Results: Considering a cohort of 1000 patients modelled for 25 yrs, anastrozole was estimated to lead to 184 discounted LYG at an additional cost of £2.1 million. Consequently, the discounted ICER of anastrozole compared to tamoxifen was estimated to be £11,747/LYG (95% CI £1946–£21,984). Furthermore, acceptability curves showed that the estimated cost/LYG at 25 yrs was below £20,000 with a probability greater than 90%. T he result compared favourably with commonly accepted thresholds for cost-effectiveness of other cancer drugs and was robust to all the parameters (including adverse events) tested in the sensitivity analysis.

Conclusions: Anastrozole is a cost-effective alternative to tamoxifen for the adjuvant treatment of postmenopausal women with HR+ early breast cancer.

57 POSTER

Neoadjuvant tamoxifen for hormone-sensitive non metastasis breast carcinomas in early post-menopausal women: a 118–month median follow-up

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Purpose: An initial analysis was published and showed the feasibility of this strategy, obtaining a conserving treatment rate of 50%. We now report the long-term analysis of this series with a 118-month median follow-up. The aim of this study is to verify that a conserving treatment after neoadjuvant endocrine therapy does not hamper overall survival.

Patients and methods: Between 1985 and 1996, 199 women from 50 to 70 years old, having a too big tumor to be treated with conserving surgery or a T4 tumor, were treated at Institut Bergonié with neoadjuvant endocrine therapy. All of these tumors had steroid receptor positivity with at least one positive receptor. Tamoxifen was given for 4 to 6 months at a 30 mg dosage per day. Median duration of treatment was 5.34 months. Ninety seven women (48.7%) benefited from a conserving treatment, 38 with an exclusive irradiation, 57 with a conserving surgery plus an irradiation and 2 with a preoperative irradiation. Remaining patients (n=102) were treated by modified radical mastectomy (n=57) or received another medical treatment.

Results are presented with a 118 month median follow-up. In the group treated with modified radical mastectomy, 46 patients (54%) had a recurrence, 16 with local relapse (18%) and among them 9 were isolated local relapse and 7 were associated with metastatic disease. In the group treated with conserving therapy, 44 (45.3%) had a recurrence. Eighteen had local relapse (18.5%) and, among them, 10 had **isolated local relapse**. The others had metastatic disease (n=26) as first recurrence. In this series of patients having benifited from conserving treatment after neo-adjuvant tamoxifen, 10 women could have their outcome hampered by their local relapse. The probability to have an isolated local relapse is 6.3% at 3 years, 8.4% at 5 years and 21.4% at 10-year follow-up. Treatment of local relapses was performed in 2 cases with second line conserving surgery, thanks to small recurrence size and in 4 cases with total mastectomy. Complete remission was obtained after this salvage surgery and no adjuvant medical treatment was delivered afterwards. Three patients refused salvage surgery and were treated by an other hormonotherapy. The onset of **metastatic disease** is equivalent in the 2 groups of patients having had a conserving surgery (20% and 41.5%) or a modified radical mastectomy (21.2% and 57.9%) at 5- and 10-year follow-up respectively.

Concerning overall survival, the 2 curves are identical, whatever the loco-regional treatment carried out, 88.6% and 79.9% at 5-year follow-up and 62.9% and 57% at 10-year follow-up respectively.

In conclusion, there was no difference in clinical outcome in terms of locoregional recurrences, metastatic free survival and overall survival between patients undergoing conserving treatment and patients who were submitted to radical mastectomy after neoadjuvant tamoxifen.

58 POSTER

Disease free survival (DFS) in breast cancer patients older than 70 years compered to younger patients groups

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Introduction: Breast cancer in the elderly is a common disease that is usually undertreated compared to younger patients (pts). The aim of our analysis was to find out the differences in tumor characteristics, treatment modalites and DFS in pts over 70 years (y) in comparison with pts 50–70y and younger than 50y.

Patients and Methods: We analysed the data of 1541 pts with operable breast cancer that were treated at the Institute of Oncology during the period September 1993–October 2002. All patients had radical local therapy and systemic therapy performed according to the institutional guidelines at that time. The differences in tumor characteristics (nodal status, grade, tumor size, tumor type, hormonal receptors [HR] and PAI 1) and treatment modalites (type of surgery, radiotherapy (RT) and systemic therapy offered) in pts over 70y (n=305), 50–70y (n=769) and less than 50y (n=473) were examined by χ^2 test. The 3-year DFS in all three groups was calculated according to Kaplan-Meier method and log-rank test.

Results: Patients >70y had compared to pts <50y statistically significant more HR+ tumors (p=>0.0001) and tumors ⩾2 cm (p=0.004), less N+ tumors (p=0.023) and less histological type of invasive ductal carcinoma (p=0.001). Borderline significance was found for grade III tumors (p=0.059). When tumors characteristics of pts >70y were compared with pts 50–70y, statistical significance was found only for tumor size (p=0.041). Regarding local treatment, pts >70y had statistically less conservative surgery done, compared to both younger pts groups (p=>0.0001). The same was found for RT (p=>0.0001). Regarding systemic therapy more hormonal therapy was offered to pts >70y than to pts <50y (p=>0.0001) and pts 50–70y (p=0.013). The opposite was shown for chemotherapy (p=>0.0001).

The 3-year DFS for patients >70y was 82% (HR+ 86% and HR− 61%), for groups of patients 50–70 years and pts <50y DFS was 83% (HR+ 85%, HR− 74%) and 79% (HR+ 82% and HR− 69%), respectively. The difference in DFS in hormonal responsive disease between pts >70y and <50y was statistically significant (p=0.0134).

Conclusion: Women over 70y do not have more indolent breast cancer than pts 50–70y, but have more favorable tumors characteristics in terms of HR+, lymph node+ and histological type than pts less than 50y.

Patients over 70y with hormonal responsive disease treated with radical local therapy and systemic therapy (mostly HT) have significantly better DFS than pts less than 50y and comparable DFS to pts 50–70y. However in hormonal unresponsive disease in pts over 70 is a trend to worse DFS compared to both younger groups and we suppose that this is a group of the elderly patients where clinical trials of adjuvant chemotherapy is urgently needed.

59 POSTER

Effects of fulvestrant in premenopausal women with oestrogen receptor-positive primary breast cancer

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Background: Fulvestrant is an estrogen receptor (ER) antagonist that has no agonist effects. While fulvestrant reduces cellular levels of markers of hormone sensitivity and proliferation in postmenopausal women, its effects on these markers in premenopausal women with ER-positive primary breast cancer have not yet been studied.

Methods: This randomised, double-blind trial evaluated the anti-oestrogenic effect (expression of ER and progesterone receptor [PgR] indices) and the anti-proliferative effect (Ki67 labelling index) of a single 250 mg intramuscular (im) dose of fulvestrant. Premenopausal patients were randomised to receive fulvestrant (n=39) or placebo (n=40) on Day 1, with surgery for primary breast cancer occurring between days 15–22. Tumour biopsy samples were evaluated before trial treatment and at the time of surgery.

Results: Patients in the fulvestrant and placebo groups were well matched, with similar proportions of patients in each group in the luteal and follicular phases of their menstrual cycle. There were no statistically significant differences between treatments for any of the primary endpoint indices (Table 1) and there was no association between plasma fulvestrant concentration and changes in the endpoint indices.

Table 1

	Lsmean	Treatment effect* (95% CI)	p-value
ER Index (H-score)			
Fulvestrant (n=29)	49	5 (−9, 20)	p=0.48
Placebo (n=31)	44		
PgR Index (H-score)			
Fulvestrant (n=26)	65	−23 (−49, 3)	p=0.08
Placebo (n=26)	88		
Ki67 Index			
Fulvestrant (n=30)	24	0 (−7, 7)	p=0.97
Placebo (n=32)	24		

Lsmean, least squares mean; CI, confidence interval; *difference in Lsmeans.

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.

61 POSTER

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.

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)

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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