1802

Adjuvant Systemic Therapy of Node-Negative (N0) Breast Cancer (BC) Patients with Immunohistochemically Detected Occult Tumor Cells (OTC) in Lymph Nodes and Bone Marrow Does notImprove Outcome. *A. Krause, B. Gerber, H. Müller, D. Richter, T. Reimer, G. Kundt, K. Friese; University of Rostock, Rostock, Germany*

The detection of occult tumor cells (OTC) in histologically tumor-free axillary lymph nodes or bone marrow has raised the question as to whether such findings become a further indication for systemic adjuvant therapy. We have studied the effects of given adjuvant treatments in relation to the detection of OTC in node negative pts. Pts. & methods: Lymph nodes and bone marrow aspirates of 484 pts. with conventionally pT1–2N0M0 BC were retrospectively examined for OTC using a cytokeratin (8, 18, 19) antibody and ABC-technique. The given adjuvant therapy (20 mg Tamoxifen over 5 years or 6 cycles of CMF) according to the St. Gallen Consensus conference recommendations was correlated with the immunohistochemical findings. The status of OTC was unknown for adjuvant treatment decision. The mean follow up time was 68 + 18 months. Results: In 180 of 484 (37.2 %) pts. OTCs were detected in lymph nodes and/or bone marrow aspirates. Systemic adjuvant therapy was given to 246 of 304 (80.9 %) pts. without OTC and to 151 of 180 (83.9 %) pts. with OTC. According to the Consensus Conferences, a systemic adjuvant treatment had to be recommend in 85.2 % of OTC-free and 90 % of OTC-positive patients. Five- and 10-year disease-free survival (DFS) and overall survival (OAS) between adjuvant treated and untreated patients were not significantly different. Conclusion: Although the detection of occult tumor cells in conventionally staged pT1–2N0M0 breast cancer patients represents a prognostic disadvantage, systemic adjuvant treatment in these pts. will not improve the prognosis.

	OTC negative			OTC positive		
	Adjuvant therapy		Log-Rank	Adjuvant therapy		Log-Rank
	yes (n=246)	no (n=58)	p	yes (n=151	no (n=29)	p
DFS 5 years	0.92	0.96		0.74	0.70	
DFS 10 years	0.71	0.87	0.23	0.64	0	0.36
OAS 5 years	0.95	0.96		0.85	0.78	
OAS 10 years	0.93	0.96	0.35	0.71	0.66	0.37

1803

Dose-Density Therapy with Docetaxel and Mitoxantrone for Patients with High Risk Metastatic Breast Cancer. *E. Koenig, C. Kurbacher, M. Breidenbach, P. Mallmann; University of Cologne, Cologne, Germany*

Docetaxel (DCT) and Mitoxantrone (MX) are active drugs in Metastatic Breast Cancer (MBC). Prior studies have shown, that the combination of DCT and MX is highly effective in MBC. This pilot study was conducted to evaluate the effectiveness and toxicity of the combination of dose-dense (DD) DCT and MX in pts. with high risk MBC. Twenty-two patients aged <71 years were enrolled. The average age was 52.7 ± 1.8. 77 % of the pts. had visceral metastasis, the average number of metastatic sites was 2. Pts. received DCT at 35 mg/m2 q1w and MX at 6 mg/m2 q2w during the first 6 weeks of an 8 week interval. Pts. with regression or steady-state continued the treatment for a maximum of two more 8 week periods. Toxicity was recorded according to the WHO common toxicity score. If necessary, pts. received granulocyte-colony stimulating factor. During this study 81 % (n = 18) benefited from the regimen with 45 % and 36 % showing PR and SD, respectively. In 18 % of the pts. a PD was registered. A grade 3 leucopenia was present in 14 pts (64 %). However, no pt was hospitalized due to leucopenic fever or any other life-threatening toxicity. Other hematologic and non-hematologic side effects did not exceed grade 2. We conclude that the DD administration of DCT and MX is a promising, relatively well-tolerated, clinically feasible regimen for MBC with unfavorable prognosis. Confirmatory large-scaled clinical trials have to be performed.

1804

Significance of DPD Activity in Tumor Tissue or Lymph Nodes in Cases of Breast Cancer. *T. Kataoka, T. Kadoya, K. Sugi, M. Takahashi, R. Haruta, S. Okimasa, H. Hashimoto, K. Sugino, T. Asahara; Hiroshima University, Hiroshima, Japan*

PURPOSE: Dihydroxypyrimidine dehydrogenase (DPD) is one of the key enzymes in the metabolism of 5-fluorouracil (5-FU) in vivo. We therefore measured the DPD activity to determine whether it could be used to predict the effects of treatment with FU derivatives. MATERIALS & METHODS: The materials used in this study were tissues obtained from 61 patients who had undergone operations during the period from January 1998 to June 1999. The 61 patients included one group of 14 patients who were given 600 mg of UFT daily for 5 days preoperatively and one group of 47 patients who were not given UFT. The DPD activities in tumor and normal tissues, in metastatic and normal lymph nodes, and in mononuclear cells in peripheral blood were measured. The concentrations of FU in the tumor and in serum of each patient in the UFT-treated group were also measured. RESULTS: (1) Mean levels of DPD activity in the tumor tissues, in lymph nodes and in mononuclear cells were significantly higher than that in normal tissues; (2) DPD activities in tumor versus normal tissues and also in metastatic versus normal lymph nodes showed strong positive correlations; (3) the concentration of FU and DPD activity in tumor tissues and also in metastatic lymph nodes showed a negative correlation. CONCLUSION: The result that the concentrations of FU were lower in patients with high DPD activities in tumor tissues or lymph nodes suggests that the decomposition of 5-FU was promoted by DPD. Thus, the dosage of FU derivatives should be adjusted so as to maintain a high concentration of FU. Moreover, the fact that DPD activities were significantly higher in tumor than in normal tissues suggests that control of the DPD activity would contribute to enhancing the effect of FU derivatives in vivo.

1805

Tamoxifen and Toremifene Treatment of Breast Cancer and Risk of Subsequent Endometrial Cancer - a Population-Based Case-Control Study. *E. Pukkala, S. Maijanen, P. Kyyrönen, R. Sankila, K. Holli; Finnish Cancer Registry, Helsinki, Finland; IARC, Lyon, France; Finnish Breast Cancer Group, Tampere, Finland*

A population-based case-control study was performed to evaluate the risk of endometrial cancer related to tamoxifen or toremifene treatment. All patients with breast cancer diagnosis since 1980 in Finland who subsequently developed an endometrial cancer by end of the year 1995, and three matched controls were identified among the 38 000 breast cancer patients of the Finnish Cancer Registry database. Detailed information on treatment of breast cancer and potential confounders related to endometrial cancer were collected from hospital records. The odds ratio (OR) for tamoxifen treatment, adjusted for significant co-factors (increased risk associated with obesity, low parity, and progesterone receptor positivity) was 2,9 (95% CI 1,8–4,7). The OR for toremifene, based on three cases and six controls, was 0,9 (95% CI 0,3–3,9). The OR related to adjuvant tamoxifen treatment reached its maximum already 2–5 years after usage (OR 5,1, 95% CI 2,1–13), while the OR for tamoxifen used for advanced breast cancer was especially high after a lag of over five years (OR 9,5, 95%CI 2,5–36). The risk increase due to tamoxifen was slightly higher if the age at the initiation was below 50, and risk was more pronounced in well differentiated endometrial cancer than in cancers of clinical gradus 2 or 3. According to this study, treatment with tamoxifen evidently increases the risk of endometrial cancer. Tamoxifen seems to have at least a promoting effect but longer treatment used in advanced disease indicated also an initiator effect. Concerning toremifene, due to its rare use up to the mid-1990s, we can not draw conclusion regarding the potential risk of subsequent endometrial cancer.