PROCEEDINGS

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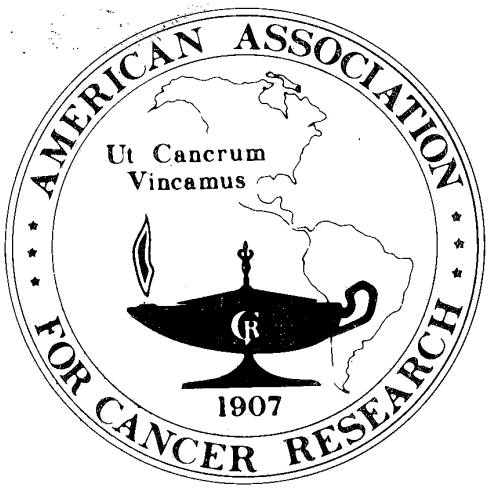

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Interaction of oncofetal antigen with malignant melanoma patients' sera. F.A. Salinas, Cancer Control Agency of B.C., 600 West 10th Ave., Vancouver, B.C., V5Z 4E6, Canada.

We have evaluated the reactivities of sera from malignant melanoma (MM) patients upon interaction with xenogeneic oncofetal antigen (XOFA) by using an in vitro system that simulates tumor burden changes. Each serum sample was mixed with XOFA at increasing concentrations (2 to 20 times). The results demonstrated a consistent inverse relationship between levels of circulating immune complexes (CIC) and levels of anti-XOFA antibody (IgG) concentration. When XOFA-containing CIC were subjected to size distribution analysis a significant relationship was found among CIC size, tumor burden and concentration of added XOFA. Predominant CIC of 10-12S were observed in sera from patients with no evidence of disease at sampling time, of 13-15S in sera from patients with small tumor burden, and of 16-18S in sera from patients with advanced disease. CIC sizes were dependent on the concentration of XOFA and anti-XOFA as well as on their relative combining reactivities. No increase in baseline levels of CIC were observed in parallel analyses of normal or non-malignant control sera. Our results illustrate a dynamic interaction of exogenous XOFA, with anti-XOFA and CIC present in sera from MM patients and suggest that analysis of size and molecular composition of CIC could explain the changes of CIC concentration observed in MM patients with different tumor burden. Such an analysis can be clinically relevant to disease prognosis. The study also suggests that the interaction of exogenous XOFA and patients' sera provide an in vitro model, that simulates patients tumor burden changes, to study host-tumor interaction.

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PHASE I CLINICAL EVALUATION OF ELSAMICIN. R. Amato, M. Raber, and L. Schacter. The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030

Elsamicin is a product of fermentation with a novel chemical structure that is not related to other known chemotherapeutic agents. Its mechanism of action is unknown. In preclinical studies it is active against the murine tumors P388, L1210, B16, M5076, as well as the MX1 and HCT-116 xenografts using the subrenal capsule assay. It is active against a variety of human tumor cell lines independent of route or schedule of administration. The mouse LD10 is 50 mgs/m² as a single injection. In dogs, 3.12 mgs/m² (5% MELD10) was uniformly lethal, while 1.8 mgs/m² was well tolerated.

We are conducting a phase I clinical evaluation of Elsamicin given as an intravenous bolus every three weeks. The starting dose was 0.6 mgs/m² (1/3 of the TDL in dogs). To date, 16 patients with metastatic solid tumors refractory to standard therapy (9 female/7 male, median performance status 1, median age 59, prior chemotherapy 15, prior immune therapy 4, prior radiation therapy 11), have received 22 courses. To date six dose escalations have been achieved, (0.6, 1.2, 2.4, 4.8, 7.2, and 10.8 mgs/m²). One patient at 4.8 mgs/m² developed grade II leukopenia associated with a grade I thrombocytopenia. One other patient developed a grade I thrombocytopenia at 7.2 mgs/m². No other patients have experienced myelosuppression. Nonhematologic toxicity has been minimal. The study is ongoing.

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TREATMENT OF ADVANCED METASTATIC MELANOMA USING SINGLE DOSE MURINE MONOCLONAL ANTIBODY - RICIN A CHAIN IMMUNOTOXIN WITH DOSE ESCALATION - A PHASE I STUDY. P. Salem, A. Zukiwski, W. Robinson, P. Bunn, R. Lamb, R.S. Benjamin, L. Spitler, N. Wedel, and S. Ackerman. The U.T. M.D. Anderson Cancer Center (MDACC), Houston, TX, The University of Colorado Medical Ctr., Denver, CO, and XOMA Corp., Berkeley, CA.

A phase I study utilizing single dose murine monoclonal anti-melanoma antibody - Ricin A chain immunotoxin (XOMAZYME-MEL) in the treatment of advanced malignant melanoma was jointly conducted at MDACC and the University of Colorado Medical Center. A total of 19 patients (pts) were treated. The immunotoxin was given as an infusion over 30 min. and in all pts except one, a single infusion was given. The starting dose was 0.6 mg/kg and was escalated stepwise by 25% to a maximum of 1.6 mg/kg. Six pts were treated at 1.6 mg/kg dose level and four of them developed grade IV fatigue (reduction in pt's activity to < 25%), and grade III myalgias (requiring narcotics). These toxicities were considered limiting. They were first noted 4 days after drug administration and they lasted approximately 1 week. Other non-limiting toxicities were: mild hypotension, decrease in serum albumin associated with weight gain and peripheral edema, and flu-like syndrome. The severity of these toxicities was also dose dependent. All pts were considered evaluable for response. There was one PR and one minor response. In conclusion, the maximum tolerated dose of XOMAZYME-MEL, when given as a single infusion of 30 minutes is 1.6 mg/kg.

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SKELETAL EWING'S SARCOMA (ES) IN ADULTS; AN OVER 40 YEARS' EXPERIENCE. N.E.J. Papadopoulos, R.S. Benjamin, C. Plager, A. Ayala, M. Romsdahl and John Murray. The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030.

One hundred ten adult (age ≥ 16) patients (pts) with ES and no metastases at diagnosis were retrospectively reviewed. There were 72 males and 38 females. Primary location included long bones (51), pelvis (25), spine (8), ribs (11), clavicle (2), skull (2), scapula (7), foot (4). The 5-year survival (5YS) of all pts was 36%. Those who received primary treatment with chemotherapy that included adriamycin (A) did the best: CYVADIC 48% and CAV 35%. For pts with extremity lesions, the most favorable site (47% 5YS), and A chemotherapy, those treated with surgery had a 73% 5YS compared with 48% for those without surgery (p=0.10) whereas those treated with radiation (54% 5YS) did no better than those treated without radiation (65% 5YS) (p=0.2). Thirteen pts had resection of the primary lesion after treatment with chemotherapy only. Ten pts with microscopic or no residual tumor had DFS of 90%. In contrast, 3 pts with residual tumor ≥ 10% all died (p=0.004). In conclusion: a) Chemotherapy should be the primary treatment for ES. b) Primary lesions should be resected if feasible. c) Degree of tumor necrosis after primary chemotherapy becomes an important prognostic factor. d) The adjuctive role of radiation therapy in the primary treatment of ES is questionable.