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.

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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.

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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.

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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.

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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