without the toxicities associated with systemic application. We report on the following aspects:

(1) *Protocol:* Intra/peritumoral application of IL-2 is most effective in the dose range of 7,000–33,000 IU/day, injected for 5 consecutive days.

(2) *Sensitive tumour types:* This therapy induced cures/complete remissions in mice with breast cancer, lymphosarcoma, fibrosarcoma, mastocytoma; rats with bladder carcinoma; guinea pigs with liver carcinoma; cattle with spontaneous ocular squamous cell carcinoma (OCC); horses with spontaneous sarcoids; human patients with T1/G1G2 marker lesions of superficial bladder carcinoma.

(3) *Potency of IL-2 therapy:* This therapy induces cures in mice with severely infiltrated and metastasized lymphosarcoma comprising at least 5% of the body weight and complete remissions of spontaneous OCC of up to cm^2, and spontaneous sarcoids of up to 20 cm^2 surface in horses.

381 POSTER

Long-term therapeutic efficacy and toxicity of recombinant interferon-alpha 2a in Polycythemia Vera

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Purpose: To assess long-term therapeutic efficacy and toxicity of recombinant interferon alpha 2-a (IFN) in a series of 38 patients with Polycythemia Vera (PV).

Methods: In all patients haematocrit (PCV) was first brought into the normal range by venesection; IFN was then begun at a starting weekly dose of 9,000,000 I.U. Complete response (CR) was defined as persistence of normal PCV without phlebotomies; partial response (PR) as >50% reduction of venesection requirement.

Results: Eleven patients (28.9%) achieved CR and 8 (21.0%) PR. Median duration of response was 40 months; 12 responsive patients are still under treatment after 13, 15, 25, 35, 40, 41, 43, 49, 50, 51, 52 and 52 months. Both in CR and PR patients IFN also mormalized leukocyte and platelet counts besides relieving symptoms as generalized pruritus. As far as late toxicity is concerned, 13.1% of patients experienced severe weakness leading to treatment discontinuation. No case of leukemia/solid tumours was observed in PV patients treated with IFN.

Conclusion: IFN is an effective and safe long-term treatment for PV.

382 POSTER

Application of a novel growth suppressing gene, *tob*, for gene therapy of pancreatic cancer *in vitro*

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Purpose: Recently, a novel gene, termed *tob*, encodes a 38-kDa protein with homologous to the growth suppressing protein Btg-1 was identified. Elevated expression of the Tob protein suppressed growth of the NIH3T3 cells. In this study, we evaluated the *tob* expression in the pancreatic cancer cell lines, and have presented to the conditions for the transfection of adeno-viral vector containing *tob* cDNA (Ad-tob vector).

Method: Human pancreatic cancer cell lines, AsPC-1, BxPC-3, SOJ, were used. RNA blot hybridization was performed on samples cell lines using the 1.0 kbp HindIII fragment of ^{32}P-labeled *tob* cDNA. Transfection of Ad-tob vector was performed in these cell lines.

Results: The *tob* mRNA was expressed in every pancreatic cancer cell line, and the level of the *tob* mRNA of AsPC-1 cells was strongest. The titer of the Ad-tob vector was 3.5×10^8 pfu/ml. Transfection of adeno-viral vector containing *lac*-Z gene to pancreatic cancer cells revealed that these cancer cells were able to be transfected with high MOI from 50 to 100 without adeno-viral toxicicity.

Conclusion: Exogeneously expressed Tob exhibits the suppression of cell growth, therefore it may be possible to apply Ad-tob vector in gene therapy.

383 POSTER

A phase I trial of escalating repeated doses of PNU-214565 in patients with advanced colorectal and other gastrointestinal adenocarcinomas

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A T-cell-based therapeutic modality for carcinomas of gastrointestinal origin was provided by generation of a fusion protein consisting of the superantigen staphylococcal enterotoxin A (SEA) and the Fab fragment of the monoclonal antibody C242, reacting with human colorectal (CRC), pancreatic carcinoma (PC) and other adenocarcinomas of gastrointestinal origin (AGO), independently of MHC class II interaction. Based on the results of prior single dose phase I studies with this fusion protein PNU-214565 (formerly designated LS 4565) the starting dose with repeated doses (four consequtive days) was determined to be 0.5 ng/kg. A total of 11 patients with CRC, 5 with PC and 4 with AGO were treated with doses ranging from 0.5 ng/kg to 4.0 ng/kg. Three patients treated at 0.5 ng/kg and 1.5 ng/kg respectively, had only mild adverse events. At 4.0 ng/kg, two patients experienced dose limiting toxicities (DLT): The first patient developed transient grade IV vomiting, thrombocyto- and leucopenia, hyperbilirubinemia together with a acute renal failure requiring 5 weeks of dialysis before normalisation. The second patient had grade IV hepatotoxicity and thrombocytopenia lasting for 5 days. Of 12 patients treated at the next lower dose, 2.75 ng, only one developed DLT, a grade IV hypotension easily managed with Dopamine. Accordingly, the maximum tolerated dose was 2.75 ng/kg. However, analysis of the compiled data from all previos trials with PNU-214565 has indicated a correlation between pretreatment anti-SEA antibodies and the dose of PNU-214565 needed to induce effects/side effects of the drug. Clinical trials are now being carried out to test this correlation.

384 POSTER

Bcl2 and p53 expression in platinum and irradiation sensitive and resistant human ovarian cancer cells

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Purpose: Apoptosis is regulated by different genes equally involved in cell cycle and cell death (eg., Bcl2, p53). Apoptotic cells observed in tumors may govern curability. Therefore, we evaluated the expression of Bcl2 and p53 in Cisplatin (CDDP) and ionizing radiation (IR) sensitive and resistant human ovarian cancer cells.

Methods: Tumor cells were cultivated in tissue culture flasks. Sensitive cells were made resistant to CDDP and IR by chronic exposure. The resistance factor at the 50% survival level was 3.6–5.1 for CDDP, and 1.7–2.0 for IR. The resistance was stable after withdrawal of the drug. The sensitive cells were diploid. The DNA index of the resistant cells was 1.76–1.84. Cell survival after cytotoxic exposure was evaluated by clonogenic assay. The expression of Bcl2 and p53 was analyzed by immunochemistry on paraffin-embedded cells.

Results: CDDP and IR sensitive and resistant cells were both associated with a positive Bcl2 and p53 expression. There was no significant difference between both.

Conclusion: The difference in sensitivity of the tumor cells to CDDP and IR did not correlate with any change in expression of Bcl2 or p53. Therefore, the different expression reported as predictor for the sensitivity of tumor cells to cytotoxicity needs to be further evaluated.

385 POSTER

Intraperitoneal (IP) interferon A2b (INF) consolidation in cCR ovarian cancer (OC) patients following carboplatin chemotherapy (CT)

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Purpose of this study was to assess the feasibility and tolerance of IP IFN consolidation treatment as well as the overall survival of OC patients following clinical complete remission (cCR) after Carboplatin CT. Since May 92, 83 women with median age 56, PS 1 entered the study. 74.4% had