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.

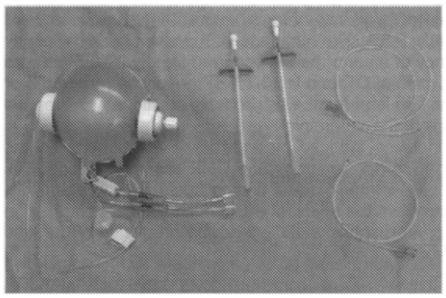

Fig. 1. ON~Q continuous local anesthetic pump with y-shaped catheter.

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 ($p=0.13$).

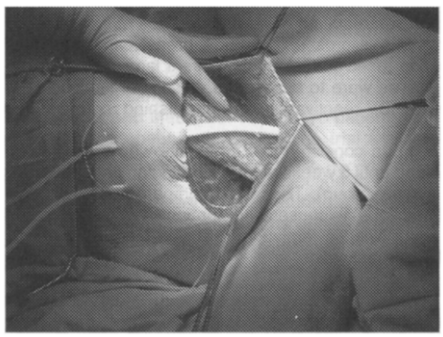

Fig. 2. Intraoperative placement of ON~Q pain pump after mastectomy.

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

during the first three cycles of CT was significantly more frequent in older premenopausal BC pts, than in younger ones. Finally, amenorrhea was permanent, according to the 4 age groups, in 3%, 3.5%, 51% and 73% pts, respectively, while the frequency of temporary amenorrhea decreased with the age from 15% to 9.8%. The number of CT cycles also significantly influenced the frequency of amenorrhea: it occurred in only 22.5% pts who received less than 6 cycles of CT, and in 53.7% of those who received 6 or more than 6 CT cycles. The later result was probably additionally influenced by the cumulative dose of the anthracycline.

In conclusion, amenorrhea induced by anthracycline regimens seems to be less frequent than in non-anthracycline CMF-based regimens. It is rather rare in very young women. These finding could be important in a multiple clinical aspects: from the adjuvant endocrine treatment planning in premenopausal endocrine-responsive BC pts to the prediction of the loss of fertility in BC survivors.

295 POSTER HIGHLIGHT

Lamivudine for the prevention of hepatitis B virus reactivation in hbsag seropositive cancer patients undergoing cytotoxic chemotherapy

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Background: Breast cancer is a rapidly increasing problem in many developing countries and cytotoxic chemotherapy is now an integral part of its management. In several developing countries, the carriage of hepatitis B virus (HBV) in cancer patients may be as high as 12% and such patients are at risk of developing HBV reactivation during chemotherapy, which is a well-described complication resulting in varying degrees of liver damage that may lead to death. In this prospective study, breast cancer patients with chronic HBV infection received the antiviral agent lamivudine prior to chemotherapy, the objectives were to assess the efficacy of lamivudine in reducing the incidence of HBV reactivation, and diminishing morbidity and mortality during chemotherapy.

Methods: The study group consisted of 27 patients who were treated with lamivudine prior to and until 8 weeks after discontinuing chemotherapy (the 'prophylactic lamivudine' group). They were compared with historical controls which consisted of 41 consecutive patients who underwent chemotherapy without prophylactic lamivudine. The outcomes, in terms of the incidence of HBV reactivation and clinical consequences, were compared.

Results: The 2 groups were comparable in most baseline-characteristics, although in the prophylactic lamivudine group, there were significantly more patients receiving anthracyclines (96% vs 51% in the controls, p<0.001). In the prophylactic lamivudine group, there was significantly less HBV reactivation (7% vs 41% in the controls, p=0.003), fewer incidences of hepatitis (11% vs 66%%, p<0.001) that were less severe (7% vs 15%, p=0.117), and less disruption of chemotherapy (26% vs 51%, p=0.02). There was no associated mortality in both groups.

Conclusions: Prophylactic lamivudine significantly reduced the incidence and morbidity of HBV reactivation in breast cancer patients undergoing chemotherapy.

296 POSTER HIGHLIGHT

Long-term safety of zoledronic acid for the treatment of patients with breast cancer and bone metastases

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Background: Zoledronic acid has demonstrated clinical benefit superior to that of pamidronate for the treatment of bone metastases in patients with breast cancer. Moreover, zoledronic acid can be administered via a more convenient 15-minute infusion. However, concerns have been raised regarding the renal safety profile of zoledronic acid. Herein, the renal safety profile of 4 mg zoledronic acid (via 15-minute infusion) is compared with that of 90 mg pamidronate (via 2-hour infusion).

Materials and methods: Patients were randomized to receive zoledronic acid or pamidronate every 3–4 weeks for up to 25 months in a multicenter, phase III trial. Data presented are from the stratified subset of 766 patients with breast cancer. A notable increase in serum creatinine was defined as an increase of ⩾0.5 mg/dL for patients with baseline serum creatinine ⩽1.4 mg/dL, an increase of ⩾1.0 mg/dL for patients with baseline serum creatinine > 1.4 mg/dL, or any increase ⩾2 times baseline value. These are sensitive and conservative criteria for determining elevated serum creatinine.

Results: A total of 454 patients completed the 13-month core phase, and 165 patients completed the 12-month extension phase. Baseline serum creatinine was similar between treatment groups, and approximately 95% of patients had normal serum creatinine (<1.4 mg/dL) at study entry. The renal safety profile of 4 mg zoledronic acid was comparable with that of 90 mg pamidronate at 25 months. Overall, 9.4% of patients treated with 4 mg zoledronic acid versus 6.5% of pamidronate-treated patients experienced notable increases in serum creatinine. However, Common Toxicity Criteria (CTC) grade 3 (>3.6 to ⩽7.2 mg/dL) or grade 4 (>7.2 mg/dL) serum creatinine was infrequent. One (0.5%) patient in the pamidronate group developed CTC grade 4 serum creatinine, whereas no patient treated with 4 mg zoledronic acid developed either grade 3 or 4 serum creatinine. Kaplan-Meier analysis of time to first episode of notable serum creatinine increase also showed that 4 mg zoledronic acid was associated with a slightly increased risk of elevated serum creatinine compared with pamidronate, which was not statistically significant (hazard ratio = 1.401; *P*=0.371).

Conclusions: With long-term use (up to 25 months), 4 mg zoledronic acid (via 15-minute infusion) has a renal safety profile comparable with 90 mg pamidronate (via 2-hour infusion) and other IV bisphosphonates.

297 POSTER HIGHLIGHT

Anastrozole therapy and lipid profile: an update

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Background: Endocrine therapy of breast cancer is aimed at inhibiting estrogen-dependent proliferation of cancer cells. Newly developed aromatase inhibitors suppress estrogens synthesis to undetectable levels. The concern exists they might increase the risk of hypoestrogenemia-related disorders, such as disturbances in lipid profile. The current study updates at the prolonged observation our previous results on effects of anastrozole – III generation aromatase inhibitor – on lipid metabolism in tamoxifen pretreated breast cancer patients.

Material and Methods: the study included 51 postmenopausal breast cancer women (median age: 67 years, range: 45–87), who were converted to anastrozole after tamoxifen treatment (median duration of therapy: 76 weeks, range: 14–193). Concentrations of basic blood lipids and body mass index values (BMI = weight in kilograms divided by squared height in meters) were measured at baseline and three times afterwards: at minimum 24 (median: 26, range: 24–33; N=51), 60 (median: 63, range: 60–70; N=51) and 130 (median: 134, range: 130–147; N=25) weeks of anastrozole administration.

Results: there was no statistically significant change over time in basic lipid parameters, that included total- (p=0.51), LDL- (p=0.61), and HDL-cholesterol (p=0.43), triglycerides (p=0.78), the atherogenic risk ratios: total/HDL-cholesterol (p=0.56) and LDL/HDL-cholesterol (p=0.33) as well as in mean BMI values (p=0.93).

Conclusion: anastrozole used in sequence to tamoxifen for approximately 3 years does not affect lipid profile and BMI values of breast cancer patients.

298 POSTER

Safety and convenience of the 15-minute infusion of zoledronic acid

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Background: Highly potent, new-generation bisphosphonates with clinical activity at extremely low molar doses can be administered using short infusion time without compromising renal safety. Among intravenous (IV) bisphosphonates approved for the treatment of hypercalcemia of malignancy (HCM) or bone metastases in patients with breast cancer, zoledronic acid has the shortest recommended infusion time (i.e., 15 min) compared with 1–2 hrs for other agents. Moreover, zoledronic acid has demonstrated clinical benefit superior or equivalent to that of pamidronate in patients with HCM or breast cancer and bone metastases.

Materials and Methods: The safety profile of zoledronic acid (4 mg via 15-min infusion) was compared with that of 90 mg pamidronate (via 2–hr infusion) based on randomized, comparative trials. Comparisons with other bisphosphonates are based on published reports.

Results: Comparative trials of 4 mg zoledronic acid versus 90 mg pamidronate in patients with HCM (N=287) and breast cancer patients with bone metastases (n=1130) have shown that zoledronic acid has an overall and renal safety profile comparable with pamidronate. Commonly reported adverse events – including fever, nausea, fatigue, constipation, and anemia – occurred in a similar proportion of patients