Material and Methods: One hundred forty-five patients, operated on for breast cancer minimally five years ago, between January 2001 and December 2003, were included. All the above mentioned methods to establish lymphoedema were performed.

Results: Prevalence of lymphoedema varies with the different methods: with water displacement volumetry and a cut-off value of 200 mL or 150 mL results were respectively a prevalence of 7% and 10%. 18% with a circumference difference of >2 cm and 19% using the sum of arm circumferences with a cut-off value of 5 cm. Self-reported lymphoedema yields a prevalence of 17%. Bio-impedance spectroscopy resistance of extracellular water (Recw) ratio is significantly smaller in the subjective oedema group ($p = 0.033$), the sum of arm circumferences (SOAC) >5 cm group ($p = 0.005$) and volume >200 mL group ($p = 0.003$), but was not able to detect lymphoedema patients. Of those patients with self-reported lymphoedema, 56% tested positive with the SOAC method, and only 36% tested positive using the water displacement method. Ninety percent of the patients with an arm volume difference of more than 200 mL reported lymphoedema. So a smaller volume difference does not exclude the presence of subjective lymphoedema.

Conclusions: When measuring lymphoedema 5 years after surgery for breast cancer, different methods result in a prevalence varying from 0.7% to 19%. Water displacement volumetry resulted in a much higher prevalence than Bio-impedance spectroscopy, in contrast with acute phase studies where BIS and volumetry yield comparable results. In this study there was a relatively high prevalence of subjective lymphoedema when compared with water displacement volumetry. These findings support the hypothesis that after 5 years the consistency of lymphoedema has changed drastically.

Thursday, 25 March 2010 18:15–19:15

POSTER SESSION

Side effects of treatment

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Long-term cause specific mortality in patients treated for DCIS; a population based study

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Background: Since the introduction of the national breast cancer screening program in the Netherlands in 1990, incidence of ductal carcinoma in situ (DCIS) has increased dramatically. DCIS is treated by surgery and, in case of breast conserving therapy, radiotherapy is also frequently used. The prognosis of DCIS is very good. However, it is still unclear what proportion of these in situ tumours would have progressed into invasive breast cancer if left untreated. Because of potential overdiagnosis, treatment-related late health effects after DCIS may be of even greater importance than late effects of invasive breast cancer treatment. Currently, there is no information on treatment-related excess mortality following treatment for DCIS.

Treatment-related late health effects after breast cancer include second tumours and cardiovascular disease. Previous studies have indeed shown increased mortality after treatment of invasive breast cancer with radiotherapy. However, most of these studies are based on outdated treatment regimens. Therefore it is still unclear to what extent contemporary radiotherapy regimens used to treat DCIS also increase the risk of cardiovascular disease and second tumours.

The aim of the current study is to assess long-term cause-specific mortality in patients treated for DCIS in a population-based design.

Materials and Methods: Data on all incident DCIS cases in the Netherlands between 1989 and 2004 were obtained from the population-based Netherlands Cancer Registry. The Netherlands Cancer Registry was established in 1989 and also collects treatment information. Date and cause of death were acquired through linkage with Statistics Netherlands until January 2009.

Results: At the EBCC, results will be presented on the evaluation of mortality rates (including the three main outcomes breast cancer, other cancer, and cardiovascular disease) in comparison with the general population. In addition, we will compare mortality rates between DCIS patients treated with surgery and radiotherapy, and those treated with surgery alone. For cardiovascular disease we will also compare mortality after radiotherapy for left-sided and right-sided DCIS.

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Prophylactic use of H1 and H2 antagonists may prevent hypersensitivity reactions and skin toxicity to docetaxel with cyclophosphamide in early breast cancer patients

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Background: US oncology 9735 study demonstrated significant improvement in DFS and OS for Docetaxel/Cyclophosphamide (TC) compared with Doxorubicin/cyclophosphamide (AC). We previously evaluated tolerability and safety of TC regimen and reported this regimen was feasible for Japanese patients with early breast cancer (Takabatake et al. Jpn J Clin Oncol 2009). In this feasibility study, relatively high incidence of hypersensitivity reactions (HSRs) or rashes were observed. Therefore, to reduce these side effects patients were premedicated with H1 and H2 antagonists in our institution. The aim of this study is to compare the rates of HSRs and rashes when TC is administered with and without prophylactic H1 and H2 antagonists.

Patients and Methods: This study was a retrospective cohort study evaluating the rates of HSRs and rashes in patients receiving TC regimen for early breast cancer at Shikoku Cancer Center from June 2006 to August 2009. Until October 2008, patients received 8 mg of iv dexamethasone (DEX) for prophylaxis: Group H(−). From November 2008, patients received H1 and H2 antagonists (50 mg of oral diphenhydramine and 20 mg iv famotidine, respectively), 30 min prior to docetaxel in addition to intravenous DEX: Group H(+). All patients received oral 8 mg of DEX day2 and day3. Medical records from all patients were reviewed to evaluate demographics, drug administration and incidence of HSRs and rashes. The chi-squared test was used for statistical analyses.

Results: Fifty eight patients received only iv DEX and 69 received H1 and H2 antagonists with DEX. Of the 58 patients in group H(−), 26 had HSRs (44.8%) and 33 had rashes (56.9%). In contrast, of the 69 patients in group H(+), 21 had HSRs (30.4%) and 26 had rashes (37.7%). There were statistically significant differences in both HSRs and rashes ($p = 0.042$ and 0.031, respectively).

Conclusion: Our study suggests that prophylactic use of H1 and H2 antagonists may prevent hypersensitivity reactions and skin toxicity to Docetaxel with Cyclophosphamide in early breast cancer patients.

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Musculoskeletal pain in the FEC-D regimen is common and frequently severe − experiences in an outer metropolitan oncology unit

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Background: The FEC-D regimen is a commonly used adjuvant chemotherapy regimen for node positive early breast cancer in our oncology unit. It has demonstrated considerable toxicity in terms of febrile neutropenia (FN) but also fatigue, myalgias and arthralgias. G-CSF can decrease the risk of FN but as the main side effect of G-CSF treatment is bone pain, there is a possible risk that it may compound the musculoskeletal side effects of docetaxel.

Materials and Methods: A retrospective analysis of the medical records of all clinic patients who had completed treatment with FEC-D between July 2007 and October 2009 was performed. Parameters measured were rates of use of G-CSF (pegylated filgrastim, Neulasta®), incidence of FN and occurrence and NCI-CTC grade musculoskeletal (MSk) pain.

Results: Of the 37 patients included, six (16%) had an episode of FN. None of these were receiving G-CSF at the time of the episode. The majority of FN occurred in either Cycle 1 of FEC or Cycle 1 of docetaxel. 25 patients (68%) received some treatment cycles with G-CSF. There were two chemotherapy discontinuations during the docetaxel treatment due to severe side effects. MSk symptoms are listed in the table.

		MSk pain			
		All grades		Grades 2 and 3	
Treatment cycle	No. treated (no. also receiving GCSF)	n (%)	receiving GCSF (% of all GCSF)	(% of total cases)	receiving GCSF (% of all cases also receiving GCSF)
FEC1	37 (6)	2 (5%)	0 (0%)	0 (0%)	0 (0%)
FEC2	37 (13)	2 (5%)	2 (15%)	0 (0%)	0 (0%)
FEC3	37 (15)	2 (5%)	0 (0%)	0 (0%)	0 (0%)
D1	**37(19)**	**26 (70%)**	**17 (89%)**	**16 (62%)**	**10 (59%)**
D2	36 (25)	19 (53%)	15 (60%)	7 (37%)	5 (33%)
D3	35 (25)	10 (28%)	8 (32%)	5 (50%)	5 (62%)

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.

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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.

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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.

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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.

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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