665 POSTER

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.

Conclusions: a) Lower percentages of endometrial cancer were detected in comparison with other studies. b) The rate of endometrial was similar to that of ovarian cancer (0.47%), while in other studies it was described to be 1.23%. c) Dose and duration of treatment makes no deference to the second primary cancer development.

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Navelbine (NVB) and Doxorubicin (DX) both at 25 mg/m², on days 1 & 8 for the management of advanced breast cancer (ABC)

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Aim: Promising results have previously been obtained with NVB 25 mg/m² on days 1 and 8, and DX 50 mg/m² on day 1, (q 21 days.) with 74% overall response rate (RR) and 21% CRs, mainly in visceral sites: (JCO, 1994). A phase II study was conducted to assess a new schedule of this combination: NVB + DX both at 25 mg/m² IV on days 1 & 8 (q 21 days.), for a maximum of 8 cycles, to improve the tolerance and to ease outpatient administration.

Results: 51 (50 eligible) chemotherapy-naive patients (pts) have been included: median age 51 y (34–73), 46% premenopausal, 42% visceral involvement; 92% ≥ 2 organs affected; PS 0, 1 and 2: 48%, 42% and 10% respectively. 297 courses (median 7) were administered. WHO grade (G) 3–4 neutropenia: 24% of pts. Low incidence of episodes of infection (5 pts at G3). G3 nausea/vomiting 20% of pts (6% of cycles) G 4 constipation: 1 pt; G1 peripheral neuropathy: 6 pts; G3 alopecia: 68%;. No cardiac impairment >G2 was observed. Overall RR: 75.5% (95%CI: 66–89%) with 18.3% CRs.

Conclusion: The excellent tolerance profile, particularly with regard to the low morbidity associated with the lack of anthracycline related cardiotoxicity and ease of out patient administration suggest that this schedule of NVB+DX can be strongly recommended as front line management of ABC.

671 POSTER

Radiation therapy of spinal metastases in breast cancer: A retrospective analysis of 108 patients

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Purpose: The retrospective analysis of the analgesic, remineralisation and decompressive effects of radiation therapy for spinal metastases in breast cancer.

Patients and Methods: From January 1990 to December 1992, 108 patients with breast cancer were treated at Bergonié Institute by irradiation for a first spinal metastasis. Three patients had previous surgery (laminectomy and Doves' frame). The indication of radiation therapy was analgesic (102 patients) or decompressive (6 patients). The usual schedule of irradiation is 30 Gy/10 fractions/2 weeks.

Results: The analgesic effect was considered as "complete" or "sub complete" (83%), "moderate" (13%) or absent (4%). The mean delay up to the maximum analgesic response was 35 days. The duration of the analgesic response and the remineralisation effect could not be retrospectively assessed due to a lack of data. The decompressive effect is complete for 5 cases and absent for 1 case. A second spinal radiation therapy were necessary 78 times (8 times in jonction field within 6 months following the first treatment). A spinal cord compression occurred out of the irradiated field in 3 cases and within in 1 case.

Conclusion: The radiation therapy for spinal metastases in breast cancer remains a palliative, especially analgesic treatment. The decompressive indication is rare. However, the assessment of compressive "risk" leads to discuss the radiological staging (contribution of MRI) and a possible previous treatment (vertebroplasty or osteosynthesis).

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Radiotherapy for choroidal metastases in breast cancer – Results of a prospective study of the ARO (ARO 95-08)

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Purpose: The primary tumor in most pts. with choroidal metastases is breast cancer. For symptomatic metastases (mts.) radiotherapy (RT) and/or chemotherapy (CT) are the treatment of choice. The best treatment for non symptomatic mts. is unknown.

Material: In 11/94 a prospective study of the ARO was started with 40 Gy in 20 fractions for pts. with symptomatic and non symptomatic choroidal mts. The endpoints of the study were tumor volume reduction, visual acuity and side effects. Until 12/96 18/30 pts. with 24 treated eyes had breast cancer as primary tumor. In 17 eyes (19 pts.) the mts. were symptomatic and in 7 eyes (6 pts.) non symptomatic. Additionally, 5/18 pts. had a CT following RT.

Results: With a median follow up of 10 months (range: 2–24 months), eight out of 18 patients were dead. All 12 symptomatic patients (n = 17 eyes) had at least a stabilization (n = 4, 24%), but in most cases a improvement in visual acuity (n = 13, 76%). A complete remission measured by ultrasound was seen in 50% (n = 12) of the treated eyes. The prominence regressed more than 50% in 25% (n = 6), less than 50% in 21% (n = 5) and was unchanged in 4% (n = 1). One patient developed a local recurrence without symptoms. One severe bilateral retinopathy following RT and later on CT and one asymptomatic opticus neuropathy was seen. The woman with the retinopathy had a decrease of visual acuity to 0.1 for both eyes after 4 months. Of the pts. with non symptomatic disease no one developed clinical signs of tumor progression.

Conclusions: RT with or without CT is highly effective in the treatment of symptomatic and non symptomatic choroidal mts. from breast cancer. However, "wait and see" and CT is another possible option for treating non symptomatic mts. The rate of severe late side effects is acceptable.

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Prognostic significance of axillary lymph node histology (pN) after neoadjuvant therapy for locally advanced breast cancer (LABC)

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Purpose: To evaluate the prognostic significance of the histopathological status of the axillary LN after neoadjuvant chemotherapy or radiotherapy in LABC.

Methods and Materials: 75 patients with LABC treated with neoadjuvant FEC or FEC + RT 50 Gy had a surgical exploration of axilla. The following endpoints have been studied: local and distant control, overall survival (OS) and disease-free survival (DFS).

Results: For the groups pNo, 1–3 pN+ and " 4pN+, the 5 yrs OS and DFS were 62, 67 and 22 per cent and respectively 47, 57 and 12% ($p < 0.01$). Patients operated after neoadjuvant FEC only, had a more favourable prognosis than those operated after FEC + RT who despite similar local control had a higher incidence of distant metastases (69 vs. 52 per cent).

Conclusions: Pathologic examination of axillary LN after neoadjuvant treatment for LABC offers important information by selecting a group of patients with favourable response to chemotherapy but this significance is lost after adding radiotherapy when the axillary control does not correlate with the risk of distant metastasis.

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Efficacy of antibody treatment with 17/1A on reduction of MRD after completion of high dose chemotherapy with transplan- tation of in vitro tumor cell purged PBSC grafts in high risk breast cancer patients

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Aim: To evaluate efficacy of in vitro immunomagnetic removal of TuCe (purging) from autologous peripheral blood stem cell (PBSC) grafts of BrCa pts. and to evaluate efficacy of immunotherapy with monoclonal antibody