394 Swedish women diagnosed with breast cancer under the age of 40 1960–96 were explored using data from the Swedish Cancer Registry and Swedish Death Cause Registry. 107 consecutive young patients with invasive breast cancer operated 1980–93 in the Southeast Swedish health care region were retrospectively followed up and their cancers reviewed and graded. The applica-

bility of the Nottingham Prognostic Index (NPI) as a prognostic instrument was investigated. The incidence of early-onset breast cancer has increased very moderately and ten-year survival rate has not improved during the last 35 years. 52%, 49% and 55% of patients diagnosed 1960, 1975 and 1988 respectively were alive at ten years. The 5-year survival increased by a factor of 1.004 per year 1960–1992. 64% had grade 3 tumours, 67% were node positive. Lymph node status was the strongest sole prognostic indicator but the use of NPI gave a more accurate prognostic information than node status alone.

O-119. AGE IS NOT AN INDEPENDENT PROGNOSTIC FACTOR

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In 3959 women with primary (<5 cm clinically) breast cancer, treated at one centre between 1974 and 1999, 1372 < 50 years of age and 2237 50+, breast cancer specific actuarial survival (OS) was a little lower in the <50's.

Divided into five groups according to the Nottingham Prognostic Index (NPI) the figures were:

	<50				50+			
NPI	n	%	10 yr OS	20 yr OS	n	%	10 yr OS	20 yr OS
EPG	144	10.5	94	88	333	14.8	95	87
GPG	229	16.7	87	75	516	23.1	84	81
MPGI	349	25.4	76	71	455	20.3	75	66
MPGII	362	26.4	56	41	574	25.7	58	43
PPG	288	21.0	28	20	362	16.2	22	8

OS is remarkably constant within all NPI groups independent of age. OS for the whole sets is better in 50+ because more lie in EPG and GPG.

Difference in adjuvant therapy (<50 more CMF, 50+ more Tamoxifen) gave no survival differences between corresponding NPI groups for the ages.

Conclusion: Survival depends on features at diagnosis (grade is higher in young women, particularly <35) and age is not an independent prognostic factor.

O-120. COMPARATIVE GENOMIC HYBRIDISATION ANALYSIS OF 40 BREAST CANCERS WITH LONG TERM PATIENT SURVIVAL DATA

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The aim of this study was to perform comparative genomic hybridisation (CGH) analysis on 40 primary breast tumours for which 7 year disease recurrence and survival data were available.

Using CGH, the mean number of aberrations per cancer was 9 with an average of 5.5 amplifications and 3.5 deletions per tumour. The most common regions of amplification were 1q (67%), 8q (47.5%), 17q (32.5%) and 20q (22.5%). Most frequently deleted areas included 17p (30%), 8p (27.5%) and 19p (25%). The CGH data are consistent with an underlying molecular pathology such as activation of myc (8q24), erb B2 amplification (17q12), cyclin D1 over-expression (11q13) and inactivation of tumour suppressors p53 (17p13) and E-cadherin (16q22). In other instances, such as amplification of 1q and 17q23 and deletion of 8p and 19p, strong candidate genes have yet to be identified.

A higher mean number of deletions was seen in cancers from patients who died during the follow-up period than in those from the survivors. Three tumours showed no copy number changes and these patients did not suffer disease recurrence. These results are consistent with acquisition of distinctive patterns of large scale (karyotypic) genetic change in malignant breast disease.

O-121. DETECTION OF ISOLATED TUMOR CELLS IN BONE MARROW IN EARLY STAGE BREAST CANCER. FINAL LABORATORY RESULTS FROM THE OSLO STUDY

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Large clinical studies are still needed to substantiate the detection of micrometastases bone marrow (BM) as an independent prognostic marker. With support from The Norwegian Cancer Society bone marrow aspirates have been collected from 917 patients with early stage breast cancer during primary surgery at 5 hospitals. BM was aspirated from anterior and posterior iliac crest bilaterally. Mononuclear cells (MNC) were prepared and analysed for tumor cells by direct immuncytochemical analysis (ICC) of 2×10^6 MNC using anti-cytokeratin mAb (AE1/AE3) and APAAP, negative controls and standardized morphological criteria (all samples). In addition, negative immunomagnetic enrichment (negative IMS) followed by ICC was performed on 615 of the patient samples (10×10^6 MNC analysed) for comparison with the standard ICC technique (2×10^6 MNC analysed). Analyses of the primary tumor specimen have been performed, including histomorphology, TNM staging, grading, immunohistochemical analysis for ER, PgR, mutant p53, CathepsinD and c-erbB2.

The basic micrometastasis analysis and primary tumor characteristics have been completed on all patients (exept for c-erbB2). Of the patients with infiltrating carcinoma, 63% were node negative (NO), 33% node positive (N+), 13% had >3 affected nodes and 62% had T1 tumors. The results show the presence of tumor cells in 13.5% of the evaluable patients after direct ICC analysis of 2×10^6 cells. The presence of tumor cells have been related to tumor-size and nodal status, showing BM-positivity in 10% of the NO cases, whereas 21% were positive in the N+ group. Of the patients with T1 tumors 10.5% were positive, increasing