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

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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.

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

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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.

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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)

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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

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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