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.

References

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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

by treatment modality, we found a 2.2 fold increase for irradiated patients (95% CI: 1.4–3.6) compared to non-irradiated patients. For non-irradiated patients, cardiovascular mortality was significantly decreased (SMR=0.5; 95% CI: 0.3–0.8) in comparison to the general population, indicating that the risk profile for breast cancer may be protective against CVD. A healthier life style after breast cancer may also play a role. The radiation-related risk increased especially after more than 10 years follow-up, and even more for patients treated before age 45 (SMR=2.6; 95% CI: 1.4–4.5). Analysis by laterality showed for the internal mammary chain field similarly increased CVD mortality for left and right side (SMR=2.1; 95% CI: 1.2–3.7) against no RT; for the chest wall field, irradiation on the left side revealed a significantly increased CVD mortality against no radiation (SMR=2.5; 95% CI: 1.1–6.4); compared to radiation to the right chest wall the risk was 1.6 fold increased, though not significantly. During the EORTC BCC4 conference results will be presented for the entire cohort of 7600 patients, including 1900 patients treated by breast conserving therapy.

292 ORAL

Cardiac safety analysis of the first stage of NSABP B-31, a randomized trial comparing the safety and efficacy of doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) to that of AC followed by paclitaxel plus trastuzumab (TH) in patients (pts) with operable, node-positive (N+), HER-2 overexpressing breast cancer (HER2+BC)

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Background: NSABP B-31 is a randomized Phase III trial comparing the safety and efficacy of AC followed by T with AC followed by TH, in the adjuvant treatment of pts with operable, N+, HER2+BC. The pivotal trial of H in pts with metastatic breast cancer demonstrated that concurrent H improved efficacy of chemotherapy (increased response rate and overall survival), but resulted in an increased frequency of congestive heart failure (CHF). To minimize risk of cardiotoxicity for women participating in B-31, a program for close monitoring of protocol defined cardiac events (CE) with planned, formal interim safety analyses was incorporated into the trial.

Methods: Women with N+, HER2+BC, free of cardiac disease, and with normal left ventricular ejection fraction (LVEF) assessed by MUGA scan were eligible. In both arms, MUGA scans were repeated post-AC, 6, 9 and 18 months following randomization. Initiation of H required post-AC LVEF $\geqslant$ the lower limit of normal and a $\leqslant$15 point percentage drop from baseline. If pts developed symptoms or findings of possible CHF, H was held if being given, MUGA was obtained and pts underwent physician-directed evaluation. Copies of reports of MUGA scans and evaluation records were received centrally, blinded as to specifics of cancer therapy and forwarded for review by members of an external Cardiac Advisory Panel, who determined if protocol criteria for CE had been met.

Results of 6 and 9 month MUGA scans were used to guide H therapy, and strict criteria for temporarily holding or discontinuing H based on MUGA results in asymptomatic pts were incorporated into the protocol.

Formal comparisons of the frequency of CE in the 2 arms were planned after 200, 600 and 1000 evaluable pts began post-AC therapy and had been followed for an additional 6 months. Early stopping rules were specified in the protocol to protect against the possibility of excessive cardiotoxicity. Results of the 1st and 2nd interim analyses were reviewed by the Data Monitoring Committee, and accrual was allowed to continue.

Results: The final planned cardiac safety analysis is being completed and results will be available for presentation in 3/04.

293 POSTER HIGHLIGHT

Locally placed catheter with anesthesia pump after mastectomy significantly reduces postoperative opioid medication with up to 68.4%

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Objective: Postoperative pain management is increasingly important especially in cancer patients. We evaluated the use of a temporarily placed thin catheter with continuously application of local anesthetic postoperatively (ON~Q by I-Flow-Corp., Lake Forrest, CA, USA) vs. without regarding postoperative need for opioids until discharge from hospital.

Method: Retrospective analysis from 1/97–12/01 of all mastectomies (n=49) at Fayette Medical Center, Alabama, USA, regarding use of postoperative pain medication with ON~Q pain management pump with continuously Sensorcaine 0.25% application for approx. 72 h (n=22) vs. control group without pain pump (n=27). Different pain medication was standardized in dose equivalents (DE) and statistically analyzed.

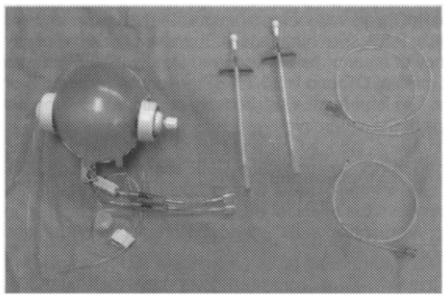

Fig. 1. ON~Q continuous local anesthetic pump with y-shaped catheter.

Results: Patient statistics in the ON~Q vs. control group was age 66.9 vs. 66.7 years, sex 22 female vs. 26 female and 1 male, weight 147 vs. 158 pounds. The procedures performed were modified radical mastectomy 17 vs. 24, simple mastectomy 3 vs. 3 and simple mastectomy with nodes 2 vs. 0. Patients with no need of postoperative pain medication were 18.2% vs. 3.7% ($p<0.001$), no use of pain medication after postoperative day 1 68% vs. 11% ($p<0.001$), total opioid usage in dose equivalents 1.25 vs. 3.36 DE (−62.8%) ($p=0.016$), opioid usage day 1 0.645 vs. 1.82 DE (−64.6%) ($p=0.016$), opioid usage day 2 0.236 vs. 0.748 DE (−68.4%) ($p=0.011$), length of stay 2.35 vs. 2.93 days ($p=0.13$), and postoperative stay in PACU 38.4 vs. 43.3 min ($p=0.13$).

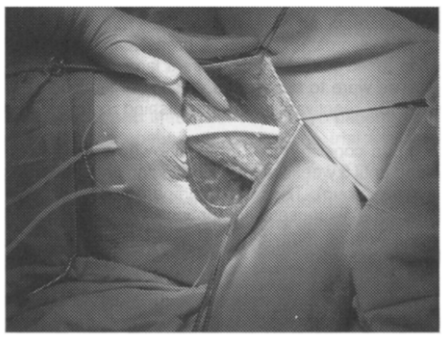

Fig. 2. Intraoperative placement of ON~Q pain pump after mastectomy.

Conclusion: Use of an ON~Q pain management pump could significantly reduce or even eliminate postoperative need for analgesics and reduce the absolute amount of opioid DE used postoperatively up to 68.4%. Length of PACU time (−10.7%) and hospital stay (−19.7%) were also reduced with use of the ON~Q. OR time for placement of catheter and pump is only slightly increased, but no complication occurred and patient's feedback is excellent.

294 POSTER HIGHLIGHT

Factors influencing the amenorrhea caused by anthracycline chemotherapy regimens in premenopausal breast cancer patients

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Amenorrhea secondary to the non-anthracycline chemotherapy (CT) regimens in premenopausal breast cancer patients has been well defined. Less information exists on an anthracycline-induced amenorrhea.

In the aim to get insight into the anthracycline-indiced amenorrhea, the hospital records of 152 premenopausal early breast cancer patients were checked. All patients have been treated with anthracycline-based chemotherapy (FAC or FEC) within five clinical studies: two international multicentric randomized, and three institutional studies. They received 4 cycles of FEC60, either pre- or postoperatively (n=31), or 6–10 cycles of FAC50, either postoperatively (n=102), or pre- and postoperatively (n=19). In total, amenorrhea occurred in 47%, and dismenorrhea in additional 9% pts. The frequency of amenorrhea was related strongly to the age of pts: in the age groups <=35, 36–40, 41–45 and >45 it reached 9%, 24%, 59% and 80.5%, respectively. In the same time the frequency of dismenorrhea decreased with age from 15% to 5%. The beginning of amenorrhea