Conclusions: There were high rates of MSk pain following the first cycle of docetaxel. Over half of these had moderate to severe pain that was not controlled with the use of simple analgesia. Most of these did not have access to stronger analgesics simply because they were not prescribed. The incidence of MSk pain was reduced with subsequent cycles possibly due to anticipation and improved analgesia. Better patient education and the pre-emptive prescribing of appropriate analgesia for the first cycle of docetaxel is important in order to improve tolerability. There was only a slightly higher incidence of grade 2 and 3 symptoms in those patients also receiving G-CSF. In view of the incidence of FN and that there was not an over-representation of grade 2 and 3 MSk symptoms in patients receiving G-CSF, consideration should be made to give G-CSF to all patients receiving the FEC-D regimen.

364 Poster

The serious uncommon side effects after radiotherapy in early breast cancer

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Background: The early and late serious side effects after radiotherapy in early breast cancer are rare (2−3%). The early most serious of them are pneumonia after radiotherapy in the treatment field and extremely rare Bronchiolitis Obliterans Organizing Pneumonia (BOOP) out of the treatment field. The late serious complications are brachial plexus injury, cardiovascular events or radiation-induced sarcomas.

Purpose: Presentation of serious uncommon side effects in early breast cancer patients after breast conservation therapy treated in Institute of Oncology in Warsaw.

Material and Methods: From 1995 to 2006 1493 early breast cancer patients with breast conservation therapy were treated. There were observed one case of BOOP and three cases of radiation-induced sarcomas of breast. The other serious side effects were not observed. The BOOP syndrome histological verified appeared 3 months after radiotherapy. In three other cases, angiosarcomas of breast without metastasis were diagnosed 10, 5 and 4.5 years after radiotherapy.

Results: In case of BOOP after two years of steroids treatment there was not permanent improvement. Only complete remission appeared when antibiotics of macrolides group were administered. In all three women with angiosarcoma of the breast simple mastectomies were performed and they are without recurrence since 1 to 3 years after treatment.

Conclusion: The proper diagnosis of serious uncommon side effects after radiotherapy in early breast cancer and suitable treatment may get benefit for patients.

365 Poster

The change of bone mineral density during aromatase inhibitor therapy alone and combining zoledronic acid in postmenopausal Korean breast cancer patients

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Background: Aromatase inhibitor (AI) is effective in postmenopausal women with estrogen receptor positive breast cancer, however it may cause bone loss and increase fracture risk. Zoledronic acid (ZA) has been shown to maintain or increase bone mineral density (BMD) in postmenopausal breast cancer patients receiving adjuvant AI. Distribution of age with breast cancer in Korea is different with that in Western, the rate of below the age of 60 and recently menopausal women are high. The aim of this study is evaluate of BMD change in Korean breast cancer patients treated with AI alone or combining ZA.

Material and Methods: Changes of BMD in lumbar spine and hip were evaluated 111 patients receiving AI treatment. 61 of them treated with ZA and 50 patients receiving AI alone. BMD was assessed at baseline and after 12 and 24 months and result were expressed as mean percentage change of BMD.

Results: The mean age of 111 patients was 54.6 years (range 42−75; 63 patients $\leqslant$55 years and 48 patients >55), the median follow-up period was 26.4 months (13−61), the mean BMD at baseline in lumbar spine was 0.9208g/cm^2 and 0.7911g/cm^2 in hip. In AI alone group, there were significant (all $p < 0.001$) losses of BMD at lumbar spine and hip, both at 12 months (3.8% and 3.0%, respectively) 24 months (4.6% and 4.3%, respectively), whereas in AI combining ZA group, there were significant (all $p < 0.001$) gains (2.5% and 1.0%, respectively at 12 months; 4.6% and 2.3%, respectively, at 24 months). The loss of BMD at lumbar spine tended to be large in below the age of 55 at 12 months (4.2% in $\leqslant$55 years and 3.1% in >55, p =0.495) but there was not difference at 24 months (4.6% in $\leqslant$55 years and 4.5% in >55, p =0.980).

The gap of bone loss at the lumbar spine was larger than patients with normal baseline BMD than osteopenic patients (5.7% and 1.8% respectively at 12 months, $p = 0.005$; 7.6% and 1.0%, respectively, at 24 months, $p = 0.032$). During follow up periods nobody experienced bone fracture.

Conclusions: ZA inhibits effectively AI associated bone loss. The bone loss in Korean breast cancer patients treated with AI alone seems to be larger than ATAC data, because of relatively high proportion of recently menopausal patients. However, for the evaluation of meaning of larger loss of BMD and risk of fracture, further large number of prospective studies and long-term follow up data are required.

366 Poster

Chemotherapy-induced venous thromboembolism is not due to endothelial cell activation

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Background: Venous thromboembolism (VTE) during breast cancer chemotherapy occurs in up to 8% of early and 17% of advanced breast cancer patients and is the cause of death in 9% of advanced breast cancer patients receiving chemotherapy. It has been hypothesised that chemotherapy induces a hypercoagulable effect though endothelial cell activation, as demonstrated clinically by local thrombophlebitis.

Material and Methods: Serum markers of endothelial cell activation (E-selectin (E-sel) and vascular cell adhesion molecule-1 (VCAM-1)) were measured prior to chemotherapy and at one, four and eight days following commencement of chemotherapy in breast cancer patients (n = 132). Duplex ultrasound imaging was performed one month following commencement of chemotherapy or if symptoms of VTE developed.

Results: See the table. VCAM but not E-sel was elevated at all timepoints in the group that subsequently developed VTE (p: 0.02−0.1). Levels of E-sel and VCAM significantly decreased in the eight days following administration of chemotherapy ($p < 0.001$). The trend for decreasing serum endothelial cell markers following chemotherapy was seen in patients who developed VTE and patients who remained free of VTE. There was no difference in the trend over time for markers of endothelial cell activation following chemotherapy in patients with and without subsequent VTE.

	Geometric mean (CI)			
	Baseline	Day 1	Day 4	Day 8
E-sel (ng/ml)				
VTE (n = 11)	29.0 (17.7−47.5)	29.3 (17.1−50.4)	27.5 (17.5−43.3)	21.0 (13.1−33.8)
No VTE (n = 121)	29.5 (26.9−32.4)	28.2 (25.6−31.0)	24.9 (22.7−27.4)	22.4 (20.3−24.7)
p	0.9	0.8	0.6	0.7
VCAM−1 (ng/ml)				
VTE (n = 11)	767 (612−960)	775 (629−956)	752 (630−898)	705 (572−863)
No VTE (n = 121)	639 (596−685)	575 (533−620)	591 (550−635)	571 (534−611)
p	0.1	0.02	0.05	0.1

Conclusion: Chemotherapy induces endothelial cell activation, however this is not the mechanism for development of chemotherapy-induced venous thromboembolism.

367 Poster

New views on treatment of aromatase inhibitors induced arthralgia

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Background: Aromatase Inhibitor (AI) induced arthralgia is one of the most frequent side effects in breast cancer hormonal therapy, which may become severe in some cases affecting patients' quality of life. The purpose of this study is to investigate alternative treatment of arthralgia, as current treatment options may often prove to be inadequate.

Material and Methods: According to Morales et al, AI-associated arthralgia syndrome is characterized by tenosynovial changes in MRI, including fluid in tendon sheaths and joints. Initially we prescribed furosemide to patients with this syndrome, especially if they were complaining for peripheral edema. The results showed that 14/16 patients had improved by this treatment. In this retrospective study, data from 288

women receiving an AI for non-metastatic breast cancer are analyzed in order to define whether chronic diuretic therapy could affect the impact of arthralgia on those patients.

Results: 42/288 patients were receiving chronic diuretic therapy for heart disease or hypertension (Group A), while 246/288 patients had never received any diuretic medication (Group B). At 43.03 months of mean follow up, in Group A arthralgia was developed in 3/42 patients (6.97%) as opposed to 39/246 patients in Group B (15.85%) − p value: 0.01. Other parameters that could affect the impact of arthralgia in both Groups are also analyzed and taken under consideration.

Conclusion: Reviewing our material, it appears that benefits arising from chronic diuretic therapy as far as AI-associated arthralgia is concerned are not statistically significant. Nevertheless, more research needs to be done in order to investigate the possibility of administering a diuretic agent as an alternative treatment to AI-associated syndrome.

368 Poster

Stellate ganglion block induced by low level laser therapy to reduce adverse reactions of endocrine therapy in breast cancer patients

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Background: Endocrine therapy is an effect and safe standard treatment for breast cancer, however many patients develop menopausal symptoms due to a low estrogenic state. In many patients, quality of life deteriorates, particularly due to hot flashes and sweating. Generally these symptoms can be treated with various methods such as Chinese herbal medicine, SSRIs, isoflavone, yoga, etc., but the results is insufficient. In 2008, Lipov etal. reported that stellate ganglion block is an effective treatment for hot flashes and night awakenings in breast cancer patients.

We report a case of a treatment using a stellate ganglion block induced low level laser therapy (LLLT) which is a non-invasive and safe method.

Material and Methods: We treated 20 patients with LLLT. All patients had received endocrine therapy, such as LH-RH agonist + TAM or TAM or AIs, and the average age was 44.1. A previous treatment for menopause-like symptoms such as hot flashes, sweating and insomnia was included in an untreated patient, but as is common, Chinese herbal medicine and SSRIs were given.

Written informed consent was obtained prior to the start of therapy. We used two machines: one was a low-level diode laser device and the other was a near-infrared laser device. The laser photoradiation site was the sixth and seventh cervical transverse process vertebrae.

Treatment time was approximately 10 minutes. We evaluated the therapeutic effects and according to symptom frequency using a hot flash score.

Results: No adverse effects of treatment were recognized, and the hot flash score mean decreased from 63.2 points before treatment to 28.0 points after treatment. In addition, we were able to confirm a decrease in the frequency of hot flashes and sweating in 85% of all patients.

Conclusions: Stellate ganglion block by LLLT is effective on hot flashes and sweating in breast cancer patients. We believe that the introduction of a safe, non-invasive procedure which is extremely simple, for treatment of the adverse reactions of breast cancer endocrine therapy could be significant.

369 Poster

The effect of exemestane and anastrozole on bone mineral density and bone turnover markers in postmenopausal early breast cancer patients: final results of 3 years after randomization of N-SAS (national surgical adjuvant study) BC04, the TEAM Japan sub-study

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Background and Aims: Postmenopausal women treated with aromatase inhibitors/inactivators (AIs) are known to be at risk for bone loss. In preclinical studies, a steroidal AI has a different effect compared with non-steroidal AIs. We aimed to investigate the difference among exemestane and anastrozole in the effect on bone mineral density (BMD) and bone turnover markers in patients with postmenopausal primary breast cancer treated with those agents as adjuvant endocrine therapy.

Patients and Methods: Of the 247 postmenopausal patients randomized in the N-SAS BC04 trial, the number of the patients included in the present study for exemestane (25 mg/day) arm was 27, anastrozole (1 mg/day) arm was 23 and tamoxifen (20 mg/day) arm was 26. In Tamoxifen arm, treatment changed from tamoxifen to exemestane at 2.75 years after randomization and, therefore, tamoxifen group was excluded in the present analysis. BMD was measured by dual-energy x-ray absorptiometry at baseline, 12, 24 and 36 months after treatment initiation. Urinary type I collagen cross-linked N-telopeptide (NTX) and serum bone specific alkaline phosphatase (BAP) were measured as bone turnover marker at baseline and 3, 6, 12, 24 and 36 months after treatment initiation. All patients are within normal limit in BMD at radomization.

Results: Although there was no significant difference in BMD level at 12 and 24 months among 2 arms, there was a significantly lower in anastrozole arm compared with exemestane arm at 36 months. NTX level did not change during 36 months period in exemestane and anastrozole arm. BAP level also constantly increased in exemestane as well as anastrozole arm.

Conclusion: Although there were no significant differences in the bone turnover marker levels between exemestane and anastrozole arms, a favorable effect of exemestane in bone mineral density profile was observed at 36 months after randomization. There might be some differences between steroidal and non-steroidal AI. Further clinical studies are mandatory to confirm these phenomena.

BMD	Entry	1 year	2 years	3 years
ANA				
mean(SD)	84.49 (13.90)	80.55 (10.91)	79.87 (9.41)	79.99 (8.84)
min–max (median)	47.0–106.3 (80.4)	59.1–98.4 (78.4)	63.8–97.3 (78.4)	70.1–96.1 (78.9)
Q1-Q3	76.1–95.4	73.5–90.0	72.5–88.5	72.2–87.7
EXE				
mean(SD)	85.77 (13.02)	86.33 (13.56)	85.67 (12.32)	86.47 (11.71)
min–max (median)	65.6–118.0 (83.8)	63.6–114.8 (83.4)	65.4–107.2 (84.0)	73.4–105.8 (80.9)
Q1-Q3	75.7–93.8	74.6–94.1	74.2–95.3	75.0–95.1

370 Poster

Bone effects of anastrozole in Japanese postmenopausal breast cancer patients: results of a two year follow-up multicenter prospective study (SBCCSG-06)

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Background: Anastrozole is superior to tamoxifen in terms of efficacy and safety for adjuvant treatment in postmenopausal patients with hormone-responsive early breast cancer. Based on therapeutic guidelines, anastrozole is widely used for adjuvant treatment in Japan. However, there are only a few reports on the safety of anastrozole in Japanese patients, especially the long-term effects on bone mineral density (BMD). The aim of this study is to evaluate the frequency of bone fracture and impact on BMD during the course of adjuvant treatment with anastrozole in Japanese patients. This is a report on the updated two year follow-up data after the first year of analysis.

Patients and Methods: The SBCCSG-06 trial included 350 post-menopausal patients with confirmed the hormone-sensitive stage I to IIIA breast cancer (oestrogen or progesterone receptor positive). All patients received anastrozole (1 mg/day) for five years as adjuvant treatment. Patients underwent clinical examination for any bone fractures and annual check-up for BMD (YAM %: young-adult-mean) during the course of treatment. The oral bisphosphonates were used concomitantly with anastrozole for patients diagnosed with osteoporosis (YAM < 70%).

Results: After a median follow-up of 29 months (ranging from 1 to 47 months), 330 women were analyzed at the time of data cutoff. Bone fractures occurred in five cases, and annual fracture rates were 0.6% (2/330) at 12 and 24 months. The overall median BMD were 85%, 82% and 81% at the time of pre-treatment, at 12 and 24 months, respectively. Paired t-test revealed that BMD significantly decreased in each period of 12 months.

Conclusions: In this multicenter prospective study, there was a significant reduction of BMD in Japanese patients after two years of treatment with anastrozole. We recommend that annual monitoring of BMD be mandatory in treated patients. Moreover, long-term follow-up data is necessary to elucidate the racial disparities of the safety profile of anastrozole.

371 Poster

Medical intervention side effects prevention throughout breast cancer treatment

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Background: Breast cancer patients quality of life is negatively affected not only due to functional deficiency caused by the malignome itself, but also due to medical treatment side effects (limited shoulder movement, arm lymphoedema on the operated breast side), which lead to functional handicap and severely affect patient's life quality.