

in each treatment group. Common Toxicity Criteria (CTC) grade 3 (>3.6 to ≤7.2 mg/dL) or grade 4 (>7.2 mg/dL) serum creatinine was infrequent. In the HCM trial, 2 (2.3%) patients treated with 4 mg zoledronic acid developed grade 3 serum creatinine elevations compared with 4 (4%) patients in the pamidronate group with either grade 3 (n=3) or grade 4 (n=1) serum creatinine. Among breast cancer patients treated with 4 mg zoledronic acid (via 15-min infusion) monthly for up to 25 months (core + extension phase), no patient developed grade 3 or 4 serum creatinine elevations compared with 1 (0.5%) patient with grade 4 serum creatinine in the pamidronate group. This compares favorably with other IV bisphosphonates, including ibandronate. Finally, a patient-preference study demonstrated that zoledronic acid was preferred by 86% of patients compared with 14% who preferred pamidronate.

Conclusions: A 15-minute infusion of zoledronic acid has an overall safety profile comparable with other IV bisphosphonates, which have longer recommended infusion times. The shorter infusion of zoledronic acid provides greater patient convenience and is preferred over pamidronate.

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POSTER

Distribution of tamoxifen in serum and breast cancer tissue and its effects on sex hormone-binding globulin (SHBG)

E.R. Kisanga¹, J. Gjerde¹, A. Guerrieri-Gonzaga², C. Robertson³, F. Mariette², A. Galli², F. Pigatto², A. Decensi², E.A. Lien¹. ¹Institute of Internal Medicine, Hormone Laboratory, Bergen University Hospital, Bergen, Norway; ²European Institute of Oncology, Division of Chemoprevention, Milan, Italy; ³University of Strathclyde, Department of Statistics and Modelling Science, Glasgow, Scotland

Tamoxifen is a front-line drug in the treatment of breast cancer. Of concern are its serious adverse effects especially when used as a chemopreventive agent. We investigated serum concentrations and the accumulation of tamoxifen and its metabolites in normal breast and breast cancer tissues during different dosing regimens. Frozen samples of serum, normal breast tissue and breast cancer tissues were obtained from patients exposed to 1, 5 or 20 mg tamoxifen daily for 28 days prior to surgery (n=38, 37 and 36 respectively). The concentrations of tamoxifen, 4-hydroxytamoxifen and N-desmethyltamoxifen were analysed by HPLC.

While 35% of the patients used tamoxifen alone, 41% used two or more drugs in addition to tamoxifen. The median (range) of tamoxifen concentrations at doses of 1, 5 and 20 mg daily were in serum (ng/ml) 7.5 (2.9–120.9), 25.2 (1.9–180.9) and 83.6 (8.7–134.4), in normal breast tissues (ng/mg) 100.5 (33.1–694), 218.7 (34.5–601.6) and 866.5 (413.4–1466), and in breast cancer tissues were 78.2 (35.9–184), 272.3 (122–641) and 744.4 (208.6–2556) respectively. Serum and tissue tamoxifen and metabolite concentrations were significantly inter-correlated and were also correlated with changes between baseline and post-treatment levels of SHBG.

In conclusion, we observed a wide range of tamoxifen and metabolite concentrations in each of the three dose groups. The concentrations of tamoxifen and metabolites in serum correlated to the levels in tumour tissues, and the oestrogen agonistic effects of tamoxifen on SHBG increased with increasing tamoxifen concentrations.

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POSTER

Effects of anastrozole on the lipid profile in postmenopausal breast cancer patients – a preliminary study

Y. Hozumi¹, T. Saito², K. Inoue³, M. Shiozawa¹, Y. Omoto¹, T. Tabei³, H. Nagai¹. ¹Jichi Medical School, Surgery, Tochigi, Japan; ²Saitama Red Cross Hospital, Surgery, Saitama, Japan

Introduction: Anastrozole, a new generation aromatase inhibitor, has been used to treat postmenopausal metastatic breast cancer, and several clinical trials of adjuvant treatment using this agent are ongoing. However, the effects of anastrozole on lipid metabolism are unknown. We previously reported the effects of tamoxifen on lipid metabolism in clinical and experimental studies (Hozumi et al., J Clin Endocrinol Metab 1998, Hozumi et al., Horm Res 2000). Moreover we reported the effect of anastrozole on lipid metabolism in ovariectomized rats (Hozumi et al., Breast Cancer Res Treat 2003). In the present study, we evaluated the effects of anastrozole on the serum lipid profile in postmenopausal breast cancer patients.

Subjects & Methods: A total of 38 postmenopausal patients, mean age 62.8 (53–79), with breast cancer were treated with anastrozole, 1 mg once daily. After an overnight fasting, serum lipid parameters [total cholesterol, triglycerides, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), apolipoprotein A1, B and lipoprotein (a)] were measured before treatment and at 3 months afterwards.

Results: A significant increase in total cholesterol ($P=0.037$), LDL-C ($P=0.015$), HDL-C ($P=0.013$) and apolipoprotein A1 levels ($P=0.03$) in the serum was noticed after anastrozole treatment.

Conclusion: Previously we showed that anastrozole did not affect lipid metabolism in ovariectomized rats. In the present clinical situation, however, anastrozole augmented serum lipid parameters although the investigation was small and preliminary. A new clinical study is underway to compare the effects of anastrozole on lipid metabolism with those of exemestane and tamoxifen.

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POSTER

Prospective investigation of the significance of cardiac markers, NT-pro Brain Natriuretic Peptide (NT-proBNP) and Troponin T (TnT), in the HERCULES study of epirubicin/cyclophosphamide with or without trastuzumab (Herceptin®)

B. Langer¹, M. Muscholl², M. Pauschinger³, C. Thomssen⁴, H. Eidtmann⁵, M. Untch⁶, H.G. Meerpohl⁷, A. du Bois⁸, H. Weber⁹, H.J. Lueck¹⁰. ¹F. Hoffman-La Roche Ltd., Pharmaceuticals Division, Basel, Switzerland; ²Cardiologic Consultant, Muenchen, Germany; ³University Hospital Benjamin Franklin, Berlin, Germany; ⁴University Hospital Eppendorf, Hamburg, Germany; ⁵University Hospital, Kiel, Germany; ⁶University Hospital Grosshadern, Muenchen, Germany; ⁷St. Vincentius-Hospital, Karlsruhe, Germany; ⁸Dr. Horst-Schmidt Hospital, Wiesbaden, Germany; ⁹F. Hoffman-La Roche Ltd., Pharmaceuticals Division, Basel, Switzerland; ¹⁰Medical University Hospital, Hannover, Germany

Introduction: The Herceptin® trial HO648g demonstrated that the combination of Herceptin® with doxorubicin was efficacious, but associated with a higher than expected incidence of cardiotoxicity. Therefore, the HERCULES trial was initiated to investigate the cardiac safety of epirubicin (E) (60 or 90 mg/m²) and cyclophosphamide (C) (600 mg/m²) with or without Herceptin® (H) (given at the standard weekly schedule until disease progression). A secondary endpoint of this trial was to determine the significance of the cardiac markers NT-proBNP and TnT, markers of congestive heart failure (CHF) and myocardial damage, respectively, as predictors of early onset cardiac dysfunction.

Patients and Methods: To date, 75 patients without pre-existing cardiac disease have been entered into the trial and followed for cardiac safety (26 EC60 + H; 25 EC90 + H; 24 EC90 only). Echocardiography was used to assess left ventricular ejection fraction (LVEF) as a measure of cardiac function every 3 weeks during chemotherapy and every 12 weeks thereafter. Serum concentrations of NT-proBNP and TnT were measured in the Herceptin® arm only weekly for the first two chemotherapy cycles and then every 3 weeks until week 43.

Results: Minor drops in LVEF were common and there was large intra-patient variation in LVEF measurements over time. Three cardiac events were reported in the Herceptin®-containing arms: one patient in the EC60 + H arm experienced an asymptomatic decline in LVEF to <50% and two patients in the EC90 + H arm experienced CHF. One additional cardiac event was seen in the EC90-alone arm (arrhythmia/tachycardia). No correlation between serum levels of NT-proBNP or TnT and cardiac events could be determined: no significant increases in these markers were observed in the three patients at, or close to, the time they experienced the cardiac event. However, the cardiac events occurred shortly following week 43 and so it is unknown whether cardiac marker levels subsequently increased. Small increases in TnT were seen in nine patients receiving Herceptin® who did not experience a cardiac event. Fluctuations in NT-proBNP, within normal limits, were also noted in many patients who did not experience cardiac events. Neither absolute LVEF values nor changes in LVEF were shown to correlate with clinical symptoms and/or cardiac marker levels.

Conclusions: The preliminary findings from a trial of EC with/without H suggest that NT-proBNP and TnT levels are not a useful indicator of early onset of cardiac dysfunction.

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POSTER

The possible life-threatening reactivation of hepatitis B during chemotherapy can be prevented by a close monitor of liver function during chemotherapy

M.C. Liu¹, Y.M. Lin², M.Y. Lee³, A.T. Huang⁴, J.L. Sung⁵. ¹Sun Yat-Sen Cancer Center, Hematology and Medical Oncology, Taipei, Taiwan; ²Sun Yat-Sen Cancer Center, Division of General Internal Medicine, Taipei, Taiwan; ³Sun Yat-Sen Cancer Center, Pathology, Taipei, Taiwan; ⁴Sun Yat-Sen Cancer Center, Hematology and Medical Oncology, Taipei, Taiwan; ⁵Sun Yat-Sen Cancer Center, Division of General Internal Medicine, Taipei, Taiwan

Purpose: To report 18 patients of breast cancer with reactivation of hepatitis B which was proven by both histology and serology during chemotherapy for breast cancer.

Materials and Methods: A patient of breast cancer and viral hepatitis B carrier developed elevation of GOT, GPT after one cycle of CMF. The biopsy showed viral hepatitis. This was the first patient who developed reactivation of hepatitis after chemotherapy. Later on, in 1999 a patient of breast cancer developed drastic change of GOT up to 1430 U/mL, GPT up to 2140 U/mL, Bilirubin up to 7.3 mg% after chemotherapy. All these confirmed the importance of monitoring liver function test (LFT) during chemotherapy for patients of HBV carrier. Since then routine HBsAg was screened in every patient before received chemotherapy at SYSCC. During chemotherapy, liver function was followed periodically for HBV carrier. Once GOT, GPT elevated to over 100u/mL, HBV DNA and liver biopsy were performed.

Results: Among the patients who developed reactivation of hepatitis B, 18 were breast cancers. All 18 patients were proved by histology and HBV DNA. Some of the patients has also a liver histology of drug effect. All the hepatitis B were treated by lamivudin successfully and chemotherapy was resumed after improved liver function test and was completed in every patient safely.

Conclusion: For cancer treatment, it is necessary to be careful for hepatitis carrier, since reactivation of hepatitis B may result in fulminant course. Reactivation of hepatitis B can be treated safely with lamivudin if we carefully monitor the LFT change. After the control of hepatitis, the chemotherapy can be completed safely.

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POSTER

Lymphedema of upper extremities after treatment for cancer of breast: incidence and risk factors analysis

W. Yao Chung. Changhua Christian Hospital, General Surgery, Changhua, Taiwan

Purpose: Lymphedema is the most significant complication of the locoregional management of breast cancer. Therapeutic procedures such as lymph node dissection, and/or radiation therapy cause local damage of the axillary lymphatic system. The overall incidence of post-mastectomy lymphedema that dependent on the criteria and follow-up period is varied, but is about 15–20% in USA. The study wants to evaluate the incidence and risk factors of arm lymphedema in patients receiving surgical treatment for breast cancer in central Taiwan.

Materials and Methods: In 2002, we retrospectively analyzed 571 patients received treatment for breast cancer at Changhua Christian Hospital between Jan, 1994 and Dec, 2000. The arm lymphedema was defined as at least 2 cm difference in circumference compared with the untreated limb at measured points. In lymphedema patients, we calculated the circumference, calculation volume and edema ratio (=excess volume/normal side volume).

Results: In total 571 patients, 8.1% (46/573) patients met the criteria of lymphedema. In MRM group, the lymphedema incidence was 8.35% (40/479), 20.86% (29/139) in MRM with radiotherapy, 3.24% (11/340) in MRM without radiotherapy. In breast conserving group, the incidence was 7.23% (6/83), 9.23% (6/65) in BC with R/T, 0 (0/18) in BC without R/T. The only significant risk factor for lymphedema is radiation therapy esp high dose (>5000 cgy). The mean time to arm edema was 22.1(± 20.9) months.

Conclusion: Radiotherapy was the predominant risk factor for arm lymphedema in patients receiving surgical treatment for breast cancer. Further prospective study is necessary to determine the accurate incidence of arm lymphedema in patients with breast cancer.

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POSTER

Changes in sensitivity related to sectioning the intercostobrachial nerve during axillary dissection for the carcinoma of the breast

A. Celebic¹, L. Djordjevic², R. Dzodic¹, M. Inic¹, D. Stojiljkovic¹, D. Babic³.
¹Institute Of Oncology And Radiology Of Serbia, Department Of Surgery, Belgrade, Serbia And Montenegro; ²Institute Of Anatomy, Medical School Of University In Belgrade, Belgrade, Serbia And Montenegro; ³Institute Of Oncology And Radiology Of Serbia, Data Centre, Belgrade, Serbia And Montenegro

Background: Side-effects of axillary surgery, primarily those relating to changes in sensitivity (e.g. pain, anesthesia, hypo- and paresthesia in the axilla, numbness of the arm), appear due to section of the sensitive intercostobrachial nerve (IBN), and may be a cause of significant discomfort in patients treated surgically for the carcinoma of the breast. The advantage of preservation of IBN to diminish sensory symptoms, has been evaluated prospectively in this study.

Material and Methods: Ninety-four patients undergoing axillary dissection for the carcinoma of the breast, hospitalised and operated at the Department of Surgery of Institute of Oncology and Radiology of Serbia in Belgrade, in the period from April 2001 to August 2002, were recruited

to this study, and followed prospectively for the period of three months. The patients were divided into three groups, according to the surgical interventions of IBN: in first group, the nerve is preserved; in second, the main trunk is preserved and peripheral branches are divided; in third group, the nerve is sectioned. Clinical testing to evaluate changes in tactile sensitivity and pain, using standard neurological methods, were conducted during the immediate postoperative period (4–7 days), after one month and after three months from the surgery. A statistical analysis using chi-square test, factorial analysis and the means of percentage has been applied to these results.

Results: Out of ninety-four patients, IBN has been preserved in 35 cases, while in 20 patients only peripheral branches have been preserved and in 39 of them, nerve has been sectioned. The greatest changes in sensitivity were found in the group of patients with the section of nerve trunk. The less intensive alterations were presented in the group with preservation of peripheral branches of the nerve. The least presence of pain, numbness and paresthesia, although also being presented, has been reported in the group with the preservation of the nerve. The incidence, intensity and the lasting of these changes, significantly increase with sacrifice of IBN ($p < 0.001$ by the chi-square test).

Conclusions: The preservation of IBN during the axillary surgery for the carcinoma of the breast, is strongly recommended in cases where the nerve is not involved by lymph nodes, and where this preservation does not compromise a control of the disease from oncological point of view.

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POSTER

Angiosarcoma of the breast: a propos three cases

J. Kulka, E. Szekely, H. Gyorffy, M. Kovacs, Z. Rusz, F. Perner, P. Lukovich, M. Dank. Semmelweis University Budapest, 2nd Department of Pathology, Budapest, Hungary

Background: Angiosarcoma of the breast is rare, the overall prevalence being around 5 per 10,000. In the last two years, however, three breast angiosarcoma cases were diagnosed in the 2nd Department of Pathology, Semmelweis University Budapest. We call attention to the likely increase of its incidence and the caution necessary in the follow-up of patients undergoing breast conserving surgery and radiotherapy.

Patients and Findings: Case 1. A 67 years old female patient developed invasive ductal carcinoma in her left breast and underwent breast conserving surgery in 1992. She received radio- and chemotherapy. In 1996, she presented with upper extremity malignant melanoma, which was excised. In 2001 haemorrhagic skin lesions of the left breast occurred, but several cytological examinations failed to prove malignancy. In 2002, left mastectomy was decided for a large mass in the breast parenchyma. High grade angiosarcoma was diagnosed. Later, contralateral axillary and breast, lung and skin metastases developed. At present she is undergoing chemotherapy. Case 2. A 69 years old female patient underwent breast conserving surgery in 1993 for invasive ductal carcinoma of her right breast. The operation was followed by radio- and chemotherapy. In 2000, she was operated for a benign tumor of the left breast. In 2002 she presented with a mass in the right breast. Preoperative cytology suggested a mesenchymal tumor. Wide local excision was performed. The tumor proved to be a low grade angiosarcoma. In November, 2003, a mass was found in the right breast on control mammography. Fine needle aspiration cytology revealed the recurrence of the angiosarcoma. Case 3. A 84 years old female patient underwent breast conserving surgery and radiotherapy for invasive breast carcinoma in 1997. In 2003 left mastectomy was performed for a large, exulcerated tumor, which proved to be intermediate grade angiosarcoma originating from the skin of the left breast. She died 4 months following the operation, after haemorrhage from the recurrent angiosarcoma.

Conclusion: With the increasing frequency of breast conserving surgery, the incidence of secondary breast angiosarcoma is likely to increase proportionally. Both primary and secondary breast angiosarcomas are aggressive, with high metastatic potential. Early diagnosis and radical surgery may extend survival time. Effective postoperative therapy is still to be established.

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POSTER

Changes to the axillary vein are associated with an increased risk of breast cancer-related lymphoedema

S. Pain, C. Bainbridge, A. Purushotham. Addenbrooke's Hospital, Cambridge Breast Unit, Cambridge, UK

Aim: This study aims to prospectively evaluate the effect of axillary node clearance (as part of breast cancer treatment) on the axillary vein, and to investigate associations between the changes observed and risk of developing lymphoedema.

Methods: A total of 70 women were studied prior to breast cancer surgery to include a Level II or Level III axillary clearance, and at 3 and 12 months post-operatively. Arm volume was calculated from sequential circumferential measurements. Doppler U/S was able to provide information