Bre 11

PROSPECTIVE, RANDOMIZED STUDY OF ADJUVANT RADIATION AND CHEMOTHERAPY OF OPERABLE CARCINOMA OF THE BREAST

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In the time of 8/76 till 12/84 patients with operable carcinoma of the breast entered in a prospective study in which the value of postoperative radiation and adjuvant chemotherapy was to be tested. The composition of the series of patients studied is as follows:

	Positive lymph nodes	Therapy after mastectomy	Group	Number of patients	Mean follow up (months)
pT_{1-3}	1-3	Radiation + Chemotherapy	IA	75	66
pN_{1B-2}		Radiation	IB		
Mo	4->	Radiation + Chemotherapy	IIA	110	61
		Chemotherapy	IIB		

The radiation included 50 Gy to the thoracic wall and the regional lymph node areas (beginning ~ 12 days after mastectomy). The adjuvant polychemotherapy was administered in form of combined treatment with adriamycin (day 1,i.v., 40 mg/m²) and cyclophosphamide (days 3-6,per os,200 mg/m²) over a 12 month period (~ 8 - max. 12 cycles), beginning ~ 12 days after radiation (groups IA and IIA) or ~ 12 days after mastectomy (group IIB).

Results: Adjuvant chemotherapy appears to delay the time of recurrence for about two years. The frequency or recurrence is not influenced. The radiotherapy reduces the frequency of thoracic wall recurrences in patients with high grade of positive lymph node, the time of recurrence is delayed for about 10 months. Data according to the menopausal status, the histological grading and the steroid hormone receptor levels are shown as well as the side effects of adjuvant treatment.

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Bre 12

3-OH-TAMOXIFEN (CYTOGENT (n)): A NEW ANTIESTROGEN FOR THE TREATMENT OF HORMONE DEPENDENT MALIGNANCIES

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Hydroxylated tamoxifen derivatives (TAM) such as 4-OH-TAM and 3-OH-TAM in comparison to TAM exhibit a 10 times higher binding affinity to the estrogen receptor protein. After completion of präclinical investigationes (Eur.J. Clin. Oncol. 21, 985-990; 1985; J. Canc. Res. Clin. Oncol. 109, A 42, 1985), phase 1 trials were performed in postmenopausal patients with advanced breast cancer. After single doses of 20, 40 and 100 mg Cytogent (3-OH-TAM-citrate) notable side-effects on respiratory, cardiac and renal functions were not observed including metabolic parameters such as bilirubin, creatinine, urea, enzymes such as SGOT, γ-GT, LDH,AP,CPK. Effects on hemograms, electrolytes as well as hormones including E_1, E_2, progesterone, testosterone, FSH, LH, prolactin, DHEA-s and hormone binding protein SHBG were absent. Upon multiple dosing with 20 or 40 mg over a period of 3 weeks, no serious side-effects and no influence on common laboratory parameters except a tentative increase in SHBG were observed. Pharmacokinetic investigations were concomitantly performed to obtain information on bioavailability (20 mg tabl. formulation). The substance was absorbed quickly and maximum concentration of 25 ng/ml (n= 4) was reached in 1.2h. The terminal half-life was calculated to be 25h and a bioavailability of 92% indicated that the tablet is almost as bioavailable as the reference solution. Preliminary results indicated after daily dosing of 20 mg Cytogent over a period of 3 weeks that the accumulation factor did not exceed 2 and 3 for parent drug and N-desmethyl metabolite, resp. Currently, multicenter studies evaluating antitumoral effect of Cytogent are underway.

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Bre 13

RISK OF BREAST CANCER IN PATIENTS WITH MASTOPATHY - A LONG TERM FOLLOW-UP.

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The significance of mastopathy in the development of carcinoma of the breast in patients is still controversial. Earlier investigations report on a high risk of malignant development in patients with mastopathy. Recent studies fail to show an increased incidence of breast cancer in this group of patients. This prospective study presents the data of 852 patients who were treated for mastopathy in our department between 1965-1984. After a mean follow up of 10 years all patients were interviewed using a standard questioneer. The answers from 549 patients (64%) are reported here.

Results: Breast cancer developed in 35 out of 549 patients with mastopathy as a rate of 6.37%. A breast biopsy was performed in 203 of the 549 patients (37%) after suspicious clinical and/or mammographic fingings. 47 of this biopsied patients (23,2%) demonstrated a proliferative mastopathy on histological evaluation and only 3 pat. exhibiting in addition epithelial dysplasia. From the 47 pat. breast cancer developed 14, this representing a malignancy rate of 29,8% after a mean follow-up of 10 years.

Discussion: The clinical or mammographic finding of mastopathy is not associated with a significant increase in the rate of development of breast cancer, the rate being 6,37% as compaired to 5% in the general female population. In contrast to this the histological finding of proliferative mastopathy is associated with a significant increase in the rate of development of breast cancer. This rate of 29,8% is six times greater than that in the general female.

Conclusion:A breast biopsy is indicated in patients with clinical and/or mammographic diagnosis of mastopathy. If the histological investigation of the biopsy speciment shows a proliferative mastopathy, then frequent follow-up are neccessary as these patients are at a higher risk of developing breast cancer.

Bre 14

MRI(Magnetic Resonance Imaging) of the Breast

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150 patients have been examined by MR at our institution.50 of them have also been examined by MR after i.v.application of 0.2 mmol Gd-DTPA/kg as paramagnetic contrast agent.

Compared to mammography the following advantages of plain MR have been found: - improved visualisation of lesions close to the chest wall and of lesions behind silicon implants, - improved differentiation of well-circumscribed benign and malignant tumors based on their signal intensities on the T2-weighted images.Calculated T1- and T2-values did not further improve the diagnostic accuracy due to too much overlap.The major draw-backs of plain MR have been its inability to image microcalcifications, high costs and long examination times.The overall diagnostic accuracy of plain MR (150pts.)(sensitivity:88%,specificity:50%) was slightly inferior to mammography (sens.:90%,spec.: 62%).

In the 50 patients examined by MR with Gd-DTPA the following has been found:All benign and malignant tumors did enhance(including carcinomas with microcalcifications),whereas scar tissue and non-proliferative dysplasia did not enhance. Thus both the visualization of lesions (especially in dense breasts)and their differentiation were improved leading to a higher sensitivity and specificity (100%,73%) compared to mammography (76%,63%) and plain MR (74%,73%).

Based on our first experiences MR of the breast with Gd-DTPA may be especially helpful in patients with extensive scarring,in patients with a prosthesis or other patients, where both clinical and radiological examination are difficult.

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This study is supported by the Dt.Krebshilfe.