

13.8%. LRR-rate with breast- and axillary surgery was 12.1% compared to 15.4% in the group treated with breast surgery only ( $p=0.76$ ). Disease free survival (DFS) was 48.7% vs. 39.5% and overall survival (OS) was 45.5% vs. 38.5% respectively.

**Conclusion:** Our results show no benefit from ALND in terms of locoregional recurrence rate, DFS or OS. However combining ALND with regional radiotherapy is associated with more morbidity.

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#### Chest wall radiation associated sarcomas are sensitive to reirradiation and hyperthermia

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**Background:** Radiation associated sarcomas occur in about 0.5 per thousand irradiated patients and are often angiosarcomas. They tend to bare an extremely poor prognosis and are believed to be radiation resistant. A series of nine radiation associated sarcomas of the chest wall is presented, treated by re-irradiation and hyperthermia in the Academic Medical Centre in Amsterdam.

**Patients and methods:** From 1984 to 2007 nine patients were referred. Eight women, one man, mean age 73 years (48–91). Mean interval from previous cancer (breast/Hodgkin's disease) was 75 months (19–132). Six had angiosarcoma, three not otherwise specified (NOS). One patient was metastasised at diagnosis and one was referred immediately after diagnosis, the others were referred after one (3 pts) two (2 pts) or three (1 pt) attempted resections or systemic treatment, with a mean interval since diagnosis of 5.5 months (3–16). One patient had no apparent tumour at referral and the remaining eight had a mean largest tumour size of 13 cm (1–25), usually an area of multiple nodules. Radiotherapy was applied to the tumour area plus a generous margin. One patient received 6 fractions of 2.5 Gy in 2 weeks, one received one fraction of 6 Gy (and refused further treatment). The other seven patients got 8 fractions of 4 Gy in 4 weeks, all with hyperthermia once weekly, aiming at 41–43°C for an hour.

**Results:** One patient stopped after one session, and was not evaluable for response. One had local and distant progression shortly after his treatment; one had minor regression; one a good partial remission and five a clinical complete remission. Three patients are alive without progression after 7, 15 and 39 months. One died of suicide two weeks after start of treatment, one of unknown cause (2 months) and four of metastatic sarcoma at 2, 4, 8 and 8 months respectively. Only one of the six responding patients developed a local recurrence before death.

**Conclusion:** It is difficult to draw conclusions from a small and heterogeneous patient cohort. Yet, with five complete remissions and one partial remission in 8 evaluable patients it is suggested that radiation associated sarcomas are sensitive to reirradiation plus hyperthermia, in contrast to what is often believed.

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#### Perioperative chemotherapy (CT) with induction sequential epirubicin (EPI) and docetaxel (DOC) followed by surgery and DOC or gemcitabine/vinorelbine (GEN) with radiotherapy for locally advanced breast cancer (LABC)

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**Background:** Anthracyclines (AC), Taxanes (TAX), Vinorelbine and Gemcitabine are among the most active cytotoxics in BC. The mature results of a multimodal treatment tailoring these drugs perioperatively in LABC are presented here.

**Patients and Treatments:** Stage III pts ECOG-PS <2 were eligible. A true-cut biopsy documentation had to be performed before the start of CT. Treatment consisted of 4 EPI (100 mg/m<sup>2</sup> D1q2w) followed by 3 DOC (100 mg/m<sup>2</sup> D1q3w); surgery 3–4 weeks from CT completion, followed by RT and CT according to response (PR/CR: DOC, NC/PD: GEN). Primary endpoints (a) response and conversion to operability/conservative surgery, (b) Time to Recurrence (TTR) and Overall Survival (OS).

**Results:** 56 women aged 32–75 (median 52 years), 24 IIIA and 32 IIIB were enrolled; 53 pts completed the entire program. Toxicity was acceptable; no treatment related death. Median RDI for all drugs was 100%. Efficacy: Clinical RR 71.4% (40pts); 33.9% cCR's. Pathological RR 67.8% (38pts); 21.4% pCR's. 33 (58.9%) and 19 (33.9%) radical and

conservative operations without increased morbidity. After a median follow-up of 62mo, median OS has not yet been reached while median TTR was 42 mo. TTR was favourably affected by path resp, RT and postop DOC ( $p=0.005$ ), while OS was longer in pts with clinical and pathological response, RT and postop DOC ( $p=0.038$ ). Preoperative CT seemed to be equally active throughout all subgroups according to histology, ER/PR and HER2 status.

**Conclusions:** The treatment program of the present study allowed for the completion of an effective therapy at the cost of acceptable toxicity. The vast majority of our patients completed the full program thanks to the type of tailoring sequential and postop CT and RT. The results of this study, conducted in the "pre-HER2 era" suggest a central role of CT for LABC and the value of eventually dose-dense, AC- and TAX-based CT in a large proportion of LABC pts, regardless of biological tumor profile. The integration of anti-HER2 and other biological therapies may further improve the longterm control of LABC.

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#### Local recurrence of breast cancer following mastectomy

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**Background:** Breast cancer is the most common cancer among Turkish women. Surgical treatment options for breast cancer include partial mastectomy with axillary dissection and radiation therapy or mastectomy. Mastectomy has long been the gold standard for treatment of breast cancer and is performed frequently in Turkey since it's first choice of our patints. Local recurrence after mastectomy depends on the initial extent of disease (tumor size, lymph node status) and type of primary therapy (radiotherapy, chemotherapy). This study examines the factors that influence of local recurrence of breast cancer in women who underwent mastectomy.

**Materials and Methods:** A 10-year retrospective review was performed using the Breast Cancer Registry data at Akdeniz University Hospital, a tertiary care facility in Antalya, Turkey. All female patients who underwent modified radical mastectomy for invasive breast cancer between 1996 and 2006 were included. Patients received radiotherapy if the number of positive axillary lymph nodes greater than three. Breast cancer registry data were reviewed for local recurrence of breast cancer. Local recurrence is defined as the reappearance of breast cancer in the skin flaps, in the mastectomy scar on the chest wall or in the ipsilateral regional lymphatics. Follow-up has ranged from 2 to 12 years. Statistical analysis of recurrence rates was performed using Pearson's chi-square analysis and logistic regression analysis.

**Results:** During this 10-year period, 412 mastectomies were performed. There were 12 (2.9%) local recurrences in study period. The mean follow-up time was 5.3 years (range 2–12 years). Patient age  $\leq 40$  years ( $P=0.055$ ), tumor size  $\geq 3$  cm ( $P=0.036$ ), axillary lymph node metastasis ( $P=0.039$ ), number of metastatic axillary lymph nodes  $\geq 6$  ( $P=0.001$ ), pathologic stage  $\geq$  stage IIB ( $P=0.001$ ), histological grade III ( $P=0.014$ ), lymphatic and/or vascular invasion ( $P=0.004$ ), estrogen receptor status negative or unknown ( $P=0.016$ ) were found that prognostic factors for local recurrence. Number of metastatic axillary lymph nodes  $\geq 6$  (HR 4.9, CI 1.31–18.6), histological grade III (HR 4.1, CI 1.01–16.97) and estrogen receptor status negative or unknown (HR 5.1, CI 1.04–25.24) were found Independent risk factors for local recurrence by logistic regression analysis.

**Conclusions:** In addition to number of positive axillary lymph nodes, predictors of local recurrence include tumor related factors, such as increasing tumor grade and negative estrogen receptor status. In conclusion, local recurrence following mastectomy was related not only initial extent of disease but also related to pathological specifications of primary tumor.

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#### Analysis of biomarkers (P27, PTEN, and IGF-IR) after preoperative systemic treatment with the combination of docetaxel and trastuzumab in patients with locally advanced HER2-overexpressing breast cancer (Tokai Breast Cancer Clinical Research Group: TBCRG)

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**Background:** There are no standard treatments for locally advanced breast cancer (Stage IIIB and IIIC including inflammatory breast cancer). We

conducted a phase II study of docetaxel (D) and trastuzumab (H) as preoperative treatment for locally advanced HER2-overexpressing breast cancer to evaluate the clinical response, pathological complete response (pCR), safety, and to perform a subset analysis based on tumor biomarkers.

**Patients and Methods:** 25 pts with HER2+ (3+ by IHC), locally advanced breast cancer were enrolled in this multicenter phase II study by the Tokai Breast Cancer Clinical Research Group (TBCRG) in Japan. Patients were treated with a combination of D (75 mg/m<sup>2</sup> every 3 weeks) and H (4 mg/kg loading dose and thereafter 2 mg/kg weekly). Four cycles of chemotherapy were repeated every 3 weeks and followed by surgery. P27, PTEN and IGF-1R were examined by IHC in core needle biopsy specimens.

**Results:** The median age was 54 years (range, 32–72) and median tumor size was 63 mm (range, 22–110). PS (ECOG): 0/1 (25/0). Clinical nodal status: N1/N2/N3 (15/5/5), Stage: IIIB/IIIC (21/4), Hormone receptor status: ER+ and/or PgR+/ER–PgR– (11/14), Menopausal status: post/pre/unknown (17/7/1). The overall clinical response rate was 68% [95% CI: 47–85%]. The pCR rate was 24% [95% CI: 9–45%]. The clinical response rate and the pCR rate of patients with ER– and PgR– tumors were 79% and 36%, respectively. On the other hand, the clinical response rate and the pCR rate of the patients with ER+ and/or PgR+ tumors were 55% and 9%, respectively. The most common Grade 3 or 4 adverse events were leukopenia 40%, neutropenia 58% and febrile neutropenia 20%. Non-hematological toxicities, including AST elevation, nausea, vomiting, and fatigue, were manageable. One patient developed interstitial pneumonia.

**Conclusion:** The combination of D and H produced a high clinical and pathological response. Subgroup analysis suggests that ER/PgR negative tumors might be correlated with pathological response in locally advanced breast cancer. Analyses of specific predictive biomarkers for D and H combination therapy are ongoing.

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#### High-dose radiotherapy treatment for locally advanced breast carcinoma

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**Introduction:** Chemotherapy followed by surgery, radiotherapy and hormonal treatment (if ER positive) is considered the treatment of choice in patients with locally advanced breast Carcinoma (LABC).

Once in a while we are confronted with a patient with a locally (very) advanced breast cancer (L.(v).A.B.C.), consisting of ulcerating tumour frequently with satellite tumours and skin infiltration. Most of the patients are aware of the serious situation and afraid for the diagnose breast cancer and the treatment of it. They refused medical help other than an event mostly bleeding of the tumour.

The aim of this study is to investigate the results of primary radiotherapy treatment in combination with hormonal therapy (pending on ER status)

**Material and Methods:** In the period February 1982 until December 2005 a total of 40 patients were identified in this situation. A surgeon, a radiation oncologist and a medical oncologist saw the patients.

The mean age was 76.5 years (48–92). This is less than 1.0% of the totally seen breast cancer patients seen in the radiotherapy department in Bronovo hospital.

It took mostly more than two contacts to assure the patient of treatment need. Trust was gained by, explanation of the results of radiotherapy cleaning the ulcer by H<sub>2</sub>O<sub>2</sub> 1.5% and absorbing gauze.

All patients were treated with megavolt (Cobalt or 6MV photons). Standard is a fractionation scheme of 2.0 Gy 5 times a week. If the condition of the patient is not well enough 4.0 Gy 2 times a week.

After 50.0 Gy a pause of 2 weeks was build in. The total treatment volume is reduced following the reduction of the tumour. The total dose depends on the condition of the patient and the treatment volume. Mostly more than 74.0 Gy (52.0–80.0 Gy) on the standard scheme and 60.0 Gy (48.0–60.0) on the alternative scheme are applied. The aim of the treatment is locally control of the tumour during the rest of life.

During and after treatment patient followed intensively.

**Results:** Median survival of the whole group is more than 5 years. (0–14.9 years; one patient died during treatment of metastasised breast cancer.)

Patients who received a Biological Equivalent Dose (B.E.D) of more than 115 Gy local control is over 85% during life time, while if B.E.D. less than 115 Gy local control is <38%.

**Conclusions:** In patients with L.(v).A.B.C. (mean age 76.5 years) treated with high dose radiotherapy (BED > 115) the local control is excellent (>85% during lifetime). The median survival is over 5 years.

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#### A low recurrence rate in patients treated for breast cancer in China

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**Background:** To assess the relation between patient and treatment characteristics and recurrence rate in patients treated for breast cancer in Tianjin (China), where the incidence of breast cancer is about 20 per 100,000 per year.

**Methods:** A random selection was made of 1,197 records out of 5,987 patients diagnosed with breast cancer between 1995 and 2000. Patient and treatment characteristics were registered. As a part of the follow-up all patients were yearly contacted by telephone to assess survival status or disease status.

**Results:** For 1,086 patients baseline information was available, for 830 patients 5-years follow-up and for 178 patients 10-years follow-up information was available. The median age at diagnosis of patients (all females) was 48.0 years (range 19–80 years). 59% of the patients (645) had a T2 tumour, and 48% of the patients (521) were in N1–3 stage. Most women (1041; 96%) underwent mastectomy; 588 (54%) received radiotherapy; 896 (82%) chemotherapy; and 374 (43%) endocrine therapy. The 10-years local recurrence rate was 4.1% (95% CI: 2.7–5.6); the 10-years contra-lateral recurrence rate was 0.1% (95% CI: 0.0–0.3), and the 10-years distant metastasis rate was 9.5% (95% CI: 7.1–11.9). Main predictor for recurrences was T-stage.

**Conclusions:** In this area without breast cancer screening the treatment for breast cancer was more aggressive than is common in Western countries. The overall recurrence rate was very small. This can be caused by treatment factors or genetic and environmental factors.

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#### Complications of surgery in management of locally advanced breast carcinoma

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In developed world, patients with locally advanced breast cancer represent a small subset of patients presenting with carcinoma of breast, seldom exceeding 5% in most of the series but same is not true for developing world. The management of locally advanced breast carcinoma provides a unique challenge to physicians. The role of surgery is limited and incidences of complications are quite high.

This study was done in university hospital of central India. Duration of study was 5 years from Jan 2003 to Dec 2007. All retrospective records of locally advanced breast carcinoma reviewed.

Locally advanced breast carcinoma comprises of 51.8% of all cases of breast carcinoma and 37.7% cases were below the 45 years of the age. 62.9% of cases of locally advanced breast carcinoma patients belong to T4bN1M0 stage; out of this approximately half below 45 years of age. All patients received anterior chemotherapy followed by surgery except 11 cases of T3N1M0 stage. Incidence of surgical complications is much higher in locally advanced breast carcinoma patients. Incidence of flap necrosis was very higher up to 14.5% patients. Other early complications hemorrhage, wound infection and seroma were 7%, 2% and 4% respectively. Incidence of local recurrence was 17% in present series.

In developing countries locally advanced breast carcinoma is still present in larger group and incidence of complications of surgery much higher in these patients.