Results: Fever and myalgia due to rINF-α2b controlled with acetaminophen was seen in 86% of the cases. Six complete response and one partial response was achieved. Pruritis significantly improved in 80% of (4/5) the cases. Recombinant interferon alpha had to be discontinued in one patient because of grade 3–4 nephrotoxicity according to WHO criteria. Recombinant interferon alpha therapy significantly improved phlebotomy requirements, MCV values, erythrocyte and platelet counts, pruritis complaints and the degree of splenomegaly.

Conclusion: Recombinant interferon alpha seems to be an effective treatment modality for the myeloproliferation of polycythemia vera and pruritis complaints.

391 PUBLICATION

Antimetastatic activity of viral oncolysates

L. Urazova, A. Gromova. *Cancer Research Institute, Tomsk, Russia*

Purpose: Antimetastatic activity of oncolysates obtained from cells of melanoma B-16 and treated by attenuated strain of Venezuelan Encephalomyelitis Virus has been studied.

Methods: Experiments were performed on C57 Bl/6 mice. The tumor strain (Melanoma B-16) was inoculated to animals. The primary tumor was removed 10 days after inoculation and postoperative immunotherapy using viral oncolysate was performed 14 days after inoculation. On days 24–26 metastases in lungs were calculated.

Results: There was found the increase in the index of metastatic spread inhibition from 88 to 100% depending on the schedule of oncolysate administering.

Conclusion: The possible mechanism of this therapeutic effect and its potential for clinical application are discussed.

Hematological malignancies and high-dose chemotherapy

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An in vivo model for multiple myeloma

M. Gramatzki, R. Burger, S. Kucher, H. Steininger, W. Baum. *Division of Hematology/Oncology, Department of Medicine III and Department of Pathology, University of Erlangen-Nuernberg, Erlangen, Germany*

The growth of malignant plasma cells in vitro is regulated by cytokines of the IL-6-family and IL-6 itself has been shown to be an important growth factor in vivo. Our aim was to develop a preclinical tumor model for human multiple myeloma. Therefore, the two plasma cell lines JK-6 and the IL-6-dependent INA-6 line were injected into irradiated SCID mice subcutaneously (sc), intraperitoneally (ip) or intravenously (iv). Some animals received recombinant human IL-6 (1 μg, ip, twice a week) (kindly provided by Sandoz). JK-6 grew as sc, ip or iv tumor with infiltration of spleen, liver, and bone marrow. In some cases, plasma cells were detected in blood smears. IL-6-dependent INA-6 cells gave rise to ip tumors which, in contrast to JK-6, led to development of ascites in these mice around day 80 to 90. Surprisingly, these INA-6 xenografts did not require IL-6 injection for proliferation in SCID mice, however when recultured in vitro after excision were strictly IL-6-dependent again. As mouse IL-6 is known not to act on human cells, the role of other cytokines of the gp130 family is currently under study. To our knowledge, this is the first xenograft tumor model for multiple myeloma with an IL-6 dependent human cell line, allowing to study growth regulation by cytokines in vivo. New therapeutic strategies including immunotherapy may be studied in this unique tumor model.

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Vinorelbine (VRL) in patients with recurrent multiple myeloma (MM): A phase II study

J.L. Harousseau[1], F. Maloisel, J.J. Sotto, Th. Facon, T. Child, S.M. Kelsey, S. Johnson, B. Descheemaker[2], L. Moore[2]. [1]*Service d'hématologie, Hôtel-Dieu, Nantes;* [2]*Pierre Fabre Oncologie, Boulogne, France*

Vinorelbine, a new semi-synthetic Vinca-alkaloid, is a potentially new alternative in the treatment regimen of MM. 33 patients (15 women, 18 men), aged 55 to 76 (median 66) with stage II–III MM, relapsing after one or two conventional chemotherapies or after one high dose chemotherapy were included. VRL was administered at 20 mg/m2 on D1 and D4 every 21 days in the first cycle. If the tolerance was good, the daily dose was escalated to 25 mg/m2 in the subsequent cycles.

Out of the first 33 patients, 2 patients were ineligible, 1 patient died after one cycle of treatment with a background of aortic insufficiency. 5 patients were non-evaluable, 2 developed a cardiac toxicity after a long-standing heart disease, and 1 a severe acute sepsis. Patients received a total of 148 cycles (1–18 cycles, median 3 cycles). The mean dose-intensity on 138 cycles (D1 and D4) of VRL was 21.64 mg/m2. From 22 evaluable patients for efficacy, 5 had a partial response (PR), and 2 a minor response (MR). 9 patients were stabilized and 6 progressed. The overall response was 33% (IC 95: 12–52%), and in intention to treat analysis 21% (IC 95:7–35%). The median time to progression among the 33 patients was 119 days (10–809). Toxicity was mainly hematologic, with grade 3–4 neutropenia mainly (cycles 1 and 2). There was no major toxicity on platelets or hemoglobin. There was one infection without grade 4 neutropenia. Non hematologic toxicity was observed very rarely (one grade 4 vomiting and diarrhea, no neurologic constipation).

Our results are comparable to those obtained with high dose dexamethasone (Alexanian et al, 1986). In summary, these preliminary data show that VRL monotherapy is active in recurrent MM. A phase II study combining VRL + dexamethasone is currently underway in relapsed MM patients.

394 ORAL

A placebo-controlled study of epoetin alfa in multiple myeloma (MM) patients with anaemia

F. Dammacco. *On behalf of the r-HuEPO multiple myeloma study group; Dept. of Internal Medicine and Clinical Oncology, University of Bari, Italy*

Purpose: This international, multi-centre, double-blind study evaluates the effect of treatment with epoetin alfa (EPO) or placebo on transfusion need and severity of anaemia in MM patients undergoing chemotherapy (CT).

Methods: 145 MM patients with anaemia (haemoglobin < 11.0 g/dL), who had received at least 6 months of CT, were stratified according to pre-study transfusion need and randomised 1:1 to EPO (150 IU/kg 3 × week, SC) or placebo, with a possible dose increase after 4 weeks depending on the haemoglobin (Hb) response. The study consisted of a 12 week double blind phase, followed by an optional 12 week open label phase (not reported here).

Results: 28% of EPO treated patients required transfusions during study months 2 or 3 versus 47% of placebo treated patients ($p = 0.02$, Fisher's exact test, "intention to treat" population). There was no significant difference between the treatment groups in the proportions of patients with pre-study transfusions (36% and 37%, $p = 1.00$, Fisher's exact test). Time to first transfusion after at least 1 month on-study was prolonged in the EPO treatment group ($p = 0.05$, log-rank test). The proportions of Correctors (achieved Hb ≥ 12 g/dL) and Responders (Hb increased ≥2 g/dL above baseline) were higher in the EPO group (38% and 47%) than in the placebo group (3% and 5%, $p < 0.001$, Fisher's exact test, efficacy population).

Conclusion: Treatment with EPO is effective in reducing transfusion need and correction of anaemia in MM patients undergoing cytotoxic CT.

395 ORAL

Cladribine (CdA) therapy in chronic lymphocytic leukemia (CLL) – Long-term follow-up of 117 patients

Gunnar Juliusson, Mats Strömberg, Jan Liliemark. *European Collaborators; Dept of Hematology, University Hospital Linköping, and Radiumhemmet, Karolinska Hospital Stockholm, Sweden*

CdA is effective therapy for CLL. We have treated 117 patients with symptoms with CdA in 5-day monthly courses. Previously treated patients had 0.12 mg/kg/day in 2 hour iv infusions (n = 53), and untreated patients had the corresponding dose 10 mg/sqm/day orally (n = 64). There were 56 patients in Binet stage C (48%), 22 in stage A (19%) and 39 in stage B (33%). Median age was 62 years (range 38–88 yrs), and the median lymphocyte count was 70 × 10 (9)/l (range 5–460). CR rate according to NCI criteria was 35%, and 32% had PR. Response rate was correlated to Binet stage ($p = 0.007$) and to number of previous regimes ($p = 0.025$), with a 41% CR rate among those with one or no previous regime. Fifty-nine patients (50%) have died, with a median survival of 20.5 months. The median observation time of surviving patients is 3 years (range 18–71 months). The three-year and median survival of patients who achieved CR (n = 41) are 82% and 5.7 years, PR (n = 38) 63% and 3.3 yrs, and NR (n = 38) 13% and 0.9 yrs. Previously untreated patients (n = 64) had a 3-yr survival of 68% (median not