RESEARCH PROGRESS REPORT SUMMARY

Grant 02215: A Cancer Vaccine for Canine Osteosarcoma

Principal Investigator: Rowan Milner, BVSc

Research Institution: University of Florida

Grant Amount: $80,877.63

Start Date: 1/1/2016 **End Date:** 4/30/2018

Progress Report: FINAL

Report Due: 4/30/2018 **Report Received:** 3/27/2019

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Original Project Description:

Osteosarcoma is a malignant cancer that carries a very poor prognosis in most large breeds of dogs. The standard of care treatment for osteosarcoma is surgery followed by chemotherapy. Unfortunately, a large number of these osteosarcomas undergo early metastasis (spread) even with early surgical intervention and chemotherapy. Infections of the surgery site, especially when limb-sparing surgery is used, have been known to stimulate the immune system post-operatively in dogs, resulting in improved survival. Since overall survival is bleak in patients with osteosarcoma, developing an osteosarcoma cancer vaccine holds promise as an adjunct treatment to surgery and chemotherapy. In a previous study of 400 dogs with melanoma we showed that a vaccine containing the ganglioside (GD3) causes a measurable immune response in normal dogs and dogs with melanoma, and prolonged survival. In this study, 40 dogs with osteosarcoma presenting to the University of Florida Small Animal Hospital will be randomly assigned to two treatment groups. Twenty dogs will be vaccinated using a ganglioside-based cancer vaccine following standard of care treatment. The outcome of the dogs receiving the vaccine plus standard of care will be compared to 20 dogs who receive standard of care without vaccination. Vaccines will be administered monthly for 4 treatments and the dogs monitored every 3-6 months for life or until lost to follow-up. The outcome of this study will help us understand the immune process associated with cancer vaccines for osteosarcoma and with an ultimate goal to improve survival for dogs with this aggressive form of cancer.

Publications:

Sahay, B., Hutchison, S., Cascio, M., Lejeune, A., Souza, C., Szivek, A., … Milner, R. J. (2018). Abstract A07: Changes in immune profiles of osteosarcoma dogs receiving a GD3-based vaccine concurrently

with carboplatin chemotherapy and surgery. *Cancer Immunology Research*, 6, A07–A07. 2017 Oct 1-4; Proceedings of the AACR Special Conference on Tumor Immunology and Immunotherapy. Boston, MA. https://doi.org/10.1158/2326-6074.TUMIMM17-A07

Presentations:

Milner RJ, Sahay B, Hutchison S, Pei S, Cascio M, Bowles K, Sayour E, Whitley E, Lejeune A, Boston S, Souza CH, Salute M. *Immune platforms to monitor GD3 based osteosarcoma vaccine given concurrently with a carboplatin chemotherapy protocol and surgery.* State of the Art (SOTA) presentation. 21 October 2016. VCS, Orlando.

Sahay, B., Hutchison, S., Cascio, M., Lejeune, A., Souza, C., Szivek, A., … Milner, R. J. (2018). Abstract A07: Changes in immune profiles of osteosarcoma dogs receiving a GD3-based vaccine concurrently with carboplatin chemotherapy and surgery. *Cancer Immunology Research*, 6, A07–A07. 2017 Oct 1-4; Proceedings of the AACR Special Conference on Tumor Immunology and Immunotherapy. Boston, MA. https://doi.org/10.1158/2326-6074.TUMIMM17-A07

Milner, R.J. GD3/GD2-Based Immunotherapy in Osteosarcoma (and Melanoma) in Combination with Standard of Care. PAWS for a Cure Symposium, Nov 12-13 2018, Merck Research Laboratories, Boston MA.

Report to Grant Sponsor from Investigator:

The investigators wish to thank the AKC Health for supporting our research. Since the start of the study we have enrolled twenty-four dogs with osteosarcoma in the treatment arm of the trial. Twenty-four dogs were able to complete the full course of the vaccine and chemotherapy. Of the dogs that completed the chemotherapy cycles and four vaccines, two were subsequently euthanized due to metastases. Owners were gracious in granting permission for a full necropsy of these two dogs. The results were very insightful. While the two dogs did show progression of their osteosarcoma because of metastases, no evidence of lung metastases were found on necropsy. One dog had small (1cm in diameter) nodules both kidney and the other had a similar small number of metastases in bone. While the results are still very early they seem to indicate that the vaccination plus the chemotherapy may have a modifying effect on the metastatic process of osteosarcoma. We are pleased to report that the median survival time for the 24 dogs is 551 days (data accrual 02/03/2019) (95% CI lower 313.54 days upper 788.45) with 8 dogs (30%) still alive, with 4 alive at > than 600 days. The study was designed to show an improvement in survival of 30% or greater compared to literature reports (9-12 months). We believe the study has achieved its goals and our survival data will be compared to dogs (case matched) undergoing amputation and six doses of carboplatin.

We are also pleased that we were able to add value to the study by developing flow cytometer panels monitoring the dog's immune cells as the vaccine and the chemotherapy are given. Early data shows that some of the immune cells that either support the immune system to fight osteosarcoma or allow the cancer to hide by making the body tolerant to the cancer, are changed as we vaccinate and give chemotherapy. Indeed, all dogs on entry to the study have shown higher numbers of these cells compared to normal dogs. The cell numbers changed overtime and increased when the cancer came back. The early findings were presented as an abstract # A07 American Association of Cancer Research AACR, Tumor Immunology and Immunotherapy Meeting, October 1-4, 2017, Boston, Massachusetts. We have completed the Phase-1 of the study and are very encouraged by the results. We are very grateful to The AKC Health Foundation for funding Phase-1 part of the trial. We look forward to Phase 2 part of the study where we will give six vaccines compared to the four-vaccines in Phase-1 part of the trial.