Conclusions: No significant differences in anti-oestrogenic or anti-proliferation markers were observed at surgery between patients treated with a single 250 mg im dose of fulvestrant and patients treated with placebo. The clinical significance of these findings is not known and the short duration of the study may not accurately reflect the clinical activity of fulvestrant in this patient population. Further clinical trials will be necessary to clearly establish the activity of fulvestrant in the premenopausal setting.

60 POSTER

Trends in the usage of adjuvant systemic therapy for breast cancer in the Netherlands and its effect on mortality

H.J. de Koning[1], M.M. Vervoort[2], G. Draisma[3], J. Fracheboud[4], L.V. van de Poll-Franse[5]. *[1]Erasmus Medical Center, Dept. of Public Health, Rotterdam, The Netherlands; [2]Erasmus Medical Center, Dept. of Public Health/NIHES, Rotterdam, The Netherlands; [3]Erasmus Medical Center, Dept. of Public Health, Rotterdam, The Netherlands; [4]Erasmus Medical Center, Dept. of Public Health, Rotterdam, The Netherlands; [5]Comprehensive Cancer Centre South (IKZ), Eindhoven, The Netherlands*

Background: Adjuvant systemic therapy was introduced in the Netherlands as a breast cancer treatment in the early 1980s. In this paper, we describe the trends in usage of adjuvant systemic treatment in the period 1975–1997 in the Netherlands. The main aim of our study was to assess the effects of adjuvant tamoxifen and polychemotherapy on breast cancer mortality, compared to the effects of the mammography screening programme.

Materials and methods: The computer simulation model MISCAN (Microsimulation Screening Analysis), which simulates demography, natural history of breast cancer and screening effects, was used to estimate the effects.

Results: Use of adjuvant therapy increased over time, but since 1990 it remained rather stable. Nowadays, adjuvant therapy is given to 88% of node-positive patients aged 50–69 years, while less than 10% of node-negative patients receive any kind of adjuvant treatment. Adjuvant treatment is given independent of mode of detection (adjusted by nodal status and size). We predict that the reduction in breast cancer mortality due to adjuvant therapy is 7% in women aged 55–74 years, while the reduction due to screening, which was first implemented in women aged 50–69 years in 1990–97, will be 28–30% in 2007.

Conclusions: Although adjuvant systemic therapy can reduce breast cancer mortality rates, it is anticipated to be less than the mortality reduction caused by mammography screening.

61 POSTER

Adjuvant pamidronate therapy prevents the development of bone metastasis in breast cancer patients with four or more positive nodes

I. Kokufu[1], N. Kohno[2], S. Takao[2], M. Yamamoto[1], S. Kohno[2], M. Miyashita[3], F. Kimura[1]. *[1]Itami City Hospital, Surgery, Itami, Japan; [2]Hyogo Medical Center for Adults, Breast Oncology, Akashi, Japan; [3]Kohnan Hospital, Surgery, Kobe, Japan*

Background: In breast cancer patients (pts), bone is the most frequent site of distant metastasis. The pathogenesis of bone metastasis is not fully understood but it has been considered that breast cancer cells produce osteoclast activating factors and activated osteoclasts resorb bone and develop into the lytic bone disease. Bisphosphonates (BPs) show highly potent inhibition of osteoclastic bone resorption and have beneficial effects on lytic bone disease in advanced breast cancer. From the mechanism of action, BPs are expected to prevent the development of bone metastases. In an *in vivo* study, a BP (risedronate) reduced the development of bone metastases by prophylactic administration. If preventive therapy has a benefical effect on the development of bone metastases, there is a significant impact on the patients' quality of life. Pamidronate (PMT), a second generation Bp, is the most potent inhibitor of osteoclast activity among the commercially available BPs. We examined whether adjuvant PMT therapy could prevent or delay the development of bone metastasis in breast cancer pts with a high risk for bone metastases.

Methods: Between 1997 and 2001, 90 pts with primary breast cancer with four or more positive nodes were assigned to the PMT group (45 mg PMT infusion 4 times every 2 weeks, 33 pts) or control group (57 pts) by patient self-preference. All pts underwent surgical treatment and the type of adjuvant systemic therapy used was based on the protocols of each center. The clinicopathological characteristics of the pts (age, tumor size, nodal status, menopausal status, hormonal status, type of chemotherapy) were well balanced between the two groups. The median follow-up period was 1650 days.

Results: Bone metastases were detected in 4 pts (12.1%) in the PMT group and in 22 pts (38.6%) in the control group (p=.008). The median number of bone metastases per pts was about 3 times higher in the control group than in the PMT group (NS). The incidence of both distant metastases and visceral and soft tissue metastases were lower in the PMT group than in the control group (p=.085 for both distant and soft tissue metastases). Five pts (15.2%) died in the PMT group and 15 pts (26.3%) died in the control group (p=0.296). Overall survival and disease-free survival rates were equal in the both groups, but bone metastasis-free survival was significantly higher in the PMT group compared to the control group (85.0% vs 63.8% at 5 years, p=.035). No serious adverse events related to the PMT occurred.

Conclusion: The incidence of bone metastasis was significantly reduced in the PMT group, and there was a tendency toward reduced incidence of distant and soft tissue metastasis in the PMT group. Bone metastasis-free survival was significantly higher in the PMT group, but no effect was seen on the overall and disease-free survival rate. We conclude that adjuvant PMT therapy (four infusions of 45 mg) significantly reduced the development of bone metastasis in breast cancer pts with four or more positive nodes.

62 POSTER

Chemotherapy (CHT) adjuvant strategies and reasons for choice in breast cancer (BC) patients (pts): results from the national oncological research observatory on adjuvant therapy (NORA)

G. Mustacchi, M. Cazzaniga, P. Pronzato, F. Di Costanzo, I. Floriani, A. De Matteis. *On behalf of NORA study group, Unversity, Medical Oncology, Trieste, Italy*

International guide lines for adjuvant therapy in BC pts are well known. At the beginning of 2003, we started collecting data from 77 Italian Oncological Centres regarding adjuvant therapeutic modalities and relapse pattern in pts with BC radically treated with surgery. About 3500 pts are expected to be enrolled, according to the following criteria: 10 pts each year starting from 2000 (retrospective cohort) and 20 pts starting from the beginning of 2003 or the date of ethical approval, if subsequent (prospective cohort). Until now, 1662 pts have been enrolled (1352 from retrospective cohort and 317 from the prospective group). Median age was 58.6 years (28–92). The majority of pts was menopausal (73.7%) at the start of adjuvant therapy. Breast conservative surgery was applied in 63.1% of the pts, histology was mainly ductal carcinoma (1258, 76.8%) and pathological T stage was T1 in 981 (60.1%), T2 in 556 (34%) and T3 in 44 (2.7%). Nodal status was positive in 700 pts (44.7%) as well as estrogen receptor status (1284, 79.6%). Data about the type of CHT and the reasons for administering it are presented. A small number of pts were part of a clinical trial (95, 5.8%), mainly CHT based (59/95, 80.8%). CHT was administered in 1075 pts (64.7%), both alone (331, 30.8%) or in combination with hormone therapy (HT) (744, 69.2%). Data about the type of CHT are available in 994 out of 1075 pts. CMF regimen, both as twenty-one or twenty-four days, was administered in 472 pts (47.5%), mainly followed by HT (296, 62.7%). On the other hand, 465 pts received an anthracycline-based CHT (465, 46.8%), alone or in combination with HT (282, 60.6%). A small number of pts received taxane-based CHT (37, 3.7%) or other drugs (20, 2.0%), mainly vinorelbine. Principal reasons for choosing CHT were biological tumour data (78.7%), tumour stage (76.7%) and standard guide lines (68.0%).

In conclusion, most of the pts underwent a CHT treatment, CMF regimen still remains a valid option, as in European tradition, even if international guide lines implemented the use of anthracycline-based therapy. In most cases, an association with HT was the preferred choice, mainly based on tumour characteristics.

63 POSTER

Zoledronic acid for the prevention of bone metastases in patients with breast cancer

R. Coleman[1], J. Gralow[2], R. Bell[3], A. Lipton[4]. *On behalf of the AZURE and SWOG/Intergroup investigators0307. [1]Academic Unit of Clinical Oncology, Weston Park Ho, Sheffield, UK; [2]University of Washington School of Medicine Seattle Cancer Care Alliance, Seattle, USA; [3]Andrew Love Cancer Centre, Geelong, Victoria, Australia; [4]Milton S. Hershey Medical Center, Hershey, USA*

Background: Zoledronic acid is the most potent bisphosphonate currently available and is highly effective for the treatment of bone metastases in patients with breast cancer. Based on evidence that daily oral clodronate may be of benefit in patients with early-stage breast cancer, studies are ongoing to investigate the potential of intravenous (IV) zoledronic acid to prevent metastasis to bone.

Materials and methods: Evidence supporting a role for zoledronic acid in the prevention of bone metastasis in patients with early-stage breast cancer was reviewed, and ongoing/planned trials are described.

Results: Preclinical studies with the MDA-MB-231 breast cancer cell line have shown that bisphosphonates have direct antitumor effects. Zoledronic

acid exhibited a 50% inhibitor concentration (IC_{50}) of 15 μM, which was approximately 50-fold lower than the IC_{50} of clodronate, and demonstrated synergistic antitumor effects with paclitaxel and doxorubicin. Moreover, in animal models of breast cancer metastasizing to bone, zoledronic acid was shown to significantly reduce skeletal tumor burden and to prevent the formation of new bone metastases at lower concentrations than any other bisphosphonate tested. These studies suggest that concentrations of zoledronic acid achievable in bone tissue are capable of inhibiting tumor growth. Therefore, studies are planned or ongoing to investigate the clinical benefit of zoledronic acid and other bisphosphonates in the adjuvant setting. The AZURE study is now recruiting patients and is evaluating the effect of zoledronic acid on disease-free survival in 3400 patients with stage II/III breast cancer receiving standard adjuvant chemotherapy and/or hormonal therapy. Patients will be randomized to placebo versus zoledronic acid (monthly × 6, every 3 months × 8 doses, then every 6 months × 5 doses). In addition, the Southwest Oncology Group will soon commence a large randomized trial to compare the benefits of oral clodronate (1600 mg/day), oral risedronate (30 mg/day), and IV zoledronic acid (4 mg every 3 wks for 6 months, and every 3 months thereafter) for 3 yrs as an adjunct to standard adjuvant therapy in women with stage I, II, or IIIA breast cancer.

Conclusions: Preclinical data and data from the metastatic setting support the investigation of zoledronic acid as an adjunct to standard adjuvant therapy to prevent bone metastasis in patients with early-stage breast cancer.

64 POSTER

Gemcitabine/epirubicin/paclitaxel as primary chemotherapy in stage II–IIIA operable breast cancer: Final results of a multicenter Italian study

A. Gennari[1], R. Degli Esposti[2], A. Bottini[3], A. Santoro[4], S. Saracchini[5], S. Donati[1], M. Roncella[6], L. Marini[7], G. Andreola[7], P. Conte[8]. [1]*Division of Medical Oncology, St Chiara Hospital, Pisa, Italy;* [2]*Division of Medical Oncology, Bologna, Italy;* [3]*Breast Unit, Cremona, Italy;* [4]*Humanitas, Milano, Italy;* [5]*Division of Medical Oncology, Pordenone, Italy;* [6]*Division of Experimental Surgery, St Chiara Hospital, Pisa, Italy;* [7]*Eli Lilly, Florence, Italy;* [9]*Division of Medical Oncology, Modena, Italy*

The purpose of this study was to evaluate pathologic complete response rate (pCR) and toxicity of preoperative chemotherapy (CT) with Gemcitabine, Paclitaxel and Epirubicin (GET) in patients with stage II/IIIA operable breast cancer. An additional endpoint was to evaluate the expression and modulation of some biological markers with prognostic and/or predictive potential. pCR was defined as the absence of invasive tumor cells in the breast. From October 2000, 44 patients have been enrolled: all patients received Gemcitabine 1000 mg/sqm days 1 and 8 plus Epirubicin 90 mg/sqm day 1 and Paclitaxel 175 mg/sqm day 1, every 21 days for 4 courses, followed by surgery. Median age was 49 years (27–67); clinical staging was IIA, 11 pts; IIB, 18 and IIIA, 15. Hormonal status was positive in 33 patients, negative in 10 and unknown in 1. Grade III/IV neutropenia occurred in 63.9% of cycles and febrile neutropenia in 1.9% of the cycles; G-CSF was administered in 3.2% of the cycles to shorten the duration of G4 neutropenia. Non hematological toxicity included G3 NV in 4.5% of patients, G3 mucositis in 6.8%, G3 diarrhoea in 2.3% and G3 alopecia in 100%. 41 patients completed the chemotherapy programme and received surgery: overall clinical RR was 90.2% (29.3% CR; 61% PR). Absence of invasive breast cancer (pCR) was documented in 6 pts (14.6%) and was associated with negative axillary nodes in 3 of them. pCR raised up to 40% and 22.2% in T < 3 cm and in node negative patients, respectively. The following biological markers were assayed at baseline and on the surgical specimens: HS, Mib1, SBR grade and Her 2-neu expression. Mib 1 > 20% was present in 83% of the patients at baseline and in 17% at surgery; Her2 neu was positive in 27% of the pts at baseline and in 9% at surgery. Final results from this study will be presented at the meeting.

65 POSTER

Pharmacoeconomic aspects of adjuvant early breast cancer treatment in postmenopausal women with anastrozole or tamoxifen: a Slovenian perspective

P. Piskur[1], M. Sonc[2], T. Cufer[2], S. Borstnar[2], A. Mrhar[1]. [1]*Faculty of Pharmacy, Ljubljana, Slovenia;* [2]*Institute of Oncology, Ljubljana, Slovenia*

Background: A cost-of-care analysis was performed to compare the costs associated with adjuvant treatment in postmenopausal early breast cancer (EBC) patients using either anastrozole (AN) or tamoxifen (TAM). Our intention was to establish which of the two approaches imposes less on society.

Methods: Cost-of-care analysis was used in this assessment. The efficacy of both drugs was obtained from an ATAC trial after the median observational time of 33.3 months. All health care costs were acquired mainly from the Institute of Oncology, Ljubljana and Institute of Health Insurance of Slovenia. In order to calculate the overall costs we had to evaluate the costs of treatment of a primary EBC, new primary EBC, and the costs of disease progression. In order to estimate the costs related to disease progression a group of 20 randomly assigned metastatic breast cancer patients was chosen. The patients' medical charts were examined and costs of treatment for a period of 3 years were calculated. Since no economic evaluation of human life exists in the Slovenian health care system, these costs could not have been included in the analysis. Additionally, the analysis that we made did not take into account the costs related to adverse effects of both treatment arms.

Results: The hypothetical cost calculation based on the treatment of 450 postmenopausal women with EBC, which is also the approximate number of new cases per year in Slovenia, showed that AN results in higher overall treatment costs than TAM. The total sum of all direct healthcare costs over 33.3 months was 4.665 million EUR (10,367 € per person) in the AN arm, and 3.081 million EUR (6847 € per person) in the TAM arm. Despite the higher overall treatment costs associated with AN we succeeded to show a conversion of drug cost ratio of AN/TAM = 7.3/1 to a ratio of only 1.5/1 in favour of TAM, considering overall treatment costs.

Conclusions: The overall treatment cost ratio of 1.5/1 in favour of TAM shows that despite its higher initial costs AN could be an acceptable choice of treatment even in countries with smaller health care budgets.

66 POSTER

The benefits of adjuvant hormonal therapy in patients with early breast cancer 35 years old or younger

N. Snoj, B. Pajk, S. Bostnar, T. Cufer. *Institute of Oncology, Medical oncology, Ljubljana, Slovenia*

Purpose: The purpose of our study was to determinate the benefits of adjuvant hormonal therapy (HT) in patients (pts) with hormone receptor (HR) positive breast cancer ⩽35 years (y).

Patients and methods: The data from 51 breast cancer pts ⩽35 y treated at the Institute of Oncology Ljubljana from September 1993 to October 2002 were analysed. All pts received radical local treatment and adjuvant systemic therapy was preformed according to the institutional guidelines.

$\chi 2$ test was used to calculate the differences in tumour characteristics; Kaplan Maier curve and log-rank test were applied to present the differences in survival between the subgroups.

Results: HR positive (+) tumours were found in 28 pts (56%) out of 51 pts; in one patient HR status was unknown. HT was preformed in only 12/28 (42%) pts with HR+ tumours (tamoxifen in 10 pts and tamoxifen and LHRH agonist in 2 pts). Sixteen HR+ pts did not receive HT, which was according to the institutional guidelines valid until 1998 (8pts), for 8 pts the reason is not known. In the majority of pts (84%) adjuvant chemotherapy was preformed.

Between the subgroups of HR+ pts, treated or not by HT, no significant differences in terms of percentage of pts treated by adjuvant chemotherapy and in terms of tumour characteristics (size, grade, number of lymph nodes involved) were found.

After the median follow up of 3.3 years the 3-y disease free survival (DFS) for the whole group of pts was 70%; for HR+ pts 72% and for HR− pts 66% (p=NS), respectively. 3-y DFS for HR+ pts treated by HT was as high as 100% and it was only 53% for HR+ pts not treated by HT (p=0.0063).

Conclusion: Our results clearly showed the benefit of HT in the HR+ early breast cancer pts ⩽35 y.

67 POSTER

Cost-effectiveness of various guidelines for adjuvant systemic therapy in primary breast cancer

M. Bolster[1], W. Kievit[2], G.J. Van der Wilt[2], E. Adang[2], P. Bult[3], E. Thunnissen[4], J. Meijer[5], L. Beex[6], V. Tjan-Heijnen[6]. [1]*University Medical Center Nijmegen, Department of Surgery, Nijmegen, The Netherlands;* [2]*University Medical Center Nijmegen, Department of Medical Technology Assessment, Nijmegen, The Netherlands;* [3]*University Medical Center Nijmegen, Department of Pathology, Nijmegen, The Netherlands;* [4]*Canisius Wilhelmina Hospital, Department of Pathology, Nijmegen, The Netherlands;* [5]*Rijnstate Hospital, Department of Pathology, Arnhem, The Netherlands;* [6]*University Medical Center Nijmegen, Department of Medical Oncology, Nijmegen, The Netherlands*

Background: During the previous decade guidelines for adjuvant systemic therapy for primary breast cancer repeatedly changed. The impact of the implementation of new guidelines on the workload of medical specialists and outpatient nurses and on the hospital-budget is rarely taken into account. In this study the change in the total number of eligible patients