all dimensions. QOL declined in both TAC and FAC treated patients during the treatment phase. While the decline in TAC subjects was statistically larger in 11/23 dimensions (including Global Health Status and Physical Functioning), it was of uncertain clinical significance and both groups returned to or exceeded their baseline scores by the 6 month follow-up visit.

Table 1. Intent-to-Treat Efficacy Analyses Prospectively Powered (n=1491)

DFS	Hazard Ratio TAC/FAC (95% CI)	P-value
Adjusted for N status (Primary endpoint)	0.72 (0.59–0.88)	0.0010
1–3 nodes (n=923)	0.61 (0.46–0.82)*	0.0009
4+ nodes (n=568)	0.82 (0.63–1.08)*	0.1629
Hormone Receptor Positive†	0.73 (0.57–0.94)	0.0132
Hormone Receptor Negative†	0.66 (0.47–0.93)	0.0163
Overall Survival		
Adjusted for N status	0.70 (0.53–0.91)	0.0080

*Ratio of Hazard Ratios: 1.34 (0.90–2.00), p= 0.1476. †Centrally reviewed.

Conclusion: Docetaxel-based therapy (TAC) significantly improves both disease free survival and overall survival compared with FAC. The higher rate of neutropenic complications is manageable, and the on-therapy differences in some QoL parameters between study arms normalized on completion of therapy. TAC represents a major therapeutic advance in the adjuvant chemotherapy for patients with early breast cancer.

51 POSTER HIGHLIGHT

Preoperative hormonal therapy vs chemotherapy in postmenopausal ER-positive breast cancer patients

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Preoperative (neoadjuvant) chemotherapy or hormonal therapy is being used increasingly to downstage locally advanced and large operable breast cancer.

Following this treatment, inoperable breast cancer often becomes fully resectable, and tumors requiring mastectomy may be successfully removed by breast-conserving surgery (BCS).

Patient selection is important to optimize neoadjuvant therapy, especially in elderly postmenopausal women with co-morbid conditions.

Patients and methods: Between March 1998 and March 2003, 117 postmenopausal (PM) women with ER(+) and/or PgR(+) breast cancer (BC) T2N1-2, T3N0-1, T4N0M0 assigned neoadjuvant treatment with either chemotherapy doxorubicin 60 mg/m2 + paclitaxel 200 mg/m2, every 3 weeks, 4 cycles, n=58 patients (pts), or hormonal therapy with aromatase inhibitors, n=59 (once daily exemestane 25 mg, n=29, or anastrazole 1 mg, n=30, 3 months).

The primary endpoint was to compare overall objective response (OR) determined by clinical (palpation) and mammography. Secondary endpoint was the number of pts who qualified for BCS + radiotherapy (50 Gy for 25 fractions).

Results:

Table 1

Neoadjuvant therapy	OR %		BCS %
	Clinical	Mammography	
Chemotherapy (doxorubicin + paclitaxel)	75.8*	62	20.6*
Anastrazole	80.0	70	33
Exemestane	90.5*	72.4	37.9*
p-value	0.096*	> 0.5	0.054*

OR rate (clinical and mammography) was statistically similar ($p > 0.05$) in the chemotherapy and ≪hormonal≫ groups. Tendency to more BCS took place in the ≪hormonal≫ arm that in the chemotherapy arm (37.9% vs 20.6% p=0.054). Local recurrence rate were similar for pts receiving chemotherapy or hormonal therapy (1.7% and 1.7%, at 34 months median follow up).

In chemotherapy arm the most frequent grade III/IV toxicity was alopecia (79.3%), neutropenia (43.1%), cardiotoxicity (6.8%), diarrhea (1.7%). Hormonal treatment was well tolerated. The most commonly adverse events were hot flushes (23.3%), vaginal discharge (6.6%), musculoskeletal disorders (1.7%).

Conclusion: Preoperative hormonal treatment (anastrazole, exemestane) is a reasonable alternative to chemotherapy for PM women with ER and/or PgR-positive cancer in clinical situation where the low toxicity of the regimen is considered an advantage, for example, for women over 70.

52 POSTER HIGHLIGHT

Participation in phase III ADEBAR: Evaluating the role of adjuvant docetaxel in high-risk breast cancer patients improves treatment strategies and individual patient care in recruiting centers

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Background: The ADEBAR study is a prospective multicenter phase III trial to evaluate whether high-risk breast cancer patients with more than 3 involved lymph nodes benefit from a sequential anthracycline-docetaxel regimen ($E_{90}C$–D: 4 cycles epirubicin [E] 90 mg/m^2 plus cyclophosphamide [C] 600 mg/m^2 q21 days followed by 4 cycles docetaxel [D] 100 mg/m^2 q21 days) compared to standard anthracycline-containing polychemotherapy ($FE_{120}C$: 6 cycles E 60 mg/m^2 d 1+8, 5-fluorouracil 500 mg/m^2 d 1+8 and C 75 mg/m^2 d 1–14, q4 weeks). With 137 actively participating centers and a median recruitment of 24.5 patients/month, ADEBAR is currently the best recruiting adjuvant chemotherapy trial in this specific risk group in Germany.

Patients and Methods: We surveyed recruiting centers by questionnaire (comprising large hospital departments and community oncology practices) to assess how participation in ADEBAR had changed their treatment strategies and patient care.

Results: The return rate of the questionnaire was 67.4% (n=93). In the year preceding ADEBAR, 54.8% of study centers had not entered high-risk breast cancer patients into a clinical trial. Outside of the ADEBAR protocol, at least 51.7% of these high-risk patients would have routinely received less effective chemotherapy regimens such as CMF, EC/CMF, or 4× EC. Forty-three percent of centers reported that participation in the trial had increased the intensitiy of their patient care (apart from study specific issues) and 53.7 % noted an improvement in their professional knowledge from being part of an investigators' network with newsletters, regular meetings, etc. Although 55.9 % reported that being part of the ADEBAR study had not changed the overall quality of their patient care, 35.5 % detected improvements.

Conclusion: Our results demonstrate that participation in clinical trial protocols benefits physicians and patients by improving treatment strategies and individual patient care in recruiting centers. Moreover, our excellent recruitment rate demonstrates that modern trials, which are easy to carry out under routine care conditions, realistically have the potential of getting centers interested in conducting clinical trials.

53 POSTER HIGHLIGHT

Neutropenic events in six European audits of breast cancer chemotherapy

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Background: European data on chemotherapy (CT) related neutropenic events (NE) and their consequences is sparse. Six retrospective audits of breast cancer CT from Austria, Belgium, Germany, Spain and the UK have been collected by the INC-EU. Results of a combined analysis are reported.

Materials and methods: Variables available in all six datasets were merged into a single dataset of individual observations and their definitions were harmonised. NE were defined as neutropenia-related hospitalisation, reduction ⩾15%, and/or dose delay ⩾7 days. Analysis addressed the incidence of NE and of low average relative CT dose intensity (ARDI). Multivariate adjusted odds ratios (ORs) were calculated by robust multiple logistic regression.

Results: A total of 2860 patients were diagnosed between 1979 and 2001 and had a mean age at diagnosis ± SD of 51.1±11.3 years

(inter-audit range: 48.5±10.9 to 53.1±11.8 years). Patients were post-menopausal 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.

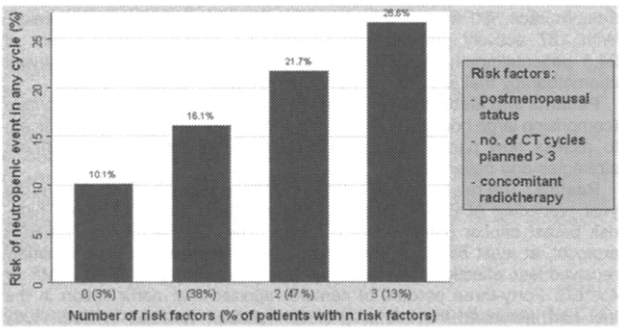

Fig. 1. Risk of neutropenic event by risk score. The more risk factors that are present the higher the incidence of observed neutropenic events in breast cancer patients receiving chemotherapy.

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 togheter 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.