**Results:** During follow-up 41 patients developed a local recurrence, of which 35 were isolated events at the time of diagnosis. The 5-year actuarial local recurrence rates for the three patient groups are presented in the Table. Despite their more favourable tumour stage, the patients undergoing M without RT had a significantly higher risk of local recurrence than the patients undergoing M with radiotherapy. A multivariate analysis, taking into account differences in tumour size, nodal status, age and adjuvant systemic treatment between the patient groups, showed that the local recurrence risk was almost 3 times lower for the patients undergoing M with RT than for the patients who underwent M without RT (HR: 0.35; 95% CI: 0.13−0.94). The risk of local recurrence in patients undergoing L with RT was not affected by the presence of positive surgical margins, neither in the univariate analysis nor after adjustment for age, tumour stage and adjuvant systemic treatment.

Table. 5- and 8-year actuarial local recurrence rates in patients with invasive lobular breast cancer (Kaplan–Meier method) according to treatment

| Follow-up | Treatment | | | | | |
|---|---|---|---|---|---|---|
| | L with RT (n = 416) | | M with RT (n = 172) | | M without RT (n = 217) | |
| | % | (95% CI) | % | (95% CI) | % | (95% CI) |
| 5-years | 3.5 | (2.5−4.5) | 2.0 | (0−4.4) | 9.1 | (4.9−13.3) |
| 8-years | 6.4 | (4.7−8.0) | 4.0 | (0−8.6) | 9.8 | (5.4−14.2) |
| P-value (logrank) | L+RT vs. M with RT: P = 0.44 | | L+RT vs. M without RT: P = 0.03 | | M without RT vs. M with RT: P = 0.02 | |

M = mastectomy; L = lumpectomy; RT = radiotherapy.

**Conclusions:** Patients with invasive lobular breast cancer whose surgical treatment is followed by radiotherapy have a very low risk of local recurrence. This low risk of local is considered to be a reflection of high sensitivity of lobular carcinoma to radiation. Radiotherapy techniques may also have become more accurate and effective in eradicating microscopic disease.

**289** Poster Discussion

**Long-term cosmetic changes after breast conserving therapy for patients with stage I and II breast cancer treated in the EORTC "boost versus no boost" trial**

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**Background:** A 16 Gy boost dose results in a better local control but also negatively affects early cosmetic outcome after breast conserving therapy for early breast cancer (Vrieling e.a., Int. J. Radiation Oncology Biol. Phys. 1999; Bartelink e.a., J. of Clinical Oncology 2007). The purpose of this study is to investigate the change in cosmesis 3-, 6- and 9 years after treatment.

**Material and Methods:** We collected pictures of the breasts from patients participating in the "Boost versus no Boost" trial treated in Tilburg and Utrecht. In this trial pictures were made before radiotherapy and every three years during follow-up. Digitalized pictures were analyzed using specific software (BCCT.core) that enables quantification of seven features (pBRA = change in nipple position, pLBC = change in level of lower breast contour, pUNR = change in nipple level, pBCE = change in distance from nipple to inframammary fold, pBCD = change in length of breast contour, pBAD = change in area of the breast, pBOD = change in non overlapping area between left and right breast), all associated with fibrosis (Cardoso e.a., Artif Intell Med 2007). Changes in the size of the treated breast were quantified and both breasts were compared. We performed a multivariate analysis on the results of these measurements.

**Results:** We retrieved 1403 sets of photographs from 347 patients with a minimum follow-up of 6 years: 169 randomized to the no boost-arm, 178 to the boost-arm. A continuous increase in time for all seven features was noted. The cosmetic outcome worsened more in the boost- than in the no boost-arm. The difference of the evolution between the two arms was statistically significant for pBRA, pLBC, pUNR, pBCD, and pBOD. In the multivariate analysis, using features representing the most relevant changes of size and shape of the breast (pBRA, pLBC, pBOD), applying a boost, postoperative complications and a maximum dose of >55 Gy in the border plane for whole breast irradiation were significantly associated with a worse cosmetic outcome.

**Conclusions:** We noted a significant worsening with time after treatment for 5 of the 7 features used for measuring changes in cosmetic results after breast conserving therapy for early breast cancer. In the multivariate analysis boost treatment, postoperative complications and a maximum dose of >55 Gy for whole breast irradiation were significantly associated with worsening of the cosmetic outcome during follow-up up to 9 years.

## Thursday, 17 April 2008 12:30–14:30

**POSTER SESSION**

# Locally advanced and recurrent disease

**290** Poster

**Clinical activity of the novel epothilone B analog, ixabepilone, in triple negative breast cancer (BC) patients**

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**Background:** Despite advances in BC treatment, many women experience progressive disease secondary to primary or acquired resistance, which may occur from the earliest stage of disease. Ixabepilone, a semi-synthetic analog of epothilone B, is the first member of a new class of antineoplastic agents, developed to have less susceptibility to tumor resistance mechanisms. Patients (pts) with ER/PR/HER2-negative (triple-negative, TNeg) BC has an aggressive clinical course with significant risk of systemic relapse and subsequent poor prognosis, TNeg BC patients have fewer treatment options than those with receptor-positive tumors. We report activity of ixabepilone in several settings of BC in the triple negative sub-set patient population.

**Material and Methods:** Ixabepilone has been administered as monotherapy, 40 mg/m$^2$ iv over 3h on day 1 q 3 wks, as well as at the same dose in combination with capecitabine, 2000 mg/m$^2$ po on days 1−14.

Data on triple negative sub-set are presented from 5 phase II studies including neoadjuvant and metastatic BC (MBC) setting and from a phase III trial of pts with anthracycline/taxane-resistant MBC.

**Objectives:** response rate (ORR), progression free survival (PFS) and main adverse events (AEs) were reviewed.

**Results:** See the tables.

In all studies from neoadjuvant to heavily pretreated metastatic disease, the safety profile was comparable between TNeg and Non-TNeg pts., neuropathy was mostly sensory, cumulative and reversible (incidence of G3 ranged from 3% in the neoadjuvant population to 21% in anthracycline/taxane-pretreated disease).

**Conclusion:** Ixabepilone has consistently demonstrated antitumor activity in patients with TNeg BC, both as monotherapy and in combination with capecitabine, from neoadjuvant to multiple resistant MBC.

| Phase II | Status | N | ORR % | pCR % |
|---|---|---|---|---|
| Neo-adj (080) n = 161 | TNeg | 42 | 64% | 26% |
| | No- TNeg | 119 | 60% | 15% |
| Taxane resistant MBC (009) n = 49 | TNeg | 18 | 6% | |
| | No- TNeg | 31 | 16% | |
| Taxane pretreated MBC (010) n = 65 | TNeg | 11 | 55% | |
| | No- TNeg | 65 | 39% | |
| TAC resistant MBC (081) n = 126 | TNeg | 42 | 12% | |
| | No- TNeg | 84 | 11% | |

* evaluated by Independent Radiological Committee.
TAC, Taxane–anthracycline–capecitabine.

| 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.

**291** Poster

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

S. Maksimovic[1], B. Jakovljevic[2], R. Raseta[2], G. Kecman[2], G. Mitrovic[3], I. Rakita[2], Z. Gojkovic[2]. *[1]General hospital Sveti Vracevi, General and Oncological Surgery, Bijeljina, Bosnia-Herzegovina; [2]Clinical Center Banja Luka, Clinic of Oncology, Banja Luka, Bosnia-Herzegovina; [3]General Hospital Sveti Vracevi, Medical Oncology, Bijeljina, Bosnia-Herzegovina*

**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.

**292** Poster

**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.

**293** Poster

**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.

**294** Poster

**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