cancer. T is synergistic with several cytotoxic drugs such as vinorelbine (V), gemcitabine and taxanes.

Objective: We have assessed the activity of vinorelbine plus tratuzumab in patients with erb-B2 overexpressing metastatic breast cancer.

Patients and methods: From January 1999 to October 2002, 15 patients have been treated with Vinorelbine 30 mg/m2/week plus trastuzumab 4mg/kg (first week) followed by 2 mg/kg/week. All patients had +++ erb-B2by immunohistochemistry in the primary tumor.

Results: Overall, 297 treatment courses were given (median = 36 courses per patient, range 4-48+). Median age was 48 (range 31-67). Median time from diagnosis to first relapse was 20 months (range 11-63). Number of prior chemotherapies for metastatic breast cancer was 1 (0-3). The most relevant toxicity was grade 3 leukopenia requiring omission of Vinorelbine in 35 courses. Grade 1-2 neuropathy in most patients receiving more than 10 courses was treated with gabapentin and did no require treatment discontinuation. One patient achieved a complete response (6.6%), 9 patients had a partial response (60%), one patient (6.6%) had stable disease for more than 2 months and 4 (26.6%) had progressive disease. Median time to progression was 24 weeks (range 4-56). Median survival was 36 weeks (range 4-130+).

Conclusions: Weekly Trastuzumab plus Vinorelbine is an active and well tolerated treatment option for patients with erb-B2 overexpressing metastatic breast cancer

998 POSTER

A phase II study of a novel taxane BAY 59-8862 in patients with aggressive refractory non-Hodgkin's lymphoma

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BAY 59-8862 (BAY) is a novel second-generation taxane. Compared to paclitaxel and docetaxel, it is 20-30 fold more potent as a growth inhibitory agent against human breast and colon tumor cell lines expressing P-glycoprotein 170. BAY is also active against multidrug resistant human colon xenografts. This phase II study was conducted to assess the efficacy (response rate) and toxicity of BAY in patients (pts) with Aggressive Refractory Non-Hodgkin's Lymphoma. BAY (75 mg/m2) was administered intravenously over 60 minutes every 3 weeks. Pts eligible were pts with Aggressive Refractory Non-Hodgkin's Lymphoma and having received no more than 3 prior chemotherapy regimens; with performance status 0, 1 or 2, adequate hematology and biochemistry; and at least one bi-dimensionally measurable lesion. Between March 2002 and March 2003, 29 pts entered the study: 9 female, 20 male; median age was 60 years; performance status 0/1/2 was 9/18/2. All were eligible and evaluable for toxicity. To date 19 pts are evaluable for response (4 pts too early for assessment, 6 pts had no repeat imaging). Number of prior chemo regimens was 1 (4), 2 (13), 3 (11), 4 (1). The median number of treatment cycles was 2 with 5 pts receiving 4 cycles of therapy and 1 pt receiving 7 cycles of therapy. Common grade drug related effects (study dependent) included nausea (9), fatigue (8), vomiting (3), peripheral neuropathy (3), anorexia (3) and skin rash (1). Grade 3-4 hematologic toxicities included neutropenia (15), anemia (6) and thrombocytopenia (3). Seven minor responses were observed out of the 19 pts now evaluable for response. Four pts continue on treatment to date. The recruitment is currently on hold and the interim analysis ongoing.

999 POSTER

Immunomonitoring in stage II melanoma patients treated with adjuvant GM-CSF

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Background: The importance of GM-CSF in the adjuvant treatment of skin melanoma has been discussed. We evaluated immunologic effects of postoperative immunotherapy with GM-CSF in stage II melanoma patients (pts).

Methods: 15 pts with stage T N M of skin melanoma were treated with low-doses of GM-CSF (1 mkg/kg, s.c., three days per week) for 1 year after surgical excision of the primary tumor(study group). Results were compared with 15 pts who received no adjuvant treatment after surgery (control group). All patients had ECOG performance status of 0. The median age was 41.2 years in the study group and 47.1 years in the control group. The men-women ratio was 1:2 in both groups.

Results: Before treatment the level of NK cells in study group was 2 times higher than normal ($p<0.001$). The level of HLA class I molecules as well as CD4, CD22, CD38 molecules was reduced ($p<0.05$). The immunological values of all others were within normal values. During therapy with GM-CSF an increase of HLA class I molecules expression, activated lymphocytes (CD38), helper T cells (CD4) and B-lymphocytes (CD22) and a decrease of NK cells (29,3 vs. 12,1) were shown ($p<0.05$). The percentage of CD8+T cells was 32,7 and 21,4 before and after treatment, respectively (t=1,95). The CTL cells depression may be explained by their migration to lymph node tissue. We observed an escalation of monocyte and lymphocyte count in study group ($p<0.05$). Three-year overall survival was 84,6% in study group and 66,5% in control group. The time to progression was 422,7 months in the study group and 356,5 months in the control group.

Conclusions: The adjuvant immunotherapy with GM-CSF induces tumor-specific immune response with an increase of HLA class I molecules expression. Despite the fact that both groups developed regional and distant metastases, survival rate of the study group patients was higher.

1000 POSTER

Pioglitazone and rofecoxib combined with angiostatic scheduling of chemotherapy in far advanced malignancies

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Purpose: Combined tumor- and stroma-cell targeted therapies might control chemorefractory malignancies.

Experimental design: A phase II trial was initiated to analyze the activity of a continuously administered molecular-targeted therapy (daily 45 mg pioglitazone po and 25mg rofecoxib po) combined with sequentially added angiostatic scheduled chemotherapy, in metastatic neoplasias with intrinsic or acquired drug resistance: Indication group A (67 cases) received capecitabine 2x1g/m^2 po from day 14 to 28, every 3 weeks, indication group B (37 cases) trofosfamide 3x50mg po daily, day 14+.

Results: Up to now 104 patients (pts) with 21 different tumor types are evaluable. Major side effects (WHO grade 3 and 4) were due to hand-foot-syndrome in 7 cases. Clinical response (CR, PR, SD > 6 months) occurred in 28% of the patients in Group A and B, in 25 and 40% of the patients with acquired and intrinsic drug resistance, respectively. A more than 50% decrease of tumor-associated CRP levels during treatment with the biomodulators alone was significantly associated with clinical response, p= 0.001.

Conclusions: This is the first study to show that novel therapeutic approaches including anti-inflammatory, angiostatic and cytostatic therapy are effective, with manageable toxicity profile in a range of chemorefractory malignancies.

1001 POSTER

Novel strategy of mature dendritic cells generation, suitable for adoptive immunotherapy of the ovarian cancer patients

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Background: The significance of adoptive immunotherapy in clinical oncology now clearly is not determined. There is increasing clinical interest in dendritic cells (DC) that are capable to initiate antitumor immune responses. Modern strategies of the generation of mature DC, pulsed with tumor antigens, have been shown to be effective methods. However, search of more simple and convenient methods of DC generation is object for future studies.

Material and methods: As a sourse of DC we used exudate from abdominal cavity, collected during 15 hours after tumour removal. CD45$^+$ 14$^+$-cells, isolated by plastic adherence, were cultured with 1.000 U/ml human granulocyte-macrophage colony-stimulating factor and 100 ng/ml lipopolysaccharide within 7 days. After 5 days of incubation DC were loaded with autologous tumor lysate (0,5 μ g/ml of protein, 1 $\times$ 10^7 cells). Surface marker analysis of DC was performed by flow cytometry and mAb- anti-CD3, CD20, CD16, CD14, CD86, HLA-DR. Function of DC in vitro and cytokines presence in DC supernatant were determined by study of their ability to stimulate of autologous and allogeneic lymphocyte proliferation. Pilot study