PR patient relapsed after 24 mo. The three patients with PD at inclusion progressed, whereas the SD patient remained stable throughout the study. No dose reductions were necessary. IL-2 induced fever, aches, fatigue and inflammation at injection sites. Maxamine injections induced short-lasting symptoms from vasodilatation, such as headache, flush, mild hypotension and tachycardia.

Conclusion: Maxamine given as an adjunct to immunotherapy in myeloma patients after PBSCT is safe and feasible. Future studies will focus on non-progressive patients.

1441 POSTER

Human monoclonal antibody immunotargeting therapy for colon cancer

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Purpose: A human monoclonal antibody (HuMAb) SK1 recognizes a glycoprotein that is expressed on the majority of colon cancer tissues. We previously demonstrated that the antibody strongly inhibits the cancer cell invasion *in vitro* and accumulates efficiently to cancer tissues *in vivo*. The current study was performed to evaluate the safety and the pharmacokinetics of escalating dose of a HuMAb SKI in patients with advanced colon cancers.

Patients and Methods: HuMAb SK1 was administered intravenously at 2, 4, 10 mg once in two weeks, totally 3 times to three consecutive groups of three patients with recurrent colon cancer who had been extensively pretreated.

Results: Among nine patients treated, slight fever that subsided without medication was seen in one patient. There were no tumors that showed complete response (CR) or partial response (PR) to the therapy. However, in 6 out of 9 patients, the rate of rise of serum CEA level reduced significantly during 4 weeks following treatment ($p = 0.042$), and the similar tendency lasted for the next 4 weeks ($p = 0.049$). In 4 patients, serum titer of anti-idiotypic IgG antibody to SK-1 continued to increase during at least 8 weeks following the treatment.

Conclusion: HuMAb SK-1 can be safely administered. This natural antibody not only possesses a direct cytostatic activity against colon carcinoma, but may induce carcinoma-related, anti-idiotypic antibody responses.

1442 POSTER

3-Fold increase in survival for stage IV melanoma patients treated with MCV allogeneic vaccine: Confirmation of previous phase II data

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Treatment of metastatic melanoma with chemotherapy and immunotherapy has not significantly improved the overall survival, although some responders on IL-2 based regimes have had a long term survival of some years. The only significant claim of increased survival has been associated with the PMCV vaccine developed by Morton and colleagues at the JWCI. In previous phase II studies they have claimed 2 year survivals of between 40–60% in Stage IV patients depending on the extent of surgery. Prior to commencement of a multi-centre randomised study we independently assessed the effect of this vaccine on patients with Stage IV melanoma. From August 1994 to August 1997, 33 patients with Stage IV melanoma, 17 female and 16 male, 13 stage IV M1a & 20 M1b, performance status = 0 were treated in a single institution phase II study in the U.K. with PMCV & BCG. The protocol stipulated extensive surgical excision prior to entry to render patients, if possible, to NED (no evidence of disease) status. Twenty-five surgical episodes were recorded for these patients to conform to the eligibility criteria. A further 60 surgical episodes have been recorded to date in patients continuing on vaccine treatment. Clinical responses, by WHO criteria, were recorded in only 3 patients (1CR & 2PR, all in soft tissue). With a median follow -up of 3 years, the survival of these patients is 110 weeks (CI 95% 72–145). This is significantly greater than historical controls from our and other U.K. institutions (median 7–11 months).

Our 2 year survival rate approaches 50% and is similar to that published by Morton et al for stage IV melanoma from the USA treated with PMCV.

1443 POSTER

Histamine dihydrochloride (Maxamine TM) potentiates the effect of interleukin-2 (IL-2) and interferon-alpha-2b (IFN-alpha-2b) in the treatment of solid tumors

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Purpose: Monocytes and macrophages can prevent activation of T cells and NK cells by release of reactive oxygen metabolites. Maxamine inhibits the release of reactive oxygen metabolites. When T cells and NK cells were exposed to phagocytes in vitro, the combination of Maxamine and IL-2 increased activated viable NK cells 12-fold and activated viable T cells > 60-fold. Maxamine has been tested in advanced melanoma and renal cell carcinoma patients as an adjuvant to IL-2 and IFN-alpha-2b.

Methods: Maxamine (1 mg, s.c., bid) was given in combination with IL-2 (4.8–18 MIU/m^2/day) and IFN-alpha-2b (3–5 MIU/day) to patients with advanced melanoma (20 patients) or renal cell carcinoma (3 patients).

Results: Maxamine caused the expected flushing but did not augment side effects associated with IL-2 and IFN-alpha-2b, and the treatment could be administered for at least one year. Mean survival for the 20 patients with advanced melanoma exceeded 15 months, and responses were observed in 2/3 patients with renal cell carcinoma.

Conclusion: The results from phase I/II studies indicate a survival benefit when Maxamine is given as an adjuvant to IL-2- and IFN-alpha-2b- based biotherapy. As a consequence two randomized phase III studies in advanced melanoma and a phase II study in advanced renal cell carcinoma are ongoing in the U.S., Europe and Australia.

1445 POSTER

Treatment of brain tumors with autologous cancer cell vaccines and radiotherapy

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Purpose: To improve the potential life expectancy of glioma patients, we have studied the combined therapeutic effect of autologous, cytokine producing cancer cell vaccines and local radiotherapy in experimental murine gliomas.

Methods: Murine gliomas were established by intracranial transplantation of glioma 261 (Gl261) cells. Autologous cancer cell vaccines were produced by transduction of in vitro growing Gl261 cells with adenoviral vectors encoding various murine cytokines (IL-2, IL-4, IL-6, IL-7, IL-12, GM-CSF, TNFa, LIF, LT). Tumor bearing mice were subcutaneously vaccinated with cytokine producing irradiated GL261 cells. In addition, vaccination therapy was combined with local radiotherapy of tumors.

Results: About 20–40% of glioma bearing mice were efficiently cured by vaccines producing either IL-2, IL-4, IL-12 or GM-CSF. The therapeutic effect of these vaccines depended on the cytokine level produced by transduced cells. The combination of vaccination and radiotherapy substantially improved survival rates: about 70–100% of tumor bearing mice were cured. The vaccination therapy induced the specific activation of cytotoxic T lymphocytes against Gl261 tumor cells as measured by cell-mediated citotoxicity assay and immunohistochemistry.

Conclusion: The combination of vaccination therapy with local radiotherapy of tumor might be efficiently used to improve survival rates of glioma bearing patients.

1446 POSTER

Immunogene therapy for murine fibrosarcoma using IL-15 gene with high translation efficiency

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Purpose: Numerous lines of evidence suggest that genetically modified tumor cells expressing cytokines can abrogate the ability of tumors to grow. IL-15 is a novel MW 15,000 cytokine that shares many of biological activities of IL-2 including induction and the proliferation of NK cells and T and B