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POSTER

Isolated tumor cells in the bone marrow (ITC-BM) of breast cancer patients before and after anthracyclin based therapy - Influenced by the HER2neu- and Topoisomerase IIa-expression/amplification of the primary tumor?

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Background: The immunocytochemical detection of ITC-BM of breast cancer patients is an independent prognostic factor in all stages of the disease. Both the expression / amplification of HER2neu and Topoisomerase IIa (TOP IIa), a key enzyme of DNA replication and main target of anthracyclines, in primary breast cancer tissue seem to have predictive value regarding the effectiveness of systemic therapies, what might possibly be expressed by a change of ITC-BM.

Methods: Tumor tissues of 52 pts that were screened for ITC-BM before and after anthracyclin based therapy (CTX) were examined for HER2neu and TOP IIa by IHC and FISH (TOP2A/HER2/CEP17 Multi-color Probe, Vysis). The correlation of these factors and their influence on clinical outcome was analysed retrospectively. Results: By IHC 30% of the tumors showed positive for HER2 (2+/3+), 23% were amplified in FISH analysis (HER2/CEP17 ≥ 2). TOP IIa overexpression ($>20\%$) was found in 23/48 pts (48%), FISH analysis was pos. in 6/42 pts (14.3%), with co-amplification of HER2 and TOP IIa in 75%. ITC-BM were present in 25% of pts before and 30% after CTX. The detection of ITC-BM before CTX correlated with HER2 (IHC and FISH), but not with TOP IIa. 43 pts had adjuvant, 6 neoadj., 3 palliat. CTX, regimens consisting of EC (6 pts), EC/CMF (18 pts), EC/Docetaxel (26 pts) and others (5 pts). 31 pts (53%) stayed neg for ITC-BM during CTX, 8 (16%) changed from neg to pos, 5 (10%) from pos to neg, and 8 (16%) stayed pos., which either was independent of the HER2- or TOP IIa status. After a median of 46 months (6-127) HER2-IHC ($p=0.005$), TOP IIa-IHC ($p=0.049$) and the detection of ITC-BM after completion of CTX ($p=0.047$) were sign. prognostic factors for overall survival (log-rank-test), whereas TOP IIa (FISH) neg. pts showed a slight but not significant trend ($p=0.09$) towards reduced distant disease free survival.

Conclusion: As shown previously, antiproliferative CTX has no or little effect on the elimination of ITC-BM. This seems to be independent of the HER2 or TOP IIa status of the primary tumor. Nevertheless, the detection of ITC-BM after CTX has, like the HER2 status, prognostic relevance for overall survival. For the development of new therapeutic strategies, it would be desirable to examine such factors on ITC directly.

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Long term results after conservative treatment for invasive breast carcinoma: A 20 year follow-up

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Background: Patients (pts) with invasive breast cancer treated by conservative treatment must be followed for a long time to ensure the efficacy of the procedure in terms of locoregional control. This study was performed to analyze the outcome of a large series of patients submitted to conservative surgery and definitive irradiation, and to evaluate the relationship between locoregional recurrence (LRR), distant metastases (DM) and survival.

Methods: From 1983 to 1998, 547 pts with early breast cancer stage I and II, underwent breast conservative treatment (BCT). Pts with axillary positive nodes received adjuvant chemotherapy, and pts with positive hormonal receptors received hormonotherapy. The following prognostic factors were analyzed for their ability to predict for a distant recurrence: pt age, menopausal status, tumor size, axillary lymph node status, histological grade, experience of LRR and interval from diagnosis to LRR. The outcome of pts after LRR (early ≤ 24 months or late >24 months) was documented and factors associated with a favorable survival following recurrence are identified.

Results: With a median f-up time of 78 (3-238) months, 25 pts experienced a LRR as their first site of recurrence and in 58 pts isolated DM were observed. The 20 years overall and cause-specific survival was $51.0\% \pm 17.7$ and $84.3\% \pm 4.6$ respectively. The 20 years cumulative incidence of LRR was $19\% \pm 12.5$ and the annual cumulative incidence of LRR within the first two years was 0.80% and between the 3th and 10th years was 0.48%. Between the 11th and 15th no LRR was observed and one pt experienced a LRR in a different quadrant from the primary tumor 16 years after the diagnosis. The cumulative incidence of DM at 20 years was 17.7 ± 2.6 and the annual cumulative incidence of DM within the first two years was 2.2% and between the 3th and 10th years was 1.3%. From the 12 th year until the end of the study none of the pts present in the study experienced a DM. The 15 years overall survival rate of pts who experienced LRR differed significantly from those pts who never experienced LRR, $72.5\% \pm 6.3$ vs $53.9\% \pm 11.7$ respectively ($p=0.005$; RR of death: 2.6; 95% CI: 1.3-5.0). The actuarial distant disease free survival (DDFS) of pts who never experienced LRR was significantly higher ($86.9\% \pm 1.9$) compared to the actuarial DDFS of pts who experienced LRR ($62.8\% \pm 9.8$) ($p<0.0006$; RR of DM: 3.2; 95% CI: 1.5-6.4). The 10 years DM probability in pts who developed an early LRR was $60\% \pm 17.3$ and $25\% \pm 10.8$ in pts who developed a late LRR (RR: 4; $p=0.041$; 95% CI: 1.05-15.2). The median f-up time for survivor pts after LRR was 44 months.

Conclusions: Long term survival rate was observed among pts who underwent BCT. LRR appears to be a significant predictor of DM and pts who sustain early LRR tend to display a more aggressive clinical course

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Interobserver variability of target volume delineation of breast tissue as well as of boost volume in 19 breast cancer patients after lumpectomy and axillary staging

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Purpose: To determine the interobserver variation in delineating the clinical target volume (CTV) of breast tissues as well as of corresponding boost volumes on computed tomography (CT) scans in breast cancer patients treated with breast conserving therapy (BCT).

Material and Methods: Nineteen consecutive breast cancer patients (mean age 53 yrs; 16 T1, 3T2) treated with breast conserving therapy agreed to participate in our study. Palpable glandular breast tissue was marked with a lead wire before CT scanning. Four radiation oncologists and 1 radiologist delineated CTV's. Indices of the corresponding CTV of all 19 patients were compared with one another specifically with respect to the delineation of breast tissue: BRI and to that of the boost volume: BOI. An index of 1.0 implicates that the location as well as the size of the CTV's is exactly the same. We then analyzed where in the breast tissue the magnitude of the observed differences was high or low (medial, lateral, cranial, caudal, outer, inner). With respect to the latter the following variables were also analyzed: i) the volume of the breast tissue; ii) the presence or absence of dense breast tissue; and specifically with respect to the boost: iii) the presence or absence of clips.

Results: The range of the BRI varied between 0.83 and 0.88. Observed differences were between the 5 physicians were largest in the upper-outer quadrant of the breast. The BOI varied between 0.45 and 0.60. Differences were less outspoken in the presence of clips.

Conclusions: Interobserver variation in the delineation of breast target volume on CT scans can be substantial (pending on the presence or absence of dense breast tissue). The differences are large in delineating the CTV of the boost volume. To reduce the interobserver variation, better imaging (including markers) and pathology studies relating glandular breast tissue to imaging may be needed in order to better visualize the true extent of the breast tissue (especially in postmenopausal patients) and the boost volume (especially in the absence of clips).

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Intramammary tumor location (ITL) does not influence prognosis, but the prevalence of axillary lymph node metastases

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The prognostic role of the ITL is discussed controversially (Lohrisch et al.,