



GRANT PROGRESS REPORT REVIEW

Grant: 00982: *Evaluation of Efficacy of Fasaret in Dogs with Osteosarcoma*

Principal Investigator: Dr. Don Bellgrau, Ph.D.

Research Institution: ApopLogic Pharmaceuticals, LLC

Grant Amount: \$199,692.00

Start Date: 4/1/2008 **End Date:** 3/31/2010

Progress Report: 24 month

Report Due: 3/31/2010 **Report Received:** 3/31/2010

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office.)

Original Project Description:

Background: Osteosarcoma (bone cancer) is a severe disease that occurs commonly in large and giant breed dogs, with as many as 10,000 cases diagnosed each year. More than 85 percent of cases occur in the limbs; treatment, which usually requires amputation of the affected limb plus follow-up chemotherapy, extends the life of dogs by an average of about 1 year. Invariably, death is due to distant spread of the tumor (metastasis), most often to the lungs or to other bones. Metastatic tumors are notoriously resistant to treatment and extended remissions or "cures" are rare, with less than 20 percent of dogs surviving more than 2 years from their diagnosis. The researchers have developed a new gene-based therapy that activates the immune system to prevent or delay recurrence and metastatic spread. The treatment is based on the brief delivery of a gene that induces tumor killing directly or indirectly (by recruiting inflammatory cells to the site), but more importantly, under the conditions this gene is expressed in the treatment setting, it also activates the immune system to recognize and kill the tumor cells. In the laboratory, this response effectively protects animals (mice) from tumor challenges that would otherwise be lethal. Presently, there is no information regarding the safety and efficacy of this therapy in companion animals. The researchers have shown that bone cancer cells are a valid "target" for therapy and have done extensive pre-clinical work to define appropriate starting doses.

Objective: This study will allow us to evaluate if Fasaret can be administered safely as an addition to standard of care for dogs with bone cancer, and if it improves the quality of life and overall survival of these patients. Specifically, the design will enable us to determine if there are side effects that would limit the application of Fasaret, and the planned 2-year follow-up will

allow us to define any increased survival attributable to Fasaret as compared to the expected ~20 percent of dogs that would be alive at this time with standard of care alone.

Original Grant Objectives:

This grant is a supplement to a NCI grant to cover the costs to the owners of 26 dogs participating in the study.

Objective 1: To determine the gene dose needed to obtain a clinical effect with limited or acceptable toxicity.

Objective 2: The effect of FasL gene transfer administered 10 days prior to standard of care treatment on event-free survival in dogs with naturally occurring OS will be compared to a historical control population.

Publications:

Two manuscripts in preparation. 3/31/2010

Report to Grant Sponsor from Investigator:

The goal of this study is to establish efficacy of Fasaret in treating osteosarcoma in canine companion animals. Fasaret is a human adenovirus vector encoding Fas ligand (FasL), a molecule that binds to a "death receptor" called Fas (CD95) that is often highly up-regulated on rapidly dividing cells such as cancers, leukemias, and lymphomas, and on activated white blood cells. Under the appropriate circumstances, engagement of the Fas receptor by FasL induces programmed cell death. Osteosarcoma predominantly affects larger canine breeds. Spontaneous canine osteosarcoma is also very similar to human osteosarcoma, which, when diagnosed, occurs during childhood. This study involves administering Fasaret to dogs at the time of bone biopsy, 10 days prior to limb amputation, should the biopsy confirm a diagnosis of osteosarcoma. Dogs receive standard of care in addition to treatment with Fasaret, which is limb amputation followed by chemotherapy. Dogs are examined for two years under the study, looking at specified time points for increased numbers of dogs that remain cancer free, to determine efficacy. A total of 50 dogs will be examined at the highest dose in this trial, 26 of these dogs being funded by the AKC CHF. All 26 dogs have been enrolled, 20 at CSU and 6 at UMN. The treatment has shown positive results at 90 day survival. Future studies will address improved dosing regimens.