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

Results of a prospectively planned combined analysis of these trials are presented.

Methods: In both trials, patients were randomised double-blind to treatment for 12 weeks prior to surgery. In the PROACT trial, additional chemotherapy was optional, whereas IMPACT patients did not receive chemotherapy. Therefore, the results from patients who received either AN or TAM alone have been combined for the primary endpoint of objective response (OR), assessed by calliper and ultrasound. OR rates are also reported for patients whose tumours were inoperable, or were scheduled to have mastectomy at baseline, the population reported in most previous studies. Surgical improvement was assessed in those patients who were inoperable or required mastectomy at baseline (improvement to any surgery/BCS at 12 weeks), defined by improvement in feasible surgery and actual surgery.

Results:

Patient population	OR (% patients)			
	AN	TAM	Odds ratio (95% CI)	p-value
Total (N=535, 69%)				
Calliper	45	36	1.42 (1.00–2.02)	0.052
Ultrasound	32	27	1.28 (0.88–1.87)	0.191
Inoperable/requiring mastectomy at baseline (N=344, 44%)				
Calliper	47	35	1.65 (1.06–2.56)	0.026
Ultrasound	36	26	1.60 (1.00–2.55)	0.048

Significant improvements were seen in both feasible surgery (47% vs 35% [1.67 (1.08–2.60); p=0.021]), and actual surgery (43% vs 31% [1.70 (1.09–2.66); p=0.019]) for AN vs TAM, respectively.

Conclusions: AN is an effective neoadjuvant treatment for post-menopausal women with hormone receptor-positive breast cancer. Overall, AN showed a strong trend towards greater efficacy than TAM, and in patients requiring mastectomy or those with locally advanced inoperable disease, AN was significantly more effective than TAM for all endpoints assessed.

48 ORAL

Correlation between response to neoadjuvant chemotherapy (NACT) with single agent taxanes and HER-2 gene amplification in patients with breast carcinoma

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Background: Taxanes are mitotic poisons that play an important role in the treatment of breast cancer. Identification of patient-specific tumor characteristics may predict response to treatment. The use of NACT is the optimal setting to observe these predictions. The objective of this study was to determine whether HER-2 gene amplification was associated with pathologic response to NACT with taxanes in patients with early-stage breast cancer.

Methods: 71 consecutive patients with stage II and III breast cancer from whom tissue was available were included. Fifty-seven patients (80%) received paclitaxel as part of a randomized clinical trial of NACT for patients with operable breast cancer (Buzdar AU et al. JCO 1999;17:3412–7). Fourteen patients (20%) received neoadjuvant docetaxel off protocol. All 71 patients received FAC postoperatively. HER-2 gene amplification was determined using fluorescence in situ hybridization (FISH). Pathologic complete response (PCR) was defined as no evidence of invasive breast cancer in the breast and the axillary lymph nodes. Breast pathologic response (BPR) was defined as no evidence of invasive breast cancer in the breast only. The association between HER-2 status and pathologic response was evaluated using the Chi Square method. The Kaplan-Meier survival analysis was used to calculate disease free survival (DFS).

Results: The median patient age was 49 years (range, 21 to 70 years). Forty-eight patients (68%) had stage II breast cancer and 23 patients (32%) had stage III breast cancer. HER-2 amplification was detected in 19 (28%) of tumors. Hormone receptor (estrogen and/or progesterone) were detected in 11 (58%) of HER-2 amplified tumors (HER-2[+]) and 31 (65%) of HER-2 non-amplified tumors (HER-2[−]). Median number of NACT cycles was 4. There were 8 PCR, 3 (16%) in patients with HER-2[+] tumors and 5 (10%) in patients with HER-2[−] tumors, (p=0.5). There were 12 BPR, 5 (26%) in patients with HER-2[+] tumors and 7 (15%) in patients with HER-2[−] tumors, (p=0.2). At a median follow up of 53.7 months there have been 17 recurrences. None of the patients who achieved pCR developed recurrent disease, regardless of HER-2 status of the primary tumor. The DFS was 89 months in both groups (HER-2[+] and HER-2[−]) (p=0.1).

Conclusion: HER-2 gene amplification was not predictive of PCR or BPR to neoadjuvant single agent taxanes in patients with early-stage breast cancer.

49 ORAL

Postoperative adjuvant chemotherapy followed by adjuvant tamoxifen versus nil for patients with operable breast cancer. First results of a randomized phase III trial EORTC 10901

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Introduction: Adjuvant Tamoxifen as monotherapy reduces recurrence and mortality in patients with hormone receptor positive operable breast cancer. However, its contribution is less established in patients receiving adjuvant chemotherapy. Experimental data suggest that Tamoxifen and chemotherapy may in fact be partially antagonistic, and recently published clinical trials confirm that concomitant administration of Tamoxifen with chemotherapy yield inferior results than chemotherapy alone. This trial, initiated by the EORTC Breast Group in 1991, investigates the impact of Tamoxifen, given sequentially after completion of adjuvant chemotherapy in patients with operable breast cancer.

Methods: Female patients with stage I–IIIA operable breast cancer receiving after surgery 6 cycles of adjuvant combination chemotherapy with either CMF, CAF, CEF, FAC or FEC were eligible, irrespective of their menstrual status and of the hormone receptor status of their primary tumor. Patients with any other malignant disease including contralateral breast cancer were excluded, except those with adequately treated cervix carcinoma or basal cell carcinoma of the skin. Patients consenting to participate were stratified by institute, chemotherapy scheme and age (above 50y or younger) and were randomized at the start of their last cycle of chemotherapy to receive either Tamoxifen 20mg daily during 3 years or no further treatment. The main endpoint of the trial was to detect a 5% increase in the 5 year survival (from 80% to 85%) in favor of antiestrogen therapy, which required to observe at least 159 deaths in each treatment arm. Secondary endpoints were relapse free survival, local control, incidence of second primary breast cancer and correlation of results with receptor status.

Results: Between 03/1991 and 05/1999, 1863 patients were randomized by 51 institutions from 14 countries. At a median follow-up to date of 6.3 years, 359 deaths and 551 events (relapse and/or death) have been observed.

Conclusions: The number of events needed to perform the first analysis has recently been reached and the data base is in its final stage of cleaning. A full report of the results of this trial will be presented at the meeting.

50 ORAL

Docetaxel-based regimen (TAC) improves DFS and OS over FAC in node positive early breast cancer patients: Efficacy, safety and quality of life at 55 month follow-up

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The BCIRG001 trial comparing the docetaxel (Taxotere®)-based regimen TAC (75/50/500 mg/m2 q3wk ×6) with FAC (500/50/500 mg/m2 q3wk×6) accrued 1491 patients with node positive early breast cancer from June 1997 to June 1999. The 2nd planned interim analysis with a median follow-up of 55 months and 399 events showed that TAC improves disease free survival (TAC/FAC Hazard Ratio: 0.72, p=.0010) and overall survival (TAC/FAC Hazard Ratio: 0.70, p=.0080) over FAC (Table 1).

Among hematological toxicities, febrile neutropenia was more frequent in the TAC arm (24.7% vs 2.5%), but with no increased incidence of grade 3/4 infection (3.9% vs 2.2%) and no septic deaths. Non-hematological toxicities (grade 3/4) with incidence >5% of pts were nausea (9.5%), vomiting (7.3%), asthenia (5.6%) in the FAC arm and, asthenia (11.2%), stomatitis (7.1%), nausea (5.1%) in the TAC arm. 91% of patients in the TAC arm and 97% in the FAC arm completed the planned 6 cycles of treatment. Quality of life (QoL), a secondary endpoint of this trial, was assessed using the EORTC QLQC30 (version 2.0) and QLQBR23 (version 1.0). The two treatment groups were well-balanced for baseline scores in