cancer women as primary therapy (N = 160) or in sequence to previous tamoxifen (N = 171) for a median period of 54 months (range: 7.5−87).

Results: Nineteen cases (5.74%) of minimal trauma fractures were identified after 9−47 (median: 25) months of anastrozole administration (median duration of AI medication in group without fractures: 31 months, range: 7.5−87; difference not significant); women who took letrozole did not experience any bone fractures. Patients who experienced bone fractures under IA were significantly younger that those without that complications (median: 47 vs. 60 years; $p = 0.01$) and more frequently subjected to surgical/radiological menopause (57.89% vs. 3.85%; $p < 0.001$). None of cases with bone fractures was pretreated with tamoxifen before AI therapy was started in contrast to those without bone fractures (tamoxifen for at least 6 months: 0% vs. 59.21%, respectively; $p < 0.05$). No statistically significant differences were observed between two study subgroups in terms of frequency and regimen of anticancer chemotherapy as well as risk factors for bone fracture, such as: initial body mass index, previously diagnosed osteoporosis/osteopenia, life-style (physical activity, cigarette smoking, alcohol abuse, diary products intake, calcium supplementation), parental history of osteoporosis/hip fracture/multiple bone fractures, co-morbidities and medications related to bone mass changes (including hormone replacement therapy), pretreatment history of minimal trauma fractures. Relatively low rate of bone fractures did not allow to perform the multivariate analysis.

Discussion: Results obtained in this preliminary study: 1) revealed that traditionally used osteoporosis fracture risk factors do not reflect the probability of AI therapy associated bone events properly, thus suggest difference between AI induced bone loss and that observed after menopause; 2) support the osteoprotective activity of tamoxifen; 3) indicates that AI-related bone fractures in unselected group of breast cancer women are less prevalent than what has been described in clinical trials.

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Some aspects of scalp cooling in breast cancer patients receiving chemotherapy

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Background: Alopecia, hair loss, is a common and distressing side effect of chemotherapy. Hair loss stigmatises by making cancer visible. Scalp cooling is worthwhile supportive care that is applied in breast cancer patients with chemotherapy schedules that cause (severe) hair loss. In 2008 scalp cooling is practised extensively in the UK and the Netherlands, but among others also in Belgium, Ireland, Norway, Sweden and Switzerland.

Methods: In 2005 a PhD-project has started comprising studies related to scalp cooling in breast cancer patients. 1. In order to optimise cooling methods the impact of post-infusion cooling times on the preservation of hair was determined in the 3-weekly docetaxel and FEC-high dose (epirubicine 90 mg/m^2 or more) regimens. Initially the post-infusion cooling times were 90 minutes. Now patients are randomised between post-infusion cooling times of 45 and 90 minutes in docetaxel and 90 and 150 minutes in FEC-high. 2. Impact of hair loss on well being and body image was measured by questionnaires completed before starting chemotherapy, 3 weeks and 6 months after the last chemotherapy session. Scalp cooled patients were compared to non-cooled patients 3. The risk of (scalp) skin metastases has been studied in the Munich Cancer Registry in non-cooled patients without metastases at diagnosis (n = 28.916). Furthermore medical records research was performed among all Dutch scalp cooled patients (n = 395) from 1997 to 2005.

Results: Results of our studies show: 1. 53% of 250 patients treated with FEC high dose and 82% of 38 patients treated with docetaxel did not require a wig after chemotherapy with 90 minutes post-cooling. Results of scalp cooling in randomised patients are not known yet, data will be presented at EBCC conference. 2. higher well being and better body image in successfully scalp cooled patients (n = 32) than in patients not receiving cooling (n = 142) who in turn have better results than not-successfully cooled patients (n = 30). 3. 694 (11%) of 6205 patients with metastases in follow up presented with skin metastases. Skin metastases alone comprised 150 patients (2.4%). While about 80% of skin metastases present on the trunk, the percentage of scalp skin metastases will be lower than 0.5%. Medical record research showed 2 patients with scalp skin metastases, these patients were treated with chemotherapy in the palliative setting.

Conclusion: More than half of the patients do not require a wig in two chemotherapy schedules that normally induce severe hair loss. Preservation of hair by scalp cooling leads to a better well being and body image. Hazards of development of scalp skin metastases by scalp cooling seem very low, but can not be excluded unequivocally.

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Electrolyte abnormalities and side effects of zoledronate in patients with bone metastases

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Background: Zoledronate is generally used for the treatment of bone metastases from different kind of neoplasms. Hypocalcemia and elevation of serum creatinine are expected adverse events during this therapy, although their actual incidence is unknown. The use of serum calcium and creatinine is therefore recommended. The primary aim of this study was to establish the actual incidence of hypocalcemia and elevation of serum creatinine during treatment with zoledronic acid. Skeletal-related events (SREs) and side effects were also assessed.

Materials and Methods: Serum creatinine and calcium levels were evaluated in 240 consecutive patients (83 males, 157 females, mean age 59.8 years) with metastatic bone lesions from different solid tumors, treated with zoledronic acid.

Results: Overall, 95/240 patients (39.6%) developed hypocalcemia: G1 in 47 patients (49.5%), G2 in 37 (38.9%) and G3 in 11 (11.6%). Median time-to-occurrence of hypocalcemia (any grade) was 2 months (range 0−35). A higher grade of hypocalcemia was associated with earlier appearance ($p = 0.0001$). Increased serum creatinine was observed in 33/240 patients (13.7%), of whom 19 had G1 (57.6%), 11 had G2 (33.4%) and 3 had G3 (9%). Median time-to-serum creatinine increase (for any grade) was 5 months (range 0−29). Elevated levels of creatinine were associated with advanced age ($p = 0.0017$).

Conclusions: The reported high incidence of serum hypocalcemia and creatinine strongly supports the need for accurate monitoring of plasma calcium and creatinine levels.

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Radiogrametrical analysis of clavicle structure – predictive factor for bone fractures in breast cancer women treated with adjuvant anastrozole?

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Background: Adjuvant anastrozole (ANS) therapy increases bone fractures risk in postmenopausal breast cancer (BC) women. Some studies showed the bone mineral density has low sensitivity to assess bone fracture risk (BFR) in general population and seems to be even less predictive in BC women treated with aromatase inhibitors. Some data suggests that other than densitometric features of bone ("bone quantity"), such as bone geometry, microstructure ("bone quality") may contribute to BFR. We studied the influence of adjuvant ANS on radiological features of bone structure and its predictive value in estimating BFR.

Patients and Methods: Data for the study were collected from 85 BC women: 48 taking adjuvant ANS as a primary endocrine therapy and non-randomelly matched group of 37 patients who received no further endocrine treatment following adjuvant chemo-/radiotherapy. The influence of ANS on bone was assessed using the radiogrametrical digital analysis of clavicle and II. rib based on chest PA X-ray radiograms routinely taken in each patient before and min. 6 months of treatment/observation afterwards (median: 16, range: 6−45 mts / 17, range: 6−43 mts, respectively) and then digitally processed using image analyzer.

Results: 1) The comparative analysis of the pairs of data taken before and during treatment revealed that the linear spongious/cortical width ratio (S/C) increases significantly in patients being under ANS in both evaluated skeletal locations (clavicle $p < 0.001$; II. rib $p < 0.01$), whereas patients from control group experienced only statistically not significant increase of the S/C ratio; 2) typical feature observed in ANS-treated patients and control cases was the increase of the contrast between cortical and spongious part of bone shadow in clavicle and II. rib (parameter C), however the difference did not reach significance; 3) comparison of changes in bone structure during treatment/observation period showed the significantly

higher increase in the value of the S/C ratio in clavicle among ANS treated patients than in the control group ($p < 0.001$) and not significant difference for data taken from the second rib; 4) there was not any difference noticed in the value of parameter C in both analyzed locations between patients treated with ANS and subjected to observation; 5) patients who experienced bone fractures during adjuvant ANS therapy (N = 11) had significantly higher increase in the S/C ratio as compared to those without fractures ($p = 0.0475$) and controls ($p < 0.001$).

Conclusions: 1) our data confirm observations that ANS exerts osteopathic activity in BC women and induces quantitative changes in bone geometry, which might be related to the increase of BFR; 2) significant increase in the S/C ratio in patients who experienced bone fractures under ANS therapy (as compared to those without that complication and control cases) suggests its potential value in prediction of BFR and will be assessed on more representative group of patients.

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Evaluation of side effects after axillary lymph node dissection for breast cancer

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Background: Main focus and purpose of the current study was to evaluate breast cancer patient's symptoms after axillary dissection measured by their subjective assessments.

Material and Methods: A total number of 516 patients, who had undergone either breast conserving therapy or mastectomy including axillary dissection for invasive breast cancer from 1999 to 2002, were enrolled in the present study.

A sample of 336 women (65.1%) completed the self-administered questionnaire and their subjective estimation of long-term sequel of axillary dissection was evaluated. Besides demographic data, responses regarding axillary symptoms such as pain, impairment of arm mobility, analgetical treatment and others were included in the questionnaire.

Results: Pain and impairment of arm mobility improved significantly in course of time in our study population. Although these results prove that most of the patients do feel less pain and arm movement restriction in course of time, still 19.4% are left with mediocre pain and 19.6% with mediocre impairment of arm mobility after 12 months. When evaluating the correlation between the types of surgery which were used (mastectomy or breast conserving therapy) and the items impairment of arm mobility, pain and usage of analgesic drugs, no significant difference ($p > 0.05$) in the postoperative effect between the two types of surgical management could be distinguished.

Furthermore our study showed that the staging of the primary breast carcinoma has no direct impact on arm mobility or on impairment of pain.

Conclusions: The results of this study demonstrate that complaints significantly ($p < 0.0001$ for the parameters pain and impairment of arm mobility) diminish in course of time in the patient collective. Still our figures clearly show that one fifth of the patient collective are left with mediocre pain and impairment of arm mobility, which proves that morbidity remains substantial.

ALND associated complications can adversely affect quality of life, e.g. delaying resumption of normal activities and returning to work. Evaluated complaints such as pain, impairment of arm mobility and analgetical usage seem to be independent from the type of surgery.

Evidence from our evaluation further state, that the initial size of the breast cancer (T1, T2, T3, T4) exerts no influence on these symptoms.

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High incidence of Antiemetic treatment failure to standard chemotherapy in women with breast cancer – A prospective QOL study in clinical practice setting in Spain – EME-Q Study

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Background: Chemotherapy (CT) Induced Nausea and Vomiting (CINV), is the most feared acute side effects by patients. Although for physicians it's frequently considered as an overcome problem, given the availability of antiemetic agents. The objective of this study was to estimate, under clinical practice conditions, the incidence of CINV with standard CT regimens in women with breast cancer.

Material and Methods: Nine oncology practice units across Spain participate in this prospective study between January 2004 and January 2006. CT naïve women with stage II to IV breast cancer and indication for a moderate to highly emetogenicity CT regimen (Hesketh classification grade 4 or 5) were proposed to participate. Information about their first CT cycle and the antiemetic prophylactic therapy ($5HT_3$-RAs, steroids and dopamine receptor antagonists -RA) were collected. Patients completed a 5-day diary recording CINV episodes during days 1−5 following CT. Nausea was measured on a 100 mm Visual Analogue Scale (VAS). Antiemetic treatment failure (lack of Complete Protection) was defined as having had either an emetic episode, significant nausea (VAS $\geqslant$25 mm), or having required antiemetic rescue medication. On day-6 patients completed the Functional Living Index-Emesis (FLIE), formed by two 9-items subscales on nausea (FLIE-n), and vomiting (FLIE-v).

Results: Overall 79 females, median age 47, were recruited. Only 27% received a grade 4 Hesketh CT regimen, 73% been grade 5. CT regimens included anthracyclines in 94% of patients (CAF 36%, CEF 27%, other 37%), ciclophosphamide in 87% and taxanes in 13%. All patients received antiemetic prophylactic treatment, 95% covering the acute and delayed phases. All patients received $5HT_3$RAs (2.5 days mean length of therapy – LOT), and steroids (2.9 days average LOT), and 44% also received dopamineRAs (1.8 days average LOT). Within days 1 to 5 after CT, 44% of the patients experienced Significant Nausea, 53% emetic episodes (47% $\geqslant$2 days), and 47% required rescue medication. In total, antiemetic therapy failed to keep Complete Protection in 80% of patients. CTIN had a great impact on patient's daily living. Patients with significant nausea had an average FLIE-n score of 4.1, as compared with 5.3 for those with mild nausea (VAS 5−25 mm) and 6.8 for those patients without nausea ($p < 0.001$). The likelihood of experiencing an impact on the IDL was also related to the number of days with nausea and vomiting ($p < 0.001$).

Conclusion: Despite the generalised use of $5HT_3$RAs, steroids and dopamine-RAs, CINV remains a highly incident problem in women with breast cancer confronted to CT. There is need for better treatment alternatives to improve this frequent side effect of CT in Spain.

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The effect of toremifene on lipid metabolism compared with that of tamoxifen in vitro

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Background: Tamoxifen (TAM) and Toremifeme (TOR) are selective estrogen receptor modulators (SERMs), which not only prevent estrogen from stimulating breast cancer growth, but also have agonistic effects in a number of physiological systems including bone and lipid metabolism. They also have effects partly similar to estrogen which produces a well-known hypertriglycemic effect. TAM is known to increase intracellular triglyceride, but the action of TOR on lipid metabolism in vitro has still not been known yet.

Material and Methods: HepG2 cells obtained from American Type Culture Collection were grown in Minimum essential medium (MEM) with supplemented with 10% fetal bovine serum (FBS), 1 mmol/l sodium pyruvate (NaPy), 2mM L-glutamine, 1% non essential amino acid (NEAA), 100 IU/ml penicillin, 100μg/ml streptomycin, and 250 ng/ml amphotericin B. HepG2 cells were preincubated overnight in serum-free MEM supplemented with 1% Bovine serum albumin (BSA). The following day, after removing the media, the cells were incubated for an additional 24 h in 1 ml media containing the appropriate compounds (TOR and 4-Hydroxytamoxifen; TAM) with or without free fatty acid (18 μmol/l oleic acid). Oleic acid was dissolved in 1% BSA. Both compounds were dissolved in 100% ethanol and added to media at a 1:1000 dilution. At the end of incubation period, the cells were washed 3 times with 1 ml ice-cold phosphate-buffered saline (PBS), and the solute cell protein was dissolved in 1 ml 0.1 mol/l NaOH and measured using the method of Bradford with BSA at the standard. To determine the intracellular triglyceride and total cholesterol, after washing 3 times with cold PBS, the cells were treated with 1 ml hexane/isopropanol (2:1) for 30 min at room temperature. These samples were transferred to the test tubes. The organic solvent was removed under nitrogen, and the lipids were resuspended in 500 μl 95% ethanol. Cellular concentrations of total cholesterol and triglyceride were measured by enzymatic kit.

Results: Intracellular concentrations of total cholesterol were decreased by both TAM and TOR, but not significantly different from control level. Neither TAM nor TOR changed the intracellular concentration of triglyceride in the absence of oleic acid. In the presence of oleic acid, TOR produced no changes in the intracellular concentrations of triglyceride; whereas TAM increased the intracellular concentrations of triglyceride at concentrations ranging from 10^{-7} to 10^{-5} mol/l of TAM ($p < 0.05$). Moreover, there was significant difference at concentrations between the two groups ranging from 10^{-9} to 10^{-5} mol/l ($p < 0.05$).