Immunization of mice with DNA vaccines encoding the human homologues of melanocytic differentiation antigens results in the induction of antibodies and T-cells which recognize both the human and mouse forms of the antigen, while DNA vaccines containing the syngeneic mouse genes are not immunogenic. Xenogeneic DNA immunization in mice leads to protection from syngeneic tumor challenge, inhibition of growth of established tumors and autoimmune depigmentation of coat. In parallel to the development of a clinical trial program for human cancer patients, we have initiated clinical trials in dogs with malignant melanoma (MM). Canine MM (CMM) is initially treated with surgery and/or radiation therapy; however, metastatic disease is common and invariably chemoresistant.

In a phase I clinical trial, 9 dogs with advanced MM (WHO stage II-IV) received four biweekly intramuscular injections of plasmid DNA encoding human tyrosinase with the Biojector needle-free jet delivery device. Blood samples were drawn for routine blood counts, biochemical screening, autoimmune induction and serological/T-cell responses. No toxicity or induction of autoimmunity was seen in any of the nine dogs, with the exception of a minimal to mild pain response at vaccination. One dog had a durable complete clinical response (CR) of lung metastases. The Kaplan-Meier median survival time of the dogs on this study was 389 days, which appears to be significantly increased when compared with stage-matched historical controls. Preliminary results indicate that the one dog experiencing the CR developed antibodies recognizing human melanoma cells and further antibody & T-cell testing of the other dogs on trial is ongoing.

The results of this trial demonstrate that xenogeneic DNA vaccination of dogs is a safe and potentially therapeutic modality for CMM. These results also warrant further evaluation of this novel therapeutic in locally controlled CMM (i.e. Phase II) and human MM. Two other Phase I canine trials with murine gp75 and murine tyrosinase (muTyr) have been recently completed and data are maturing. Importantly, no toxicity has been noted in any of the dogs on these trials as well. We are currently accruing CMM patients for a muTyr + huGM-CSF trial and two human clinical trials utilizing the xenogeneic approach have recently opened to accrual.

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Biographical Profile

Philip Bergman received his DVM from Colorado State University in 1990 and his PhD from MD Anderson Cancer Center in Texas in 1999. He is currently the Head of the Donaldson-Atwood Cancer Center and Director of the Flaherty Comparative Oncology Laboratory, both parts of the Animal Medical Center in New York. Dr. Bergman currently holds an adjunct associate faculty position at Memorial Sloan-Kettering Cancer Center and the Sloan-Kettering Institute for Cancer
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