(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.

287 POSTER

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

postoperative drainage from the back drains was significantly less in the quilted group (Median: 718 ml vs 1144 ml; P=0.016). Symptomatic seromas were drained in 95% (19/20) and 72% (13/18), respectively of the control and quilting patients (P>0.05). However, there was a significant decrease in seroma volume (Median: 72 ml vs 255 ml; P=0.024) and frequency of seroma aspiration (Median number of times: 1 vs 3) for patients in the quilting group (P=0.026). The quilting sutures did not lead to an increase in postoperative complications, or morbidity.

Conclusion: The study is ongoing and our preliminary analysis and results confirm the findings of the previous non-randomised trial and demonstrate the value of quilting the LD donor site. The technique is simple and reliable and we believe that it has a role in reducing the impact of postoperative seroma formation.

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289 ORAL

Effect of anastrozole on bone mineral density and bone fractures: results from the 'Arimidex' (anastrozole), Tamoxifen, Alone or in Combination (ATAC) trial

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Background: Low oestradiol levels in women are associated with decreased bone mineral density (BMD) and increased fracture risk. Aromatase inhibitors, used to treat breast cancer, reduce oestrogen levels in postmenopausal (PM) women. The ATAC trial is a randomised, double-blind trial of 9366 PM women with early breast cancer. Patients received anastrozole (A) (1 mg/day), tamoxifen (T) (20 mg/day) or a combination of the two (C). Bone fractures, a more clinically relevant endpoint than BMD, were investigated in the main ATAC trial. ATAC also includes a BMD sub-protocol. Here we report BMD results after 2 years of therapy and fracture rates over time.

Materials and Methods: The effects of A, T and C on BMD in a subset of 308 women from the ATAC trial were measured by dual energy X-ray absorptiometry (DXA) at the lumbar spine (LS) and total hip (TH). Fracture incidence was assessed every 6 months (mths) up to 48 mths of treatment in the overall study population.

Results: Estimated % changes (95% confidence interval (CI)) from baseline in LS- and TH-BMD, following an ANOVA on log-transformed data, after 1 and 2 years of therapy are shown in Table 1. At 1 and 2 years, A was associated with bone loss at the spine and hip and T with an increase in BMD, the differences between A and T being statistically significant. The rate of bone loss with A was approximately constant over 1 and 2 years. Changes from baseline in LS- or TH-BMD (1 and 2 years) were not significantly different between T and C. The absolute T-score change (median) from baseline at 2 years for LS-BMD was −0.36 (−1.3–0.2) for A, 0.18 (−0.8–0.8) for T and 0.11 (−0.7–1.1) for C; and for TH-BMD was −0.30 (−1.1–0.5) for A, 0.09 (−0.7–0.9) for T and 0.06 (−0.4–0.5) for C.

Table 1.

		LS-BMD		TH-BMD	
		Year 1	Year 2	Year 1	Year 2
A	%	−2.6	−4.0	−1.7	−3.2
	95% CI	−3.3 to −1.8	−5.0 to −3.0	−2.3 to −1.0	−4.1 to −2.4
	n	71	58	71	58
T	%	1.2	1.9	0.8	1.2
	95% CI	0.4 to 2.0	0.9 to 2.9	0.1 to 1.6	0.3 to 2.0
	n	69	64	68	63
C	%	0.1	0.8	0.8	1.1
	95% CI	−0.7 to 1.0	−0.3 to 1.9	0.0 to 1.5	0.1 to 2.1
n	64	51	62	48	

At a median duration of therapy of 31 mths fracture incidence was 5.9% and 3.7% for A and T, respectively (relative risk [RR] A/T 1.59); following a safety update (median duration of therapy 37 mths) RR for fractures was very similar (1.60). Six-monthly fracture rates remained relatively stable for both A and T. After 24 mths, the 6-monthly fracture rates seen with A did not appear to increase over time with further treatment. Overall fractures of hip + spine + wrist showed similar patterns.

Conclusions: Therapy with A continues to be associated with a modest loss in BMD, while T was associated with a small increase in BMD at 2 years (due to its bone-sparing properties). The more clinically relevant and mature fracture data show that after an initial increase, relative risk of fracture has not increased further over time with A. Given the efficacy and numerous tolerability benefits of A compared with T, the overall risk:benefit favours A in early breast cancer therapy.

290 ORAL

Anastrozole has a protective effect on the endometrium: data from the ATAC ('Arimidex', Tamoxifen, Alone or in Combination) trial

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Background: Recent safety data from the ATAC trial have for the first time allowed a direct comparison of the endometrial effects of the aromatase inhibitor anastrozole (AN) with tamoxifen (TAM) in postmenopausal women. The side effects of tamoxifen on the endometrium are well known, and anastrozole showed clear benefits with respect to reduced incidence of endometrial cancer (EC) (0.1% vs 0.5% for AN vs TAM, p=0.007) [1]. It was, therefore, of interest to compare the EC incidence rates seen with anastrozole in the ATAC trial with those of an age-matched standard population, to determine whether or not anastrozole provides a protective effect relative to norm.

Material and Methods: In recognition of regional differences, age-specific EC rates (per 1000 patient years) were obtained for the USA from US SEER (Surveillance, Epidemiology and End Results) data (previously adjusted for the prevalence of hysterectomy [2]), and for Europe from the European cancer (EUCAN) registry [3], which were then adjusted for prevalence of hysterectomy [4]. Expected incidence of EC in each age-specific group from the ATAC trial (North American and European patients) and their duration of follow-up was calculated and compared with the observed incidence. From these a Standard Incidence Rate (SIR) was calculated (Table 1). ATAC data from Argentina, Australia, New Zealand and South Africa (4.3% of patients) were omitted from calculations as age-specific EC rates could not be established.

Results:

Table 1

Treatment	Observed incidence of EC (~5300 yrs patients)	Expected incidence of EC	SIR (95% confidence interval)
Anastrozole	3	4.14	0.73 (0.15–2.12)
Tamoxifen	11	4.10	2.68 (1.34–4.80)
Combination	5	4.10	1.22 (0.40–2.85)

Conclusions: EC rates with anastrozole were lower than the rates expected in a normal age-matched population. In agreement with previous findings, EC rates observed with tamoxifen were clearly higher than expected rates. These data indicate a probable protective effect of anastrozole versus endometrial cancer development, and support the initiation of randomized trials to assess the effectiveness of anastrozole as a treatment for EC.

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291 ORAL

Cardiovascular mortality following breast cancer treatment

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We studied mortality from cardiovascular disease (CVD) in a group of 7600 patients who were treated in the NKI and the DDHK for early stage breast cancer between 1970 and 1987. In data collection, specific attention was given to the radiation fields used. In the analysis, we compared CVD mortality not only between irradiated and non-irradiated patients, but also between the study population and the general female population. For 92% of the patients medical status was complete up to at least January 1998. So far, we evaluated the patient group treated between 1970 and 1981 (n=3900). Median follow-up time was 12.6 years; for 34% of the patients follow-up time was longer than 20 years. Compared to the general female population, the number of cardiovascular deaths in the study population was within the range of normal expectancy. However, when we analyzed