absence of taxanes in the neoadjuvant chemotherapy regimen (p = 0.02). In the multivariate analysis, only the clinical N2 stage was associated with a higher rate of locoregional recurrences. There were no significant difference in overall survival (52% at 5 years, 38% at 10 years, p = 0.32) or disease-free interval (at 5 years 32%, at 10 years 26%, p = 0.35). Factors associated in univariate analyses with a decreased overall survival were age over 50 years, the absence of achievement of a clinical response ⩾50%, absence of hormone receptors and the absence of taxanes in the neoadjuvant chemotherapy regimen. In multivariate analysis, only the absence of hormone receptors and either complete or partial clinical tumor response remained significant.

Factors associated in univariate analyses with a higher rate of disease recurrences were the absence of achievement of a clinical response ⩾50%, absence of hormone receptors and the absence of taxanes in the neoadjuvant chemotherapy regimen. In multivariate analysis, only the absence of hormone receptors and of clinical tumor response remained significant. Late toxicities were not significantly different between the two treatment groups except for a higher rate of fibrosis in the no-surgery group (p < 0.0001), and more lymphedema in the surgery group (p = 0.002).

Conclusion: Our data suggest an improvement in locoregional control in patients treated by surgery, in conjunction with chemotherapy and radiotherapy, for IBC. Efforts must be made to improve overall survival.

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Re-irradiation plus hyperthermia for recurrent breast cancer gives high local response and locoregional control

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Background: Locoregional recurrent breast cancer, especially in previous irradiated area, generally implies a poor prognosis. Treatment options are limited.

A cohort of 130 patients, treated in the AMC from 1982–2003, was analysed to evaluate the response and long term locoregional control and toxicity of re-irradiation (re-RT) and hyperthermia (HT) for locoregional recurrent breast cancer in previously irradiated area.

Patients/methods: Median age was 57 years. Median follow-up was 109.2 (63.0–187.2) months. All patients received extensive previous treatments, including surgery and irradiation to a median dose of 50 Gy in 5 weeks. Most (90%) received one or more lines of systemic therapy. Initial tumor stage included stage 1−4 (36, 50, 13 and 2%, respectively). Concurrent metastases occurred in 41 (32%) patients. Ninety patients (69%) had one or more previous locoregional recurrences before re-RT+HT. Median time interval between primary treatment and current recurrence was 36.9 (2.8–240.2) months. At start of re-RT+HT the median tumor size was 10 cm (0.5−30) and comprised >25% of the ipsilateral chest wall in 38% of patients. Thirty-five patients presented with lymphangitis cutis carcinomatosa and 38 with regional tumor activity. Recurrences were classified as single (n = 22), multiple (n = 60) or diffuse (n = 35).

Re-RT consisted of 32 Gy (15−40), given twice a week. Four (1−8) sessions of superficial hyperthermia were added once a week using CFMA-434 MHz applicators. Aim temperature was 41−43ºC for one hour. Concurrent chemotherapy was given in 22% and concurrent hormone therapy in 32% of patients.

Results: Overall clinical response rate, including regional disease, was 83% (CR+PR): 67 patients (52%) had a complete remission and 40 (31%) a partial remission. Fifteen (12%) patients showed no response and 2 had local progression. After CR the three-year local control rate was 38%. For the total cohort the three-year overall survival was 18%.

Most frequent acute toxicities were erythema and epidermolysis. Fibrosis was the most frequent late toxicity. Acute and late ⩾ grade 3 toxicity occurred in 26% and 16% of patients, respectively. One grade 5 (lethal) event occurred due to infection of a late radiation ulcer.

Discussion/Conclusion: The combination of re-irradiation and hyperthermia appears to achieve good locoregional control with an acceptable risk of side effects, particularly in view of the high tumour burden and resistance to previous treatments.

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Trends in survival in metastatic breast cancer

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Background: In the last 20 years new treatment options in breast cancer have evolved. We wanted to determine whether the survival of patients with metastatic breast cancer have improved during this period.

Materials and Methods: All pts with a diagnosis of disseminated breast cancer established 1985–2004 in the county of Kalmar were identified from the patients registry. Patient and tumour data was retrieved from patient records and the pathology database. Survival curves were constructed and median survival in months was determined for each 5 year interval 1985–2004 for the whole cohort and by grade. The percentage of patients surviving more than 2, 3, 5 and 10 years after first metastatic event was determined for each group. Separate analyses were performed for pts with ER/PR positive and HER2 positive tumours resp to determine whether the survival changed in the first 50% of the cohorts compared to the last.

Results: The median survival of the 557 pts in the whole study population was 10, 14, 16 and 22 months in each successive five-year period from 1985 to 2004.

For pts with grade 3 tumours (N = 288) the median survival increased from 10, 12, 15 to 17 months resp. The percentage of pts with grade 3 tumours surviving more than 3 years improved from 14 to 34% and the 5 years survival increased from 8 to19%.

The median survival for pts with grade 2 tumours (N = 168) was 17, 22, 23 and 27 months resp. The percentage of pts surviving more than 2 years increased significantly from 33 to 51%.

Only 43 pts had grade 1 tumours. The median survival for this group was 33 months and did not change.

ER/PR positive pts were 276. The median survival was 22 months and did not change over time. Sixty-four percent of pts diagnosed before 1997 survived more than 2 years and 44% more than 3 years. Corresponding figures for pts diagnosed 1997 and later were 68 and 48% resp.

Forty HER2+ pts treated before 2000 had a median survival of 14 months and the same number diagnosed year 2000 and onwards 21 months. Two-year survival improved from 20 to 43%, 3-year from 12 to 33 and 5-year survival from 5 to 15%. Fifty-eight of the HER2 positive tumours were of grade 3. In this subset 46% of pts diagnosed 2000 or later survived more than 2 years, 32% more than 3 years and 21% more than 5 years as compared to 10, 3 and 3% resp for those diagnosed before the year 2000.

Conclusions: Survival in metastatic breast cancer improved 1985–2004. The most striking improvement was achieved in the HER2 positive subset. The median survival of ER/PR positive patients did not increase.

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Circulating cross-linked N-telopeptide of type 1 collagen and VEGF in patients with bone metastases from breast cancer treated with zoledronic acid

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Background: Breast cancer is the most frequent tumor in women and 80% of patients with metastatic disease have bone metastases (BM), which are responsible for high morbidity and for reduced quality of life. Zoledronic acid (Zometa®, Zol), routinely used to treat patients with BM, inhibits bone resorption and has antitumor properties. It has also been reported to have an antiangiogenic effect.

Material and Methods: The present study evaluated serum levels of vascular endothelial growth factor (VEGF) and cross-linked N-telopeptide of type I collagen (NTX) in 31 consecutive patients with advanced breast cancer. Patients were eligible if they were at first diagnosis of bone metastases and if they had not previously undergone bisphosphonate treatment. All patients received the standard Zol schedule of a 4-mg infusion every 28 days. Patients were monitored for about 9 months and blood samples were collected before the first infusion of Zol and every 3 months thereafter.

Results: The baseline VEGF median value was 298 ng/ml (25–1264). The median value at 3 months was 345 ng/ml (62–977), 307 ng/ml (112–1307) at 6 months and 394 ng/ml (172–1004) at 9 months, none of which reached statistical difference. In contrast, NTX median values significantly decreased with respect to baseline (median value 16, range 3−45 nm BCE) at 3 (10 nm BCE, range 5−35) and at 6 months (10 nm BCE, range 5−21) (p < 0.001), but not at 9 months (12 nm BCE, range 5−45). The NTX serum median level at 3 months was 34% less than that of the baseline. Blood samples at 6 and 9 months showed a decrease of 38% and 26% with respect to baseline, respectively. There was no correlation between VEGF and NTX values.

Conclusions: The present work shows that standard monthly treatment with zoledronic acid induced a rapid and long-lasting decrease in NTX levels in the majority of patients, in marked contrast to literature data on urinary NTX in a similar patient setting. Conversely, no change was observed in circulating VEGF values, which may be due to the small cases series or to the fact that monthly treatments have less effect on VEGF than non standard weekly administration. The study is ongoing to validate these data.