and evaluation of disease free survivals interval and overall survival rates require further investigation and longer follow-up.

51 POSTER

Sequential doxorubicine (DOX) and docetaxel (DOC) as neoadjuvant chemotherapy in locally advanced breast cancer (LABC): A pilot study

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DOX is the best single agent for treatment of breast cancer and plays an important role for adjuvant treatment. Many observations showed that taxanes, especially DOC, still could remain active in DOX resistant cases. It is therefore logical to try to combine these 2 agents. Instead of giving them simultaneously at reduced dosis, we gave full dosage of both sequentially to patients with LABC. Between 06/97 and 12/97, 8 patients (stage IIIb), received first 2 cycles of DOX 75 mg/m^2 (q3w), followed by 2 cycles DOC 100 mg/m^2 (1 hour infusion, q3w). Clinical, biochemical and radiological evaluation of response were performed after the 2nd and 4th cycle. Thereafter, loco-regional treatment was administered and systemic treatment was planned in function of observed response. All patients had objective regression, according to the UICC criteria (2CR, 6PR). In 1 pt. we found no invasive tumor after surgery, only DCIS. Evaluation of early response after 2 cycles proved very difficult because of poor sensitivity and specificity of clinical examination and mammography. There were no serious complications. Dose reduction during 2nd course of DOC (75%) was only necessary because of mucositis (1) and myalgia (1). We conclude that a high response rate can be achieved within 12 weeks with the proposed regimen. Because of the poor reliability of clinical and radiological evaluation, new techniques like MRI or PET-scan deserve consideration. This regimen could also be compared to others for inducing response in LABC. Further research should also focus on optimizing loco-regional and maintenance systemic treatment.

52 POSTER

Neoadjuvant hormonal therapy in locally advanced breast cancer

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Background: Management of locally advanced breast cancer (LABC) it's not consensual. In post-menopausal women, particularly in the elderly, primary hormonal therapy (HT) is an option, to convert an inoperable tumour into operable.

Objective: To evaluate the influence of a neoadjuvant HT protocol in local control of the disease (tumour downstaging and HR status).

Methods: We used a prospective non-randomised study between Jan/93 and May/94, which included 28 pts. An initial evaluation was made through clinical examination, ultrasonography and incisional biopsy with HR determination. The neoadjuvant HT consisted in a minimum of two months therapy with Tamoxifen (20 mg/day). In all pts, a clinical and/or ultrasonographic revaluation was made. A radical mastectomy was then proposed, with a new HR determination. The treatment was completed with adjuvant Radiotherapy and HT. The median Follow-up was 50 months (range: 11–62).

Results: The median age was 72 years (range: 52–86). *Initial evaluation*: Twenty-two (79%) pts were in stage III-B and six (21%) pts in stage III-A. In 27 pts, ductal invasive Ca was found and lobular invasive Ca in one. The ER were positive in 24 (86%) pts and PR n 18 (64%) pts. Ultrasonography was used to study tumour size and axillary lymph nodes. *Post-HT evaluation*: Clinical and/or ultrasonographic response was observed in 20 (71%) pts, with two complete remissions. No relevant side effects were found. *Postoperative evaluation*: Tumour downstaging occurred in 22 (79%) dts; in three other pts, there was a significant decrease in tumour size. HR status changed in 10 (36%) pts.

Conclusions: 1- Neoadjuvant HT can play an important role in LABC management, mainly in the elderly. 2- Tamoxifen had a good response rate (71%) and was well tolerated. 3- Correlation between clinical and pathologic responses occurred in 22 (79%) pts.

53 POSTER

Photodynamic therapy versus laser induced thermotherapy in the treatment of local recurrences and skin secondaries of breast cancer

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Aim: The effect of photodynamic therapy (PDT) and Laser induced thermotherapy (LITT) as palliative methods in otherwise pretreated patients on locoregional recurrences should be investigated.

Material and Methods: The PDT was currently performed on 6 women using the Photosan 3 (HPD) as a photosensitizer, the irradiation was performed with laser light at a wavelength of 630 nm 48 h, 72 h and 196 h after photosensitization. – In 10 women with locally advanced breast cancer and pretreatment with surgery (primary and secondary mastectomy, m. latiss. dorsi-flap), irradiation and chemotherapy, an interstitial laser application was performed percutaneously into the center of the diseased tissue. The laser used was a Nd:YAG laser with a wavelength of 1064 nm. Heat expansion was controlled digitally and monitored by ultrasound and colour coded duplex sonography (CCDS), respectively.

Results: All patients are scheduled for long-time follow-up. The initial results of PDT are promising. – LITT enabled the precise coagulation of the tumour without ulceration or destruction of the skin, although these areas had been pretreated by radiotherapy up to 60 Gy, before.

Conclusion: PDT and LITT are safe and minimal invasive methods for palliative treatment of subcutaneous local recurrences of breast cancer.

54 POSTER

Diagnostic problems of evaluating bone metastasis from breast cancer by proliferative activity: Comparison of findings between bone scintigraphy and MRI and their relationship to prognosis

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Purpose: Bone metastases from breast cancer are frequently observed, however, diagnosis and treatment are difficult in many cases. We evaluated the relationship between diagnosis of bone metastases of breast cancer and clinicopathological factors.

Methods: We enrolled 51 breast cancer patients with vertebral matastases diagnosed by plain radiography, bone scintigraphy or MRI. Diagnosis of bone metastases was classified into the following groups: the A group: those who showed similar findings in plain radiography, bone scintigraphy and MRI; the C group: those who showed no abnormalities in radiography or scintigraphy, and their lesions were diagnosed by MRI.

Results: Twenty-four of 51 patients were included in the A group, while 14 were included in the C group. Regarding the relationship with clinicopathological factors, a significant number of patients with ER-negative tumors demonstrating a high level of DNA polymerase α, short disease-free intervals (DFI) and metastases to other organs were included in the C group. Prognoses of patients were apparently poor in the C group.

Conclusion: Bone scintigraphy sufficiently reflects foci in patients with ER positive or low proliferative tumors, while false negative bone scintigraphy is likely in patients with ER negative or highly proliferative tumors. MRI was useful in diagnosing such patients. Therefore, consideration of malignancy such as proliferative activity and ER is thought to be necessary during postoperative follow-up of breast cancer patients.

55 POSTER

Changes in biochemical markers of bone turnover in breast cancer patients with bone metastases

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The understanding and the monitoring of metastatic bone disease remains unsatisfactory. this study we compared several markers of bone turnover in 25 breast cancer patients with bone metastases, aged 48–70 years. All patients were treated with pamidronate 60 mg i.v. every month in addition to standard endocrine or chemotherapy. Blood or urine measurements included total and bone alkaline phosphatase, osteocalcin (BGP), hydroxyproline, pyridinoline (Pyr), deoxypyridinoline (DPyr) and ICTP were performed baseline, 1, 3 and 6 months after starting therapy. The mean values

of alkaline phosphatase, Pyr, DPyr and ICTP were significantly increased in 7/25 (28%), 21/25 (84%), 22/25 (88%) and 17/25 (68%) patients respectively ($p < 0.001$). Therpy significant reduced Pyr (84.4 ± 12.3 vs. 32.5 ± 7.6 nmol/mmol creatinin) and DPyr (16.7 ± 7.1 vs. 9.4 ± 3.7 nmol/mmol creatinin). There were no changes in osteocalcin and hydroxyproline levels. These results indicate that sequential measurement of Pyr and DPyr can be used to monitoring the results of therapy of bone metastases.

56 POSTER

A combination therapy with mitomycin-C, etoposide, doxifluridine and medroxyprogesterone acetate as second-line therapy for advanced breast cancer

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Purpose: To determine whether there is a effective therapy for the patients with advanced breast cancer refractory to doxorubicin-containing chemotherapy, we performed combination therapy of mitomycin C, etoposide, doxifluridine and medroxyprogesterone acetate as second-line therapy.

Method: Patients with breast cancer who failed to the previous CAF therapy were designated as those refractory to CAF therapy. A total of 32 patients were included in this trial from January, 1989 through December 1995.

Results: Observed responses included 6patients (18.7%) with complete response (CR) and 7 (21.9%) with partial response. Two (50%) out of 4 patients who had bone pain due to bone metastasis noted pain relief. CR and PR were obtained in 4 out of 12 patients who had not responsed to the previous CAF therapy. While grade III myelosuppression was observed in 3 patients, pther adverse effect were minimal.

Conclusion: It is suggested that this combination therapy may be recommended for advanced breast cancer patients as a second-line therapy.

57 POSTER

Mastectomy in addition to chemotheraphy improves relapse free survival in women with localy advanced breast cancer

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Purpose: The mainstay of treatment for localy advanced breast cancer (LABC) is chemotherapy (CT). Additional mastectomy improves relapse free survival (RFS) and overall survival (OS) in women with LABC.

Methods: We analysed 135 women with LABC in period from 1992 to 1997. Among them, 84 patients with mean age 51, 25 (min 38, max 65) had undergone mastectomy and postoperative RT in addition to CT while 51 patients with mean age 57, 6 (min 44, max 74) were treated with CT and radical RT. Mean follow up period for both groups of patients was 23 months (min 6, max 48 months for group with mastectomy and min 10, max 40 months for group without mastectomy). In these two groups we studied RFS and OS according to age, nodal status and tumour size.

Results: In the operated group of women (84) mean time to progression (TTP) was 20 months (min 6, max 36) and in nonoperated group of women (51) mean TIP was 14, 3 months (min 6, max 24). 2 years RFS was 22% and OS was 48% for operated group, while for nonoperated group 2 years RFS was 1% and OS was 42%.

Conclusion: LABC represents disease stage with a very poor prognosis. Although there was no statisticaly significant difference in OS among two analysed groups of patients, there was statisticaly significant difference in RFS depending on prognostic factors previously mentioned.

58 POSTER

Improving results in the treatment of locally advanced T4 breast cancer

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Between 1990 and 1997 63 patients with T4 N1–3 M0 breast carcinoma were treated at our Institute. Storically, at first *from 1990 to 1995*, 43 patients aged from 36 to 71 years (median 51), PS 0–1, 20 premenopausal, with T4 breast carcinoma, following the tru-cut biopsy for the histology (31 infiltracting ductal, 8 infiltracting lobular, 4 mixed) and prognostic factors (ER15+/28−; PgR 12+/31−; 23G2, 20G3; Ki67 7+/36−) were treated with 3–5 cycles of primary standard chemotherapy (FEC 50, or HD-Epirubicin, or MMM). *Clinical response:* CR 1/43 (2.3%), PR > 50% 25/43 (58.1%), PR < 50% 15/43 (34.8%) and NC. 2/43 (4.6%). *Surgery* was performed in 41 pts (95.3%), 38 (88.3%) demolitive and 3 (7%) conservative. *Pathological response* was pTo 2/41 (4.8%), pT1 5/41 (12%), pT2 18/41 (44%), pT3 6/41 (14.6%) while 10 (24%) remained pT4. Lymphnodes were involved in 100% of cases, 1–3: 11 (27%); 4–10: 17 (41%), >10: 13 (32%). At median *Follow-up* of 57 months (27–93) the median DFS is 21 months (3–75) and OS 37 months (10–75). 33 pts (76.7%) relapsed and 10 (23.3%) are disease-free. 25 pts (58%) died and 18 (42%) are still alive. Relapses were directly proportional to the LN number (1–3: 64%; 4–10: 82%; >10: 85%), while survival inversely (64%, 35%, 31% respectively).

Afterwards *from 1996* we initiate a study to evaluate the effectiveness and the toxicity of a combination of Lonidamine (450 mg/die), CDDP (50 mg/mq), Epirubicin (100 mg/mq), Vinorelbine (25 mg/mq), day 1–21. Until now we treated 20 T4 pts in age from 39 to 68 years (median 50), 11 premenopausal, PS 0–1, 17 infiltracting ductal, 3 infiltracting lobular, ER11+/9−; PgR 7+/13−; 18G2, 2G3; Ki67 9+/11−. *Clinical response:* CR: 7/20 (35%); PR > 50%: 13/20 (65%). *Surgery* was feasible in 100% of 18 evaluable cases, 12 demolitive (67%) and 6 conservative (33%). *Pathological response:* pTo 2/18 (11%); pT1 5/18 (28%); pT2 8/18 (44%); pT3 1/18 (6%); pT4 2/18 (11%); pLN0: 4/18 (22%); pLN 1–3: 5/18 (28%); pLN 4–10: 6 (33%); pLN > 10: 3/18 (17%).

Conclusions: the L-PEV regimen is more active than the first that we used, in terms of global clinical response (100% vs 60%), clinical CR (35% vs 2.3%) and patholocical CR (11% vs 4.8%) of the primary and nodes (pLN0 22% vs 0%). Since in the our first trial relapses and survival were strictly correlated to the pathological status of LN, the high activity of L-PEV also at nodal level may better the outcome of these patients.

59 POSTER

Continuous infusion of adriamycin + cyclophosphamide + 5-fluorouracil in disseminated breast cancer

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Purpose: The aim of this study is to improve the treatment efficacy of the patients suffering from disseminated breast cancer by increasing the dose of chemodrags using a continuous infusion.

Methods: The program includes three chemotherapeutic agents: adriamycin in a dose of 20 mg/m2/24 hours, from 1 to 5 days i.v. as a 120-hour continuous infusion, 5-fluorouracil in a dose of 500 mg/m2 on the 1-st and the 8-th days i.v. and cyclophosphamide in a dose of 600 mg/m2 on the 1-st and the 8-th days i.v. Continuous infusion is performed through a catheter plased in v. subclavia. The treatment according to this program has been performing at Chemotherapy Department since 1995. A total of 21 women aged 38–64 have been treated. There were 6 women in premenopause, 15 patients in postmenopause. Performance status (ECOG) was 0–2. All the patients were histologically diagnosed as having breast cancer. The localization of metastases was the following: periferal lymphatic nodes – 14, lungs – 4, bones – 8, intracutaneous – 5. Each patient reseived 2 or more courses of chemotherapy. The total number of courses was 50.

Results: Complete regression was observed in 6 cases (28.6%), parcial regression in 10 (47.6%), no change 4 patients (19.0%), progression 1 case (4.8%). Complication included leukopenia. I–II gr.-20 courses, III–IV gr.-6 courses; anemia I–II gr.-4 courses, stomatitis I–II gr. 15 courses, III gr.-2 courses, nausea/vomiting I–II gr.-12 courses, III gr.-2 courses, alopecia – practically in all the patients.

Conclusion: The total effect of the program was considered to be rather high – 76.2%. Toxicity was acceptable. Long-term results are being studied.

60 POSTER

Sonomammography an objective tool for assessment of chemotherapeutic response in locally advanced breast cancer

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Purpose: Primary chemotheraphy in locally advanced breast cancer (LABC) produces objective clinical response. In a prospective study the role of sonomammography has been evaluated as a tool for monitoring the objective tumour response following primary chemotherapy.

Methods: Patients with LABC were treated with Primary Chemotherapy. Ultrasonography was done using 7.5 MHz probe before commencing each