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Clinical course, prognosis and therapy of bone metastases in breast cancer patients

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Purpose: Although bone metastasis is a frequent event in breast cancer patients (75% of all patients with advanced disease display osseous metastases) the knowledge of clinical course and prognosis of this complication has been poor and contradictory in former investigations.

Methods: In the present study 648 patients with metastatic breast cancer (1972–1992) had postoperative care at the womens hospital of the University of Heidelberg. Follow-up data of these patients were statistically analyzed.

Results: Best prognostic factors at the time of primary surgery were tumor size nodal status and tumor grading; on the other hand progesterone receptor and the site of metastasis were the most relevant factors at the time of metastasis. It was significant that osseous metastases occur later than visceral metastases (25 vs. 14 months; $p < 0.001$). Patients with primary bone metastases had a better overall survival, than patients with primary visceral metastasis (28 vs. 13 months; $p < 0.001$). Median survival time after first bone metastasis was not improved by new treatment concepts in the period between 1972–1992 ($p < 0.21$).

Conclusion: We could show that the primary site of metastasis is decisive for the patients fate, whereas the localisation of the second metastatic site was not of prognostic relevance. Osseous metastasis is a more common event in patients with well differentiated tumors. It is remarkable in our study, that a change in the therapeutical concept has had no influence on the time of disease-free and overall survival in patients with bone metastases.

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Anthracycline as second line chemotherapy (CT) for metastatic breast cancer (MBC) patients previously treated with taxotere (TXT)

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In a retrospective study, we evaluate the efficacy of Anthracycline in MBC according to TXT response.

Between 4/92 and 5/96, 62 patients (pts), have been enrolled in 4 phase II studies with TXT as first line CT for MBC. Taxotere was administered as single agent or in combination with Vinorelbine. Overall Response Rate (ORR) was 68%.

Among these 62 pts, 53 failed with a median time to progression: 22 weeks (2–160). Twenty four on 53 received Anthracycline-based regimens as second line CT for MBC, **23** are evaluable for response Median number of cycles administered: 4.6 (1–9). Of the 23 pts, eighteen had received adjuvant Anthracycline.

Results: Observed responses included 7 PR (30%), 6 NC and 10 PD. The median duration of response was 18 weeks (7–52). Response according to previous TXT response as first line was as follow:

Taxotere non Resistant	Taxotere Resistant*	Overall
6 PR	1 PR	7 PR (30%)
6 NC, 6 PD	4 PD	6 NC, 10 PD

*Progressive disease while on first line Taxotere therapy (secondary resistant or refractory to TXT).

Conclusion: These data provide the first evidence that Anthracycline-based regimens are active as salvage therapy, in patients previously treated with Taxotere, with a response rate of 30%.

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Static disease (sd) of long duration (≥24 weeks) is an important remission criterion in breast cancer patients treated with the aromatase inhibitor anastrozole (AN)

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Purpose: The importance of SD of long duration in advanced breast cancer patients (ABC) patients has previously been reported for megestrol acetate (MA)(1). This analysis assessed the value of long SD in patients treated with Arimidex™ (AN).

Methods: Initial results of a combined analysis of two randomised trials comparing AN (1 and 10 mg) and MA in postmen ABC have previously been reported (2) A survival update was carried out at a median follow-up of 31 months. A sub-group analysis compared survival in patients with long SD with that for those with CR/PR.

Results and Conclusions:

	CR/PR		Long SD		Other	
Treatment	n	2 yr surv	n	2 yr surv	n	2 yr surv
MA	31	70%	71	72%	151	30%
AN 1 mg	33	85%	78	86%	152	35%
AN 10 mg	31	84%	68	77%	149	38%

With each therapy, patients with long SD showed comparable 2 year survival to that for those with CR/PR. This is an important finding, as 30% of patients in this study were classified as long SD. These data support the previous finding with MA, and show that long SD was an important remission criterion in this comparison of AN and MA.

[1] Robertson JFR et al. Eur J Cancer Clin Oncol 1989, 23, 469–475
[2] Buzdar AU et al J Clin Oncol 1996, 14, 2000–2011.

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Radiation (XRT) with electron beam rotation technique of chest wall in locally advanced breast cancer

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Purpose: Different XRT techniques are being used for chest wall XRT after mastectomie. We review our results with the electron beam rotation technique in a series of 130 breast cancer patients. End points of the study were overall survival (OS), disease free survival (DFS) and local control (LC) as well as acute and late side effects.

Material and Methods: From 1/1990 to 6/1995 89 pat. underwent chest wall rotation technique beam XRT after primary mastectomy + ALNE (group 1) and 41 pat. after excision of local recurrence (group2) with 4 × 2.5 Gy/week to 50Gy (4–12 MeV electrons depending on the thickness of the chest wall). XRT of locoregional lymphnodes and local boost of 10Gy was administered depending on the R- and N-status.

Results: After a median follow up of 29 months (65% stadium III/IV) the 3 year OS, DFS, and LC were 75.4%, 46.7%, and 73.1%, respectively. LC in group 1 was 78% vs. 60% in group2. Sign. predictors of OS, DFS and LC were resection status (R0 vs. R1/2) and hormon receptor status (+vs.-). In group1, tumor grading (G1 vs. G2/3) was found to be an additional sign. prognostic factor. Seven pat. developed symptomatic pneumonitis (5%) and one a chronic cutaneous ulcus. A significant correlation between the degree of acute skin reaction and persistant hyperpigmentation was observed.

Conclusion: In locally advanced or recurrent breast cancer the postoperative XRT with electron beam rotation technique of the chest wall is a effective therapy with 73.1% local controll after 3 years. The rate of acute and late toxicity is low. The degree of acute skin reaction correlates with the degree of persistant hyperpigmentation.

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Long term breast cancer treatment with tamoxifen and second primary tumors

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Tamoxifen after twenty years in the treatment of breast cancer has been shown to be the least toxic among any other treatment. There are though publications that implicate tamoxifen in the second primary development of endometrial cancer. The aim of the present study is to contribute with our material to the relationship of Tamoxifen and second primary tumors.

Material: 422 breast cancer patients were reviewed. The great majority were post menopausal and tamoxifen had been given as adjuvant therapy.

Treatment: Tamoxifen 20–40 mgs was given continuously for 2–16 years. 168 patients had been on treatment for 5–16 years and 254 for 2–5 years. Follow up was 3–16 years median 7 years.

Results: 7 second primary cancers were detected out of 422 patients (1.65%). There were 2 ovarian cancers, 2 endometrial cancers, 1 cervical cancer, 1 gastric cancer and 1 lymphoma of the stomach. Of the two patients with endometrial cancer one was on 20 mgs of Tamoxifen daily and the other on 40 mgs daily and the duration of the treatments was 4 years and 7 years, respectively.