

(inter-audit range: 48.5±10.9 to 53.1±11.8 years). Patients were postmenopausal in 51% of cases and 64% were hormone receptor positive. The diagnostic spread was stage I 18%, II 63%, III 15% and IV 4%. Concomitant radiotherapy was reported in 35%. Fifty-seven percent received CMF-based regimens, 39% anthracycline-containing, and 4% other regimens. Use of colony-stimulating factors (CSF) was reported in 13% (inter-audit range: 1–18%). NE were observed in 20% of patients (inter-audit range: 15–27%). Repeated NE were seen in 8% (inter-audit range 6–11%). Neutropenia-related hospitalisations, dose reductions, and dose delays were seen in 4%, 6% and 13%. Mean ARDI ± SD was 96±8% vs 87±11% in patients without and with NE ($p<0.005$). ARDI * 85% was observed in 10% vs 35% of patients without and with NE ($p<0.005$; OR 5.0, 95% CI 4.0–6.4; multivariate adjusted OR 4.8, CI 3.8–6.0). NE were independently associated with postmenopausal status (OR 1.2, CI 1.0–1.5); use of a non-anthracycline-containing regimen (OR 1.3, CI 1.1–1.6; unadjusted association not uniform across studies); number of CT cycles planned (OR 1.2 per additional cycle, CI 1.2–1.3); and concomitant radiotherapy (OR 1.5, CI 1.2–1.9). NE from cycle 2 onwards were additionally associated with cycle 1 NE (OR 10.4, CI 5.0–21.6); negative hormone receptor status (OR 1.4, CI 1.0–2.0); and higher disease stage (OR 1.2 per stage, CI 1.0–1.3); but not with menopausal status. A risk score based on menopausal status, number of CT cycles planned, and concomitant radiotherapy administration appears to differentiate patient groups with increasing NE risk (10–27%) as shown in Figure 1.

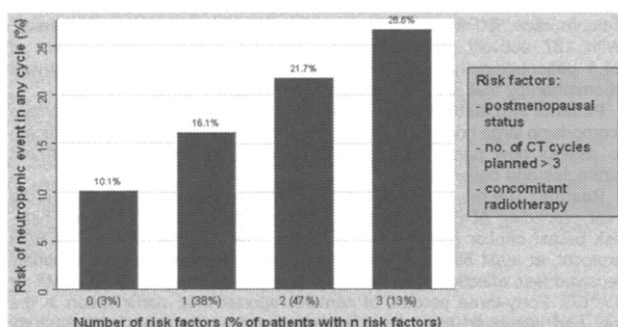


Fig. 1. Risk of neutropenic event by risk score. The more risk factors that are present the higher the incidence of observed neutropenic events in breast cancer patients receiving chemotherapy.

Conclusions: NE occur in a relevant proportion of patients receiving breast cancer CT and are associated with low ARDI which may affect treatment outcomes. This data adds to the growing evidence supporting the development of risk models to enable better targeting of preventative measures. Prospective data from ongoing EU and US studies should enable the relationship between risk factors for NE to be more clearly defined.

54 POSTER HIGHLIGHT Efficacy of adjuvant chemotherapy according to hormone receptor status in young breast cancer patients

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Purpose: breast cancer at a young age is associated with an unfavorable prognosis. Very young breast cancer patients receive chemotherapy irrespective of tumor stage or grade. However, chemotherapy alone may not be adequate adjuvant systemic therapy in hormone receptor positive young breast cancer patients. Therefore we studied the effect of adjuvant chemotherapy in young breast cancer patients in relation to hormone receptor status.

Patients and Methods: paraffin embedded tumor material was collected from 480 early stage breast cancer patients who participated in one of four EORTC trials; 10801, 10854, 10901, 22881. All patients were younger than 41 years at time of diagnosis. Estrogen receptor- and progesterone receptor status were scored by immunohistochemistry using a tissue micro array. Patients were followed up for overall survival and distant disease-free survival; the median follow up period was 7.3 years.

Results: overall, patients with ER-positive tumors had better overall survival rates compared to ER-negative patients (HR 0.63, 95%CI 0.43–0.93, $P=0.02$). However no significant difference in overall survival (HR 0.87, 95%CI 0.50–1.52, $P=0.63$) and distant disease-free survival was found between patients with ER positive tumors or ER negative patients

in the subgroup that did receive chemotherapy. Patients with ER positive tumors who did not receive adjuvant chemotherapy had better overall survival (HR 0.63, 95%CI 0.43–0.93, $P=0.02$) rates than ER negative patients. Outcome results were similar for PgR status.

Discussion: Patients with ER positive tumors benefit less than those with ER negative tumors from adjuvant systemic chemotherapy. Therefore, chemotherapy alone in breast cancer patients aged 40 years or less with hormone receptor positive tumors is sub optimal adjuvant systemic treatment. The addition of adjuvant hormonal treatment with or without endocrine ovarian suppression may result in improved survival.

55 POSTER HIGHLIGHT Hormone adjuvant strategies in breast cancer (BC) patients (pts): results from the National Oncological Research observatory on Adjuvant therapy (NORA)

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NORA is a national observatory aimed at investigating adjuvant therapeutic modalities and relapse pattern in patients (pts) with breast cancer (BC), radically treated with surgery in 77 Italian Oncological Centres (OCs). About 3500 BC pts will be enrolled consecutively, 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, data about 1662 pts are available. Median age was 58.6 years (28–92). Most of the pts were menopausal (73.7%). More than half of the pts underwent breast conservative surgery (63.1%), were T1 (60.1%) or T2 (34%) and node +ve (44.7%). Estrogen receptor (ER) status was positive in 1284 pts (79.6%). The majority of the pts received a medical therapy (97.5%), with (59.3%) or without radiotherapy (RXT). Data about hormone therapy (HT) choice and the principal reasons leading to it are presented. Irrespective to RXT, HT was administered alone (540/1621, 33.5%), or as a part of a combination program: chemotherapy (CHT) followed by HT: 671, 41.4%; concomitant CHT and HT: 73, 4.5%. Tamoxifen was administered in 1004 out of 1662 pts (62.8%), as HT alone (475, 45.5%) or sequential to CHT (569, 54.4%). Aromatase inhibitors (AI) represented the treatment of choice in 112 pts (6.9%), alone (52/112, 46.4%) or after CHT (53.6%). HT was chosen in 821 ER+ pts (63.9%) as single modality, or together with CHT (714, 55.6%). We asked investigators to indicate the three main reasons for choosing hormone therapy, both as the only therapy or combined with CHT: biological tumour data (80.5%), standard guide lines (70.2%) and tumour stage (52.9%) were referred as the principal criteria. In conclusion, tamoxifen is still the wide used HT, mainly as a part of combination program together with CHT. AI have been used in a small percentage of pts. NORA results provide useful information about adjuvant strategies in BC pts, allowing us to better understand factors involved in our choice.

56 POSTER HIGHLIGHT Cost-effectiveness of anastrozole vs tamoxifen as adjuvant therapy in postmenopausal women with early breast cancer: a UK National Health Service perspective

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Background: Results from the ATAC trial (Lancet 2002; 359:2131–9), at a median follow-up of 33 months, indicated that anastrozole ($n=3125$) was superior to tamoxifen ($n=3116$) in terms of disease-free survival in the adjuvant treatment of postmenopausal women with hormone receptor-positive (HR+) early breast cancer. Updated data (median follow-up 47.2 months for efficacy and 37 months for safety) confirmed these findings (Cancer 2003; 98:1802–10). Using the updated data, the direct medical costs and incremental cost-effectiveness ratio (ICER) per life year gained (LYG) for managing this group were calculated for anastrozole compared to tamoxifen within the UK National Health Service (NHS) setting.

Methods: A probabilistic Markov model was developed using the updated ATAC data. The model projected outcomes for both anastrozole and tamoxifen to 25 years (lifetime horizon) by extrapolating pooled Kaplan-Meier curves using parametric statistical methods. General mortality data were obtained from UK national statistics. It was assumed that anastrozole and tamoxifen would be given for a maximum of 5 years and that recurrence rates after this treatment period would be equivalent in the two groups—a conservative approach. Resource utilisation data associated with treating adverse events pre-specified in the ATAC study were obtained from published literature. Other resource utilisation data were estimated from structured telephone interviews with 6 UK physicians. Unit costs in GBP were obtained from 2002 NHS reference costs and 2003 drug costs (BNF). Costs and benefits were discounted at 6% and 1.5%, respectively. Sensitivity analyses were conducted. The perspective was that of the UK NHS.

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%. The 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.

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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 benefited 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 hormoneotherapy. 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.

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POSTER

Disease free survival (DFS) in breast cancer patients older than 70 years compared 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 modalities 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 modalities (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.

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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.