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CLINICAL EXPERIENCE WITH rH GM-CSF(LEUCOMAX) IN ADVANCED NEOPLASIAS

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RH GM-CSF is a major regulator of myelopoiesis, induces production of other cytokines and elicits systemic immune response(Burdach S,1993). Using the retroviral vector MFG in conjunction with short term culture technique,it has achieved (in primary renal,ovarian and pancreatic tumor explants) an autologous GM-CSF vaccine for clinical trials(a gene therapy for human cancers)(Jaffee EM et al,1993).

We have studied the effect of rh GM-CSF (Leucomax) on myelosuppressive states in a number of 1o patients with advanced neoplasias.
There were 3 men and 7 women,aged 24-68 years.
Diagnosis: 5 cases of advanced breast cancer,esophagus,NSCLC,Melanoma,STS and Hodgkin's disease each one case;8eight cases have had metastatic cancer,2 patients have had minimal residual disease (MRD).
The goal of the treatment was to decrese the myelosuppression and thus to continue chemotherapy, and to decrease immunosuppression and its consequences.A course of Leucomax consisted in administration of 3oo micrograms sc,daily for 5 consecutive days.All cases received 1-2 courses of Leucomax. Results.All patients have had a beneficial effect;neutrophil count recovered to normal levels within 4-5 days.
These results show that Leucomax is a useful agent in the treatment of myelosuppression,cancer and immunosuppression.

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IMMUNOTHERAPEUTIC APPROACHES DIRECTED AGAINST MINIMAL RESIDUAL CANCER.

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Occult micrometastatic spread largely determines the prognosis of patients with solid epithelial tumours which account for more than 80% of all cancer-related deaths in western industrialized countries. Our group has recently demonstrated the reliability and prognostic relevance of an immunocytochemical assay with monoclonal antibodies against cytokeratins that allows the specific detection of individual micrometastatic carcinoma cells derived from various epithelial organs. With regard to adjuvant therapy, the question arose whether our immunocytochemical assays can be used for predicting and monitoring the therapeutic response of micrometastatic tumour cells in bone marrow. In a pilot study, seven breast patients were treated with 6 x 100 mg of the mAb BR55-2 (SDZ ABL 364) to the Lewis Y blood group precursor antigen. Five out of the seven antibody-treated patients showed a distinct reduction of CK-positive/BR55-2-positive tumour cells. In contrast, no response was observed in the three placebo-treated control patients or those two patients who received BR55-2 but presented only with CK-positive/BR55-2-negative tumour cells.
Numerous study have shown that patients with solid cancer metastasis are quite resistant to antibody therapy. We therefore designed a randomized clinical trial in which the epithelial-specific monoclonal antibody 17-1A was targeted to microscopic residual disease in patients with colorectal cancer (stage Dukes C). 189 patients were randomly assigned to an observation regimen or to postoperative treatment with 500 mg of 17-1A antibody, followed by four 100 mg infusions each month. Toxic effects of 17-1A antibody were rare, consisting mainly of mild constitutional and gastrointestinal symptoms. After a median follow up of five years, the antibody treatment reduced overall death rate by 30 percent and the recurrence rate by 27 percent (Riethmüller et al., Lancet 343:1177-1183, 1994). This effect was most pronounced on the manifestation of distant metastases as first event ($p = 0.0014$), an effect which was not seen for local relapses ($p = 0.74$).
Our data provide first prove that monoclonal antibody treatment applied in the stage of minimal residual disease can be indeed effective. Monoclonal antibodies to cytokeratins are reliable probes for the detection of individual cancer cells in bone marrow, and the use of these cells as surrogate markers for the efficacy of adjuvant anti-cancer therapy is desirable.