Phase III	Status	n	ORR %	PFS (months)
AT resistant MBC I + C vs C (046), n 752	TNeg I + C	91	27%	4.1 (3.35−4.37)
	TNeg C	96	9%	2.1 (1.45−2.8)
	No- TNeg I + C	284	37%	7.1 (6.14−8.08)
	No- TNeg C	281	16%	5. (4.1−5.55)

* evaluated by Independent Radiological Committee.
AT, anthracycline–taxane; C, capecitabine; I, Ixabepilone.

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Prognostic significance of positive axillary lymph node matastases and extracapsular extension in T1 to T3 breast cancer

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Background: Extracapsular extension (ECE) of axillary metastases has the importance as a risk factor for recurrence. Poorer survival in breast cancer has been suggested, but its prognostic value has not been uniformly confirmed.

Methods: From January 2000 to December 2007, 421 breast cancer patients operated on at the Department of General Surgery in General hospital "Sveti Vracevi" in Bijeljina. We selected 211 (50.1%) cases with pT1 to pT3 node-positive breast cancer. The prognostic significance of ECE of axillary metastases was evaluated with respect to disease-free survival, overall survival, and the patterns of disease recurrence. Such prognostic significance was then compared with that of other clinical and pathologic factors.

Results: 109 patients (25.8%) presented with ECE. 35 patients (32%) were identified as having three or less lymph nodes involved, 31 patients (28.4%) patients four to six, 23 patients (21.1%) seven to nine, and 18.5% patients ten or more nodes, respectively. With a median follow-up of 89 months, factors with independent prognostic value for disease-free survival by multivariate analysis included absence of estrogen receptors ($P < 0.005$), pN category ($P < 0.01$), presence of lymphovascular invasion (LVI; $P < 0.005$), and ECE ($P < 0.001$). An independent negative prognostic effect on overall survival was observed for absence of estrogen and progesterone receptors ($P < 0.05$), pN category ($P < 0.05$), and presence of LVI ($P < 0.005$) and ECE ($P < 0.001$).

Conclusions: ECE demonstrated a stronger statistical significance in predicting prognosis than the pN category and was also related to an increased risk of distant recurrences. We suggest that the decision on adjuvant therapy should consider the presence of ECE of axillary metastases and peritumoral LVI as indicators of high biological aggressiveness. Balancing the risks and benefits of irradiation, we continue to recommend that complete axillary irradiation is not routinely indicated after adequate axillary dissection.

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Economic impact of recurrence in postmenopausal women with breast cancer

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Background: Health care resource utilization among breast cancer patients is substantially high and patients who experience recurrent breast cancer require more costly care than patients who do not develop recurrent disease. Research has also shown that the cost associated with a distant recurrence is significantly greater than the cost associated with a contralateral or locoregional recurrence. Distant metastasis has also been shown to account for the greatest number of breast cancer recurrence events early in the course of the disease (2−3 years after surgery). In this study we evaluated the cost associated with breast cancer recurrence in postmenopausal women diagnosed with breast cancer between 1995 and 2005.

Method: This retrospective analysis was conducted using patients identified from the Henry Ford Health System, who were at least 45 year old at the time of diagnosis without a stage IV or unknown tumor. Patients had at least one year of continuous enrollment and received at least one of the following treatments: surgery, chemotherapy, radiation, or hormone therapy. Total health care costs incurred after distant, contralateral or locoregional recurrence were calculated up to one year after breast cancer recurrence or death and presented as mean cost per month.

Result: A total of 1,649 women were identified based on the inclusion criteria. The mean age was 61 years, and Stage I tumors were the most common (38%). The majority of the patients had surgery (99%). Other initial and subsequent treatments included radiation (71%), chemotherapy (27%), and hormone therapy (51%). Of the 232 patients who experienced a recurrence, distant recurrence (44%) was more common than contralateral (23%) or locoregional recurrence (34%). On average, patients with distant, contralateral, and locoregional recurrence incurred cost for approximately 7, 12, and 11 months, respectively. The mean cost per month associated with a distant recurrence ($37,969) was significantly greater that for contralateral ($10,934) recurrence or locoregional ($9,129) ($P < 0.0001$).

Conclusion: Distant metastasis is the primary cause for breast cancer deaths. This study finds that in postmenopausal women, the greatest number of breast cancer recurrences was distant, and these are associated with significantly higher cost of care compared to locoregional or contralateral recurrence.

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Clinical and biological 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.

Materials and Methods: Women with infiltrating ductal carcinoma (IDC) and invasive lobular breast carcinoma (ILC) were diagnosed and treated in Surgical clinic Nis between 1997 to 2001. 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 cancer had 102 (8.80%) and 1057 (91.20%) had infiltrating ductal carcinoma. The 5-year survival rates were for ILC 65% 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.

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Optimizing local control in locally advanced breast cancer: do we still need surgery?

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Background: Multimodality treatment is considered the standard treatment for patients with locally advanced breast cancer (LABC). This treatment usually consists of neo-adjuvant therapy followed by locoregional radiotherapy. Surgery is mainly used to remove residual disease after completion of neo-adjuvant therapy in order to ensure optimal local control. There is still debate however about the extent of surgery needed, since there is no survival benefit. Purpose of our study was to evaluate the disease outcome after neo-adjuvant therapy and locoregional radiotherapy in patients with locally advanced breast cancer, looking specifically at the extent of surgery.

Material and Methods: 109 patients with non-metastatic LABC (cT3−4N0−2) were retrospectively analyzed. All patients were treated between 1995 and 2005 in 3 different hospitals with neo-adjuvant therapy and locoregional radiotherapy ($\geqslant$50 Gy). Data about the surgical procedures and follow-up were collected.

Results: After neo-adjuvant treatment most patients ($N = 92$) underwent surgery. Surgical procedures consisted of any form of breast surgery with ($N = 66$) or without ($N = 26$) complete axillary lymph node dissection (ALND). With a median follow-up of 3.3 years the overall LRR-rate was

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 41−43ºC 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^2 D1q2w) followed by 3 DOC (100 mg/m^2 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 $\leqslant$40 years (P = 0.055), tumor size $\geqslant$3 cm (P = 0.036), axillary lymph node metastasis (P = 0.039), number of metastatic axillary lymph nodes $\geqslant$6 (P = 0.001), pathologic stage $\geqslant$ 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 $\geqslant$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