20 mg/day (n = 50), or Anastrazole 10 mg (n = 50). Both BMD and Osteocalcin were assessed initially before treatment then at regular intervals for both groups. Use of Tamoxifen was associated with significant annual decrease in Osteocalcin. P = 0.001, whereas Anastrazole group had gradual increase of the annual levels P < 0.01. BMD decreases significantly in Anastrazole group versus Tamoxifen 2.6%, 0.4% respectively (P < 0.001). Osteoporosis T < −2.5 was reported significantly higher in Anastrazole group (P < 0.01). Women with initial osteopenia in Anastrazole group showed significant decrease in BMD P < 0.05. The addition of bisphosphonate for patients with early osteoporosis markedly improved both Osteocalcin level and BMD.

**Conclusion:** Tamoxifen preserves BMD in post menopausal breast cancer patients whereas Anastrazole accelerates age associated fall in BMD especially in the first year of therapy, more over the addition of bisphosphonate can help to decrease the skeletal related events associated with treatment to ensure better quality of life with treatment.

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**The association of HER-2 status with disease outcome in premenopausal early breast cancer patients treated with adjuvant ovarian ablation**

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**Background:** Steroid receptor (SR) – positive breast cancer (BC) patients (pts) have better prognosis and higher response to endocrine therapy, although some of them experience early relapse. We investigated the influence of HER-2 gene amplification on disease outcome in premenopausal women with SR-positive BC treated with adjuvant ovarian ablation (A-OA).

**Patients and methods:** One hundred and forty eight premenopausal pts with progesterone receptor (PgR)-positive BC were treated from 1988 to 1993 with A-OA only. The guidelines for the treatment of BC at that time proposed adjuvant endocrine therapy only in PgR-positive grade 3 node-negative BC pts and 1−3 node-positive pts, irrespective of tumor grade. SRs were determined prospectively by the classical biochemical DCC method, while HER-2 gene amplification was determined retrospectively by CISH in 66 women whose archival paraffin tissue samples were retrieved. Log rank test, cumulative hazard function (Peterson's method) and Cox regression models were used for statistical analysis.

**Results:** Sixty-six premenopausal BC pts, median age of 45 years (range 35−54), were treated with A-OA by irradiation after the radical mastectomy. The median SR contents were: estrogen receptor (ER) 22 fmol/mg protein (range 0–199) and PgR 65 fmol/mg protein (range 14–511). Median follow-up was 156 months (range 12–234). Disease relapse experienced 35 patients, while 26 women died, all from BC. According to HER-2 status, HER2 positive subgroup (10/66 pts) had almost similar risk of disease relapse [Hazard ratio (HR): 1.17; 95% CI: 0.512−2.69; Likelihood ratio test: p = 0.71)] and death (HR: 1.09; 95% CI: 0.411−2.90; Likelihood ratio test: p = 0.86) as HER-2 negative subgroup (56/66 pts). The ratio of hazard functions of disease relapse and death between HER-2 negative and HER-2 positive groups ranged from 1.46 to 3.68 at 3−10 years of follow-up and from 1.66 to 3.59 at 6−10 years of follow up, respectively.

**Conclusion:** There is no strong association of HER-2 status with disease outcome in SR-positive early premenopausal BC pts treated with A-OA, although the likelihood of disease recurrence from 3−10 years of follow up seemed to be higher for HER-2 negative in comparison to HER-2 positive pts. According to our opinion, the potential of oestrogen deprivation therapy in premenopausal SR positive/HER-2 positive BC pts deserve further investigation within randomized clinical trials.

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**Strong age dependent increase in the use of adjuvant systemic treatment for early stage breast cancer in the period 1990–2006: a population based analysis**

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**Background:** This study evaluated the impact of changing guidelines on the patterns of adjuvant systemic treatment for patients with early stage breast cancer from 1990 through 2006. Special attention was paid to patients aged 70 years and older due to absence of clear guidelines for this age group.

**Methods:** Patients diagnosed with early stage breast cancer (stage I−IIIa) in the period 1990–2006 were selected from the cancer registry of the Comprehensive Cancer Centre South (n = 8,261). Based on the publication date of the guidelines and the changing indications for adjuvant systemic treatment, results were shown separately for the periods 1990–1997, 1998–2001, 2002–2006 and the age groups $\leqslant$35, 36−49, 50−69 and $\geqslant$70 years. To determine probability ratios (PR) of receiving adjuvant systemic therapy per tumor and patient characteristic, multivariate analyses were performed by SAS Proc Genmod using a modified Poisson regression approach.

**Results:** The use of any adjuvant systemic treatment increased significantly over time: 37% in 1990–1997, 51% in 1998–2001 and 53% in 2002–2006 (p for trend <0.0001). Patients aged $\geqslant$70 years compared to patients aged $\leqslant$35 years had less chance of receiving chemotherapy, or a combination of hormonal and chemotherapy (PR = 0.01; 95% CI, 0.01−0.02 and PR = 0.01; 95% CI, 0.00−0.02, respectively), and a higher chance of receiving hormonal therapy alone (PR = 2.39; 95% CI, 1.94−2.95). Tumor size, positive nodal status and undifferentiated tumors were positively associated with the probability to receive adjuvant systemic treatment. Patients with ER- and PR-negative tumors were more likely to receive chemotherapy (PR = 1.59; 95% CI, 1.47−1.71) and less likely to receive hormonal therapy (PR = 0.28; 95% CI, 0.23−0.33) or both chemotherapy and hormonal therapy (PR = 0.13; 95% CI, 0.08−0.20).

**Conclusions:** Trends in adjuvant systemic treatment over a large period of time (1990–2006) showed that treatment with hormonal therapy and chemotherapy increased significantly. The use of chemotherapy, alone, or in combination with hormonal therapy decreased strongly with age, while the use of hormonal therapy alone increased with age. Part of these age-related differences is attributed to the absence of clear guidelines for patients aged 70 years and older.

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**Prognostic relevance of hormone receptor and HER2 status in T4 breast cancer patients who failed to receive a pathological complete response following primary chemotherapy. Long term results from a single institution**

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**Background:** Pathological Complete Response (pCR) following primary chemotherapy in both the breast and the axilla is the main determinant for improved DFS and OS in patients (pts) with breast cancer, irrespective of hormone receptor (HR) status, HER2 or chemotherapy regimen. On the contrary, failure to achieve a pCR (<pCR) identifies an heterogeneous group of pts with different risks of recurrence and death even if they received the same standard neoadjuvant chemotherapy. The aim of our study was to evaluate the prognostic relevance of HR and HER2 status in terms of survival in <pCR T4 breast cancer patients.

**Material and Methods:** We analysed 58 of 74 consecutive stage T4 patients, observed between 1996 and 2007, who achieved <pCR following primary PEV regimen (cisplatin 50 mg/m$^2$; epirubicin 100 mg/m$^2$; vinorelbine 25 mg/m$^2$) for up to 6 cycles (4−6). All pts, subsequently, received surgery, radiation, adjuvant chemotherapy and hormone therapy when indicated. Median age was 51years (29−70); 45 pts (78%) were T4abc and 13 pts (22%) were T4d; 52 pts (90%) had clinical axillary nodes involvement; 39 pts (67%) were ER+, 19 pts (33%) were ER−; 23 pts (40%) were PgR+, 35 pts (60%) PR−; 18 pts (31%) ER−/PR−; 22 pts (38%) ER+/PgR+; 6 pts (10%) HER2+, 40 pts (69%) HER2−, 12 pts (21%)

HER2 unknown; 12 pts (21%) HER2−/ER−/PR− (as Triple Negative) and 34 pts (59%) not-Triple Negative.

**Results:** After a median follow up of 99 months (8–135), Kaplan–Meier estimated DFS and OS at 10y were 40% and 50% for overall group, respectively. Pts with either HR− or Triple Negative disease had significantly worse DFS and OS compared to patients with either HR+ or not-Triple Negative.

**Conclusions:** Our data confirm that failure to achieve pCR following primary chemotherapy does not equate with poor outcome in all pts. Indeed, pts with HR− and Triple negative tumors have poorer survival, probably because they do not benefit from standard endocrine and or anti-HER2 therapies; therefore, they should be considered for innovative therapies following primary treatment.

| | ER− PgR− (18) | ER+ PgR+ (22) | p value | Triple Neg (12) | not Triple Neg (34) | p value |
|---|---|---|---|---|---|---|
| 10 y DFS % | 27.8 | 50.0 | 0.012 | 33.3 | 50.0 | 0.127 |
| 10 y OS % | 30.3 | 72.7 | 0.001 | 41.7 | 70.6 | 0.027 |

**255** Poster

**Adjuvant trastuzumab in routine clinical practice – the Sheffield experience and impact of cardiac monitoring guidelines on treatment delivery**

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**Background:** Adjuvant trastuzumab was introduced into routine practice in the UK in 2006. National treatment guidance and cardiac monitoring recommendations were defined by the NCRI Breast Group and based on the HERA trial protocol[1,2]. Early experience of the use of adjuvant trastuzumab in routine practice within a UK cancer network has been evaluated.

**Material and Methods:** 68 consecutive patients (pts) under the care of Weston Park Hospital, Sheffield, who had either completed (n = 61) or should have completed (n = 7) a one year course of adjuvant trastuzumab (3 weekly cycles; loading dose and 17 maintenance doses) were identified from pharmacy records. Baseline characteristics, delivery of adjuvant trastuzumab and results of three monthly assessments of cardiac function were reviewed. Left ventricular ejection fraction (LVEF) was to be assessed by MUGA scan at baseline, 3, 6, 9 months on treatment and on completion of trastuzumab; treatment was to be interrupted or discontinued as defined in the HERA study[2].

**Results:** 57 (84%) pts completed treatment on schedule and 4 (6%) completed all 18 cycles despite at least one delay in treatment because of temporary falls in LVEF. The remaining 7 pts stopped treatment early: 5 (7%) discontinued treatment early because of insufficient recovery in LVEF following delays in treatment and 2 (3%) discontinued treatment early for other reasons (1 relapse, 1 patient choice). One patient (1.5%) developed symptomatic, partially reversible cardiac failure (New York Class II) during treatment. There were no marked differences in baseline characteristics between pts who completed treatment without delays, and those with LVEF changes that triggered treatment delays or prevented completion of treatment. LVEF remained constant throughout treatment with median values at baseline, 3, 6, 9 months and end of treatment of 59%, 58%, 59%, 58% and 57.5% respectively.

**Conclusions:** Adjuvant trastuzumab was well tolerated by the majority of patients, with 90% completing 18 cycles. Median values of LVEF were well maintained and it is unclear whether all the delays and interruptions for LVEF falls were clinically necessary. Less stringent guidelines for cardiac monitoring are being developed by the NCRI and the impact that this guidance would have had on treatment decisions will be presented.

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**256** Poster

**Baseline assessment of fracture risk in women with breast cancer using current and emerging guidance**

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**Background:** The importance of monitoring bone health in women diagnosed with breast cancer (BC) has become increasingly apparent, especially considering the known negative effects of some cancer therapies on bone. Recent studies noted a 31% increased fracture risk in BC survivors. Current WHO and ASCO clinical guidelines recommend therapy based on bone mineral density (BMD), but emerging guidelines now recognize the contribution of both clinical risk factors and BMD to a patient's overall fracture risk. This retrospective, case-controlled study was conducted to determine the percentage of women with newly diagnosed breast cancer who may be at increased risk for fracture and require preventive therapy using current and emerging guidelines.

**Material and Methods:** This study compared 88 pre- and 402 postmenopausal women (PMW) with BC with an equal number of healthy, age and body mass index-matched women. BMD was assessed using dual-energy x-ray absorptiometry (DEXA) at the lumbar spine (LS) and total hip. Quantitative ultrasonometry (QUS) was performed at the os calcaneus and at the phalanges. Measurements of BMD were performed at a mean duration of 15 and 242 days after diagnosis of cancer in pre- and PMW, respectively.

**Results:** Baseline characteristics were well balanced between the BC and healthy control groups. When stratified by estrogen receptor-positive (ER+) status, 18.8% of premenopausal women and 36.9% of PMW were osteopenic, and 8.9% of PMW were osteoporotic at the LS. In ER+ PMW with BC, osteoporosis was detected in 15.9% of patients >65 years of age, in 8.3% of patients 55 to 65 years old, and in only 1.4% of patients <55 years old. Applying the current WHO and ASCO treatment guidelines, approximately 9% of ER+ PMW with BC would receive bone protective therapy. After applying the emerging guidance, clinical risk factors alone identified 6.5% of patients who should receive therapy. When both clinical risk factors and BMD were included in the fracture risk assessment, 28.6% of women were eligible for bone protective therapy.

**Conclusions:** Fracture risk assessment using clinical risk factors alone does not increase the proportion of PMW with BC eligible for bone-protective therapy. Including both BMD and clinical risk factors increased the number of eligible women and may more effectively identify patients at risk for fracture, although further studies are needed.

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**Is three-day steroid medication compulsory to prevent fluid retension in TAC adjuvant chemotherapy for node-positive breast cancer?**

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**Background:** TAC (docetaxel, doxorubicin and cyclophosphamide; 75−50–500 mg/m$^2$) chemotherapy has been used as one of the adjuvant treatments for the node-positive breast cancer these days. Also, it has been proving itself as effective as FAC chemotherapy protocol for the similar subset of breast cancer patients. Fluid retension is well known as one of the major complications that may result from the use of TAC chemotherapy. So, it is suggested that steroid should be given to the patients having TAC chemotherapy for three days starting from day 0 (previous day) to day 2 (the very next day of chemotherapy). Steroid itself may provoke many adverse effects to the patients. We tried to determine if abbreviated use of steroid is good enough to prevent fluid retension from TAC chemotherapy.

**Patients and methods:** From Jan. 2006 to Nov. 2007, we randomly assigned patients (node-positive breast cancer) into two subgroups after getting informed consent which had been approved by our institutional review board. Group one was comprised 30 patients who were given steroid medication as suggested (three-day prescription; 16 mg oral dexamethasone daily), and group two (n = 30) were given steroid as follows: 12 hours before chemotherapy (15 mg oral dexamethasone), 30 minutes before starting chemotherapy (15 mg) and in the evening of day 1 (chemotherapy day). All patient were followed up while measuring circumferences of extremieties, body weight, and patients' interview daily for 10 days. All other reported adverse reactions were evaluated during the study period.

**Results:** All patients were chemo-naive women with no other co morbid disease affecting renal or any other systemic function. Mean age was 42.3 years (group 1) and 45.5 years (group 2). Each group evaluated 180 cycles of TAC chemotherapy. The incidence of neuropenia (grade III or more), febrile neutropenia, infection, fluid retension and other known adverse