and Carboxyterminal crosslinked telopeptide of type I collagen (ictp) before treatment, 3 months and 15 months after treatment were measured with commercially available test kits. Also, 34 out of 79 evaluable patients completed Functional Assessment of Cancer Therapy core questionnaire (FACT-G) with its additional breast cancer subscale (BCS) at baseline, 4, 8, 12 weeks after NHT. Incomplete questionnaires were included for cross-sectional analysis.

Results: BMD at the femur for group A patients did not change after 24 months but it was lowered for group C patients and raised for group B patients. The values for group B patients was significantly greater than group A ($p = 0.011$) and C patients ($p = 0.003$). Changes for bap at 3 months and ictp at 3 and 15 months were not different between 3 groups. However, the changes of bap at 12 months were higher in group B patients than the other groups. The difference between group B and A patients were statistically insignificant but was significant between group B and C patients ($p = 0.017$). FACT-G scores and FACT-B scores (sum of FACT-G and BCS scores) did not show statistical significance among groups, but BCS scores of group A patients were significantly higher than that of group C patients 12 weeks after treatment ($p = 0.021$). Negative changes of FACT-B and FACT-G scores were observed in group B and C patients, but positive changes in group A patients after 4 weeks of treatment. Significant difference of FACT-B score ($p = 0.008$) and FACT-G score ($p = 0.019$) were observed at that time point.

Conclusion: The sub-study suggested that impact on BMD and bone turnover proteins as well as QoL might be different in patients receiving combination of steroidal aromatase inhibitor and cyclo-oxygenase-2 inhibitor preoperatively.

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Chemotherapy-induced amenorrhea and adjuvant endocrine therapy for premenopausal women with early breast cancer

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Background: Amenorrhea is a common side-effect to chemotherapy of premenopausal women. The incidence of chemotherapy-induced amenorrhea (CIA) varies depending on the patients' age, dose and the type of chemotherapy. CIA affects choice of hormonal therapy and fertility. Menopausal status is important to determine adjuvant endocrine therapy for hormone receptor (HR)-positive women who received chemotherapy.

Patients and Methods: From September 2004 to June 2008, 60 premenopausal women who received adjuvant chemotherapy were available for the analysis. Thirty patients were treated with anthracycline-based chemotherapy and 30 with a combination of anthracyclines and taxanes. Menstrual status was monitored and serum estradiol (E2) and follicular stimulating hormone (FSH) levels were measured after the end of adjuvant chemotherapy.

Results: The patients were divided into three groups by menstruation and E2/FSH levels: 12 women (20%) in the premenoposal group (menstruation continue all courses and end of chemotherapy), 16 women (27%) in the E2 premenoposal group (cessation of menstruation but the serum E2 was within premenopausal level at the end of chemotherapy) and 32 women (52%) in the postmenopausal group (cessation of menstruation and the serum E2 was postmenopausal level at the end of chemotherapy). The median age of the patients in the premenopausal group, the E2 premenopausal group and the postmenopausal group was 35.6, 41.2 and 47.7, respectively. The patients in the postmenopausal group were significantly ($p < 0.05$) older than those in the premenopausal or in the E2 premenopausal group. Cessation of menstruation was present in 73% of patients treated with anthracyclines and in 87% of patients treated with anthracyclines and taxanes. Seven of 9 HR-positive women in the premenoposal group received tamoxifen and GnRH agonist. The other 2 patients received tamoxifen alone and become menopause. Seven of 11 HR-positive women in the E2 premenoposal group received tamoxifen and GnRH agonist. Three of 4 women who received tamoxifen alone resumed menses. Four of 5 HR-negative women the E2 premenoposal group who did not receive endocrine therapy resumed menses. Two of 26 HR-positive women in the postmenopausal group received tamoxifen and GnRH agonist treatment, 13 received tamoxifen alone, and 11 patients received aromatase inhibitor (AI). One patient in the postmenopausal group who received AI resumed menstruation. Six patients of HR-negative in the postmenopausal group continued amenorrhea.

Conclusions: In the premenopausal patients who received adjuvant chemotherapy, age and the level of serum E2/FSH are important to determine menopausal status and chose followed endocrine therapy.

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Molecular and cellular basis of anti-estrogen behavior in breast cancer cells

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Background: Breast cancer is the most common type of malignancy among women in the world. Approximately 70% of breast tumours express the estrogen receptor alpha (ERα) and are considered hormone-responsive. Endocrine therapies have long been the treatment of choice. However, the estrogen-like agonist effect and development of resistance of the available selective estrogen receptor modulator such as tamoxifen require developing new treatments that act through different mechanisms. The objective of our study is to design tools that can help to understand the molecular mechanisms involved in ligand-dependent modulation or degradation of ERα.

Materials and Methods: We selected a set of anti-estrogens with different structures and compared their effect in breast cancer cell lines on:

1. ERα degradation
2. Intra-cellular localisation of ERα
3. Regulation of transcription of ERα- endogenous target genes
4. Regulation of transcription by mutants of the ERα

Results: Using this mechanistic study we could classify the tested anti-estrogens into three groups based on their function: SERM, SERD and a new group for EM652. SERM (selective estrogen receptor modulator) include compounds such as OH-tamoxifen and RU39411, that stabilise ERα, that re-localize ERα into the nucleus upon binding, that increase transcriptional activity in mutants affecting the recruitment of cofactors or the binding of their side chain and that lack inhibitory capacities of the basal expression of endogenous genes. SERD (selective estrogen receptor modulator) include compounds such as ICI182780 or RU58668, which induce nuclear proteasome-dependent degradation ERa which occur in large nuclear foci that colocalize with the proteasome and that inhibit basal gene expression of the endogenous progesterone receptor gene (PGR). Finally, EM652 was found to affect ERα degradation and localisation similarly to SERM but inhibited basal gene expression of the endogenous PGR.

Conclusions: This approach can be used to screen the newly designed compounds based on specific antiestrogen structural features.

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Low frequency of breast cancer recurrence following introduction of adjuvant trastuzumab in HER-2 positive early breast cancer: an audit of relapses in a UK Cancer Centre and the implications for future practice

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Introduction: In England and Wales, Trastuzumab (Herceptin™) was endorsed by NICE (National Institute for Health and Clinical Excellence) for use in advanced breast cancer (ABC) in March 2002 and for early breast cancer (EBC) in August 2006. However, following publication of the first adjuvant trastuzumab studies in October 2005, there was rapid uptake of its use in the adjuvant setting prior to licensing and NICE approval. Revised NICE guidance in February 2009 suggested there was insufficient evidence to recommend Trastuzumab in ABC following use in EBC.

Method: The case notes of HER-2-positive EBC patients treated with adjuvant trastuzumab following standard chemotherapy in Newcastle between January 2006 and April 2009 were reviewed. Relapses following adjuvant trastuzumab were examined including demographic data, the time from chemotherapy to relapse and outcome of treatment for ABC. We assessed retrospectively if patients would have been eligible for the HERA trial, the model for UK practice.

Results: 95 patients received adjuvant trastuzumab. There have been 4 relapses following adjuvant chemotherapy and trastuzumab. Of the 4 patients, one would have been eligible for inclusion in the HERA trial with the others excluded on the basis of locally recurrent disease and previous non-breast malignancy (1), inflammatory disease (1) and T4 disease (1). In the HERA eligible patient, relapse occurred 9 months after completion of Trastuzumab. She was treated with trastuzumab containing therapy and lived for 13 months following relapse. Two of the other relapses occurred during trastuzumab therapy. Both of these patients has rapidly progressive disease and died 1 and 7 months after the diagnosis of recurrence. The final patient relapsed 21 months after completion of trastuzumab for local recurrence and is responding to a further trastuzumab containing regimen.

Conclusion: Relapses following adjuvant trastuzumab are rare in our dataset although follow up of these patients is short. Relapse during treatment appears to be associated with poor outcome. However,