the individual response of metastatic breast cancers to docetaxel and trastuzumab, however, the clinical responses were observed in all patients with Bcl-2-negative tumors.

Conclusion: weekly docetaxel and trastuzumab is safe and effective combination method for HER-2-overexpressing metastatic breast cancer.

281 POSTER

An exploratory analysis examining proportion of patients responding for 1 year or more in two phase III studies of fulvestrant versus anastrozole

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Background: Fulvestrant ('Faslodex') is an estrogen receptor (ER) antagonist that has no agonist effects. Two Phase III trials have shown fulvestrant to be at least as effective as anastrozole and associated with a longer median duration of response (DOR; 16.7 months vs 13.7 months, respectively) in patients with advanced breast cancer who had progressed on prior endocrine therapy. This abstract reports an exploratory combined analysis of DOR by categorical time period (⩾1 year), in the patients who experienced an objective response (OR; complete [CR] or partial response [PR]) or clinical benefit (CB; CR + PR + stable disease [SD] ⩾24 weeks) in these two trials.

Methods: Duration of OR and CB was calculated from the date of randomisation until disease progression and percentages were calculated using the total number of patients per treatment group as the denominator (fulvestrant n=428; anastrozole n=423).

Results: A total of 186 patients gained CB with fulvestrant treatment (CR: n=20; PR: n=62; SD ⩾24 weeks: n=104) compared with 173 patients receiving anastrozole (CR: n=11; PR: n=59; SD ⩾24 weeks: n=103). Table 1 shows the proportion of patients with OR or CB in these studies who maintained their response ⩾1 year.

	Fulvestrant 250mg [n=428] (%)	Anastrozole 1mg [n=423] (%)
Total number of patients with OR	82 (19.2)	70 (16.5)
Number of patients with OR ⩾1 yr	43 (10.0)	30 (7.1)
Total number of patients with CB	186 (43.5)	173 (40.9)
Number of patients with CB ⩾1 yr	82 (19.2)	59 (13.9)

OR, objective response; CB, clinical benefit.

A greater proportion of patients on fulvestrant achieved OR and CB for ⩾1 year, these data being supportive of previously reported increased median DOR observed with fulvestrant in these trials.

Conclusion: Fulvestrant is as effective as anastrozole in terms of all major efficacy endpoints evaluated and may have advantages with respect to proportion of patients with prolonged DOR.

282 POSTER

Breast cancer with synchronous metastases: trends in survival over a 14-year period

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Purpose: Although new drugs have been approved during the 1990s for the treatment of metastatic breast cancer, it is not clear whether or not their use has changed the outcome of patients in daily practice. This study sought to determine whether survival has improved over time for breast cancer patients who had metastases at diagnosis.

Methods: 724 patients have been treated in 3 French Cancer centers for an initially metastatic breast cancer between 1987 and 2000. 343 have been diagnosed between 1987 and 1993, and 381 have been diagnosed between 1994 and 2000. Tumor characteristics, treatments and outcome of these patients were compared by χ^2 test, log rank test and Cox regression analysis.

Results: Characteristics were not different between the patients diagnosed between 1987–93 and those diagnosed between 1994–2000. Ten percent of patients treated between 1987 and 1994, and 58% of patients treated between 1994 and 2000 have received either a taxane or a new aromatase inhibitor. The 3 year overall survival rates were 27% for patients treated between 1987–1993 and 44% for patients treated between 1994–2000 (p<0.001). The treatment period (1994–2000 versus 1987–1993) was a prognostic factor in multivariate analysis (relative risk: 0.6, p<0.001).

Conclusion: The survival of breast cancer patients presenting with metastases at diagnosis has improved over the time. This study highly suggests that this improvement is related to treatment.

283 POSTER

Intravenous and oral ibandronate reduce the risk of skeletal-related events (SREs) in patients with breast cancer and bone metastases

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Background: Ibandronate is a highly potent aminobisphosphonate that has recently been approved in Europe for the treatment of metastatic bone disease. Phase III clinical trials have investigated the impact of intravenous and oral ibandronate on the occurrence of SREs in women diagnosed with breast cancer and bone metastases.

Methods: Three multicenter, randomized, double-blind, placebo-controlled trials were conducted. In a trial of intravenous ibandronate, a 6 mg dose (n=154) was compared with placebo (n=158) infused over 1–2 hours every 3–4 weeks. In two trials of oral ibandronate, a 50 mg daily dose (n=287) was compared with placebo (n=277). Data from the oral trials were pooled for analysis, as pre-specified in the study protocols. The primary efficacy endpoint was the Skeletal Morbidity Period Rate (SMPR), defined as the number of 12-week periods with new bone complications. Secondary analysis of SREs was conducted using a multivariate Poisson regression model. A post-hoc analysis using the Andersen-Gill method (time to multiple SREs) was also performed, as used to assess SREs in a 2-year trial of zoledronic acid in patients with metastatic bone disease [1].

Results: Mean SMPR was significantly reduced with ibandronate (6 mg dose, 1.19 versus 1.45 with placebo, p=0.004; 50 mg dose, 0.95 versus 1.18 with placebo, p=0.004). The multivariate Poisson regression analysis demonstrated that intravenous ibandronate 6 mg led to a statistically significant 40% reduction in the risk of SREs compared with placebo (RR 0.60, 95% CI = 0.43, 0.85; p=0.0033). The effect of oral ibandronate 50 mg on the risk of SREs was similar (38% reduction versus placebo, RR 0.62, 95% CI =0.48, 0.79; p<0.0001). The Andersen-Gill analysis showed a 29% reduction in SREs for intravenous ibandronate (RR 0.71, p=0.018) and a 35–42% reduction for oral ibandronate (p<0.005) compared with placebo.

Conclusions: In patients with metastatic breast cancer, intravenous ibandronate 6 mg and oral ibandronate 50 mg similarly reduced the occurrence of SREs. The risk reductions reported with intravenous and oral ibandronate for the prevention of bone events appear to be comparable to zoledronic acid [1], warranting further investigation in comparative studies. As an effective alternative to intravenous bisphosphonates, oral ibandronate offers the choice of convenient at-home dosing to eliminate time-consuming hospital visits for bisphosphonate therapy.

References

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284 POSTER

Longitudinal changes in serum her-2/neu oncoprotein levels in trastuzumab-treated metastatic breast cancer patients

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Background. To evaluate longitudinal variations of serum HER-2/neu extracellular domain (sHER-2) in metastatic breast cancer patients receiving combined trastuzumab treatment.

Patients and methods. 33 patients were monitored by serial sHER-2 ELISA (Oncogene Science) before and during treatment. Results were compared to time to progression (TTP) and survival from treatment initiation. Non parametric statistical tests were used.

Results. Median sHER-2 before 1st injection was 41.37 ng/ml (range 7.54–1597.00 ng/ml, n=32). Mean sHER-2 levels differed significantly between responders (n=20) and non responders (n=13) (P<0.0001). Median TTP (266 days, range 35–1000 days) was unrelated to clinico-biological variables at diagnostic or number and site of metastases before trastuzumab-based treatment. Patients with sHER-2 levels ⩽30 ng/ml

(n=14) before 1st injection had a significantly longer TTP than the opposite group (n=18) (P=0.0346) and sHER-2 levels were of prognostic value for overall survival from 1st injection (P=0.0150).

Conclusions. Our results show that monitoring serum HER-2/*neu* levels during metastatic breast cancer can provide a real time assessment of a woman's HER-2/*neu* status and can provide important information for making therapeutic decisions.

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Thursday, 18 March 2004

POSTERS

Locally advanced and recurrent disease

285 POSTER

Salient characteristics of infiltrating ductal carcinoma and invasive lobular carcinoma of the breast

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Background: The roles of breast conservation versus radical surgery in the breast carcinoma treatment remain unclear. The aim of this study was to compare local recurrence, 5-year survival, and incidence of contralateral breast cancer in women with invasive lobular carcinoma to that in women with infiltrating ductal carcinoma.

Methods: Women with infiltrating ductal carcinoma (IDC) and invasive lobular breast carcinoma (ILC) were diagnosed and treated in Surgical clinic Nis between 1987 to 1995. The women were divided into groups based on their histology and treatment (breast conservation or modified radical mastectomy). The incidences of contralateral breast cancer, local recurrence, and 5-year survival were compared within each histologic group and treatment category.

Results: Invasive lobular or ductal breast carcinoma were diagnosed in 2078 women. Invasive lobular cancer had 135 (6.49%) and 1557 (74.92%) had infiltrating ductal carcinoma. The 5-year survival rates were 65% for ILC and 70% for IDC, respectively (p=0.5). The local recurrence rates were 2.8% and 4.3% for ILC treated with lumpectomy and axillary nodal dissection (LAND) and modified radical mastectomy (MRM), respectively, which were not significantly different from that obtained with IDC (LAND=2.4%, MRM=1.9%). The incidence of contralateral breast cancer during the observe period was 6.6% and 6.2% for ILC and IDC.

Conclusions: Invasive lobular carcinoma and infiltrating ductal carcinoma can be safely treated with breast conservation with no difference in local recurrence or survival. In the absence of a suspicious finding on clinical or radiologic examination, routine contralateral breast intervention is not recommended.

286 POSTER

Conservative local treatment versus mastectomy after induction chemotherapy in locally advanced breast cancer (LAMANOMA, EORTC 10974/22002). Why this study failed?

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Introduction: It is currently generally accepted that treatment of locally advanced breast cancer (LABC) should be multidisciplinary and that primary chemotherapy results in high response rates and improved locoregional control. However, the precise balance between radiotherapy and surgery in achieving optimal loco-regional control remains uncertain.

Objectives and progress of the trial: The main objective of the EORTC 10974/22002 phase III study was to show that conservative local treatment (exclusive radiotherapy or tumorectomy followed or preceded by radiotherapy) is not inferior to mastectomy plus postoperative radiotherapy in terms of overall survival (primary endpoint), time to loco-regional failure and quality of life (secondary endpoints) in patients after primary chemotherapy.

The study was opened in October 2001. Initially 47 centers from 21 countries representing 4 cooperative groups declared participation. Estimated number of patients per year was between 499 and 539. Seventeen centers were found ineligible due to various reasons, leaving 30 centers. In contrast to initial estimates, the trial enrolled only 23 patients in 21 months. Our aim was to clarify this discrepancy.

Methods: Thirty institutions that initially declared participation were sent a questionnaire including 20 specific questions, of which 10 inquired about the causes of low patient accrual (more than one answer was allowed) and 10 about competing studies and standard therapeutic strategy used in a center in LABC.

Results: The number of returned questionnaires was 25 (83%). The answers were: standing by current therapeutic strategy (7 centers), most frequently (6 centers) depending on response to primary chemotherapy, the lack of consensus on participation in a local team (6), large proportion of patient refusals (5), ethical and/or logistical problems (5), too few patients with LABC (4), another study in LABC (1) and other causes (9).

Conclusions: No dominant reason of this study failure was detected. To decrease the risk of overestimation of the number of patients in future EORTC studies, interested centers will be asked to answer a detailed questionnaire evaluating their feasibility and accrual potential.

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Immediate breast reconstruction in stage III breast cancer patients

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Purposes of this paper: to evaluate safety of primary breast reconstruction and to assess the extent to which the reconstruction operation is consistent with oncological intervention itself, with radiation therapy and chemotherapy.

Material and Methods. The analysis includes the results of treatment 33 patients with stage III breast cancer (9 at IIIa and 24 at IIIb) on whom, after effective chemotherapy, a modified radical mastectomy was performed with immediate reconstruction. TRAM flap was used in 28 patients, an endoprosthesis using a flap from the latissimus dorsi muscle in 4 patients, and an expander in one patient. Radiation therapy was given with cumulative focal dose 40–60 Gy pre- or post-operatively, and adjuvant chemotherapy and endocrine therapy were also employed.

Results: Local recurrence was seen in 3 patients (10%). Three-year disease free survival is 53±12%, overall survival is 75±11%. Estimated indicators of five-year survival are disease free – 43±21%, overall – 63±14%. Data for five-year results in stage III breast cancer patients, treated without breast reconstruction, from our Center are identical. We have not reviewed serious complications; TRAM flap has a high tolerance to radiation therapy.

Our preliminary results indicate that immediate breast reconstruction in stage III breast cancer patients do not cause progression of the disease. Pre-operative chemotherapy, radiation therapy, and adjuvant chemotherapy and endocrine therapy remain important components of effective treatment. Immediate breast reconstruction using a TRAM flap is entirely consistent with these components.

Thursday, 18 March 2004 16:00–17:15

PROFFERED PAPERS

Side effects of treatment

288 ORAL

A randomised trial of the effect of quilting Latissimus Dorsi flap donor site on seroma formation

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Introduction: Donor site seroma following Latissimus Dorsi (LD) Flap harvesting is common, affecting up to 60% of patients. Closure of the dead space of the LD donor site is reported to significantly decrease the incidence of seroma (56% vs 0% [1]). We present the preliminary results of an RCT designed to investigate the effect of this technique following immediate breast reconstruction with an LD flap.

Methods: Consecutive patients undergoing skin-sparing mastectomy (SSM) and immediate LD flap reconstruction since February 2002 were entered into the study. Patients were randomised to routine wound closure (Control group) or closure of the dead space using absorbable 2/0 vicryl quilting sutures at 3–4 cm intervals (Quilting group). Informed consent was obtained and all patients were blinded to the closure performed. All participants had two Exudrains inserted in the donor site and a breast and axillary drain as appropriate. Volume of postoperative wound drainage and incidence and volume of symptomatic seroma were recorded.

Results: Forty patients have been entered into the study with complete data available on 38 patients (19 patients in each group). The volume of