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**468** Poster

**Serum lactate dehydrogenase (LDH) is a significant prognostic variable for survival in patients with metastatic breast cancer – a multivariate analysis**

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**Background:** Advanced breast cancer that metastasizes to bone increases the risk of skeletal-related events that can be debilitating and potentially life-limiting. However, detailed evaluations of prognostic factors for survival in patients with advanced breast cancer and bone metastases (mets) have not been reported. Therefore, we conducted a retrospective analysis of data from a pamidronate-controlled trial of zoledronic acid (ZOL) in patients with bone mets from breast cancer to investigate potential prognostic variables for overall survival.

**Material and Methods:** Only patients treated with ZOL (n = 435) who had assessments of biochemical markers of bone metabolism and complete data sets of baseline (BL) variables were included in this analysis. The 23 BL variables assessed included demographics, disease history and distribution, FACT-G, ECOG performance status (PS), type of bone lesions, bone mets history, and laboratory assessments of bone markers, blood counts and markers of renal and hepatic function, including LDH. Multivariate analyses were used to assess risk ratios (RRs) for death over 24 mo. A reduced model was generated by stepwise backward elimination until only significant ($P < 0.05$) variables remained.

**Results:** Although many variables, including bone marker levels, were significant prognostic factors in univariate models, only 7 factors remained significant in the reduced multivariate model. In this model, advanced age correlated with increased risk of death vs patients $\leqslant$50 yr old (50−60: RR = 1.83, $P < 0.01$; 60−70: RR = 1.78, $P = 0.01$; >70: RR = 2.53, $P < 0.01$). Other significant variables included: impaired vs fully active ECOG PS (RR = 1.74; $P < 0.01$), prior vs no prior chemotherapy (RR = 1.97; $P < 0.01$), FACT-G score <65 units ($P < 0.05$ for comparisons with $\geqslant$75 units), presence of lytic vs mixed bone lesions ($P = 0.02$), weight <60 kg ($P < 0.02$), and LDH levels. Patients with LDH $\geqslant$ULN but <2$\times$ULN had a 2-fold increased risk of death, and LDH >2$\times$ULN correlated with a 6-fold increased risk of death vs LDH <ULN ($P < 0.0001$ for both). Although on-treatment levels of bone markers have been correlated with survival previously, bone marker levels at BL were not significant in the multivariate model.

**Conclusions:** This model confirms the significance of previously described prognostic factors such as age and ECOG PS. However, the finding that LDH level correlates strongly with survival is new in the breast cancer setting and merits further investigation.

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**Re-evaluation of the old preoperative prognostic markers CA 15-3 and CEA using a cohort of 1093 patients treated for breast cancer 1998–2006 at a single institution**

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**Background:** Prognostic markers are essential for choosing the individual therapy for patients with newly diagnosed breast cancer. Using our own cohort from 1998–2006 we studied this group concerning preoperative serum CA 15-3, CEA and outcome.

**Material and Methods:** Since 1998 all patients with breast cancer were entered in our tumor registry. The data base (in SPSS) is maintained by a study nurse. Once yearly follow-up is obtained using our own out-patient clinic data, information from general practitioners and the general cancer registry. Informed consent is taken from the patients at time of diagnosis. CA 15-3 or CEA are defined elevated if above 25 U/ml or 4.6 $\mu$g/l respectively.

**Results:** 1093 patients with newly diagnosed primary breast cancer were evaluated in this study. Mean follow-up was 34 months. Clinico-pathological features as well as survival pattern of the cohort were found similar as those described in the literature. Independent prognostic factors were nodal status (N), hormone receptor status (HR), tumor grading, tumor size and age. Twenty-five or five percent of the patients showed elevated preoperative CA 15-3, or CEA, respectively, whereas in 5% of the patients the levels of both tumormarkers were increased.

The Cox model and subgroup analysis revealed that patients of the age group 35−50 years with elevated CEA levels had a significantly poorer overall survival (OAS) ($p = 0.0005$) than patients with normal CEA levels. An increase in CA 15-3 levels even negatively affected both disease-free (DFS) ($p = 0.0002$, for age group 35−50 yrs) and overall survival ($p = 0.0002$, for age group 35−65 yrs). Multivariate analysis further showed that CEA is an independent prognostic factor for overall survival adjusted for T, N, HR and age ($p = 0.012$). CA 15-3 was found to be an independent prognostic factor for both overall and disease-free survival adjusted for the same factors ($p = 0.003$ and $p = 0.006$). The outcome of a small group of patients with elevated CEA levels alone or in combination with higher CA 15-3 levels is poorer than the outcome of patients with elevated CA 15-3 levels alone (DFS $p = 0.021$, OAS $p = 0.008$).

**Conclusions:** Preoperative levels of CA 15-3 and CEA are of prognostic value for patients that have been newly diagnosed with breast cancer. More patients showed elevated CA 15-3 levels than higher CEA levels. Since measuring CA 15-3 and CEA is easy and not expensive, this method could be recommended as a routine method to obtain additional information on the patient's prognosis.

**470** Poster

**Persisting risk after BCT in N+ and N− patients – a single institution analysis from 1485 patients**

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**Background:** To find risk groups for local recurrence (LR) and disease free survival (DFS) for node-negative (N−) and node-positive (N+) patients after breast-conservation surgery (BCS) + radiotherapy (RT) $\pm$ adjuvant systemic therapy (ST).

**Material and Methods:** From 1984 to 1997, 1485 patients with breast cancer underwent BCS, ST and RT in our institution. Complete data were available in 1347 patients: N−: 958, N+: 389 patients. Recursive partitioning analysis was carried out to find cut points in the prognostic variables with a $p \leqslant 0.05$ for the end points local recurrence (LR) and DFS. Co-variates included were age, T-stage, N-stage, ratio of involved lymph nodes and excised nodes (NR), location of the index tumour (Loc), ST (chemo/horm), ER/PR status, menopausal status and the presence of surgical marker clips. The relative hazard ratio (RHR, HR relative to median patient) was estimated in sub-groups of at least 20 patients, as well as the 10 yr. DFS.

**Results:** After a mean f/u of 107 months the rate of LR at 10 years was 6.3% (N−: 5.5%, N+: 8.6%), and the DFS was 79.8% (N−: 83.9, N+: 68.4). For N−: For LR hormone therapy was the most relevant variable, followed by Loc and age. For DFS again the application of hormones is most important, followed by age, T-stage and Loc. For N+: For LR age is the most relevant prognostic factor, followed by T-stage and PR. For age the cut point is at 38.5 years. The 10 yr. LR rate for the elder ones is 93.5 years, for the younger ones 63.3 years. For DFS the N-ratio is the most significant prognostic factor: cut off at 48.5%, 10 year results: elderly: 72%, younger: 32%. In the next level age follows, with a cut off at 37.5 years and the most extreme difference in the 10 year DFS of 45% (75.6 vs. 30.6 years). In the 3rd level PR becomes relevant. All results presented are significant: $p \leqslant 0.05$.

**Conclusion:** After standard therapies for BCT certain situations in prognostic factors result in an unfavourable outcome. In the N neg group the lack of hormone therapy results in a negative outcome. Tumour location may influence local control and disease free survival; the medial tumours reveal the worst prognosis. They may need more aggressive systemic therapy and probably radiotherapy to the internal mammary chain.

In N+ patients age is the most relevant factor followed by tumour size and PR for LR; for DFS the NR is the most significant variable followed by age, tumour size and PR. The NR has an impact on survival only, but not on LR. Compared to the common prognostic factors more attention should be paid to the application of hormones, to PR neg patients and to medially located tumours in terms of a more aggressive therapy.