



## RESEARCH PROGRESS REPORT SUMMARY

**Grant 02534:** Clinical Trial for Evaluation of Propranolol and Doxorubicin in the Treatment of Canine Hemangiosarcoma

**Principal Investigator:** Erin Dickerson, PhD

**Research Institution:** University of Minnesota Office of Sponsored Projects Administration

**Grant Amount:** \$334,306.00

**Start Date:** 7/1/2019      **End Date:** 6/30/2024

**Progress Report:** End-Year 4

**Report Due:** 6/30/2023      **Report Received:** 7/30/2023

---

*(The content of this report is not confidential and may be used in communications with your organization.)*

### **Original Project Description:**

Canine hemangiosarcoma is a largely incurable cancer in dogs, and treatment approaches to improve outcomes have remained relatively stagnant over the past few decades. Treatment remains a challenge partly because the cancer is frequently detected at an advanced stage and because these tumors are often resistant to chemotherapies. Recently published reports showed that propranolol, a drug used to treat heart disease in humans and dogs, substantially increased the survival time of human angiosarcoma patients when used in combination with standard of care treatments. Propranolol was also shown to sensitize hemangiosarcoma cells to doxorubicin, providing a more effective way to kill tumor cells. Because angiosarcoma is strikingly similar to canine hemangiosarcoma, this multi-institutional clinical trial has been designed to determine the efficacy of propranolol in dogs with hemangiosarcoma when used in combination with surgery and chemotherapy. The main goal of the study is to establish whether propranolol in combination with doxorubicin following surgery improves outcomes for dogs when compared to the use of chemotherapy and surgery alone. The investigators will also evaluate the plasma concentrations of propranolol achieved during dosing to assess whether the levels of propranolol correlate to survival times. If successful, the findings from this approach will be rapidly conveyed to the veterinary community, and the guidelines provided to clinicians for the use of propranolol and doxorubicin for the treatment of canine hemangiosarcoma.

### **Publications:**

“Repurposing Old Drugs for New Cancer Treatments.” Accessed May 5, 2023.

<https://www.dvm360.com/view/repurposing-old-drugs-for-new-cancer-treatments>.

**Presentations:**

An overview of the study was presented at the 12th Biennial AKC Canine Health Foundation National Parent Club Canine Health Conference (NPCCHC) held August 9-11, 2019 in St. Louis, MO

A summary of the study design and goals was given at the annual Veterinary Cancer Society meeting held November 4-6, 2021 (virtual meeting). The presentation was part of a special session on hemangiosarcoma.

A summary of the study design and pre-clinical data supporting the rationale for the study were presented to the Minnesota Veterinary Medical Association at their annual meeting, held February 10-11, 2022 (virtual meeting).

An overview and preliminary analysis of the study was presented at the College of Veterinary Medicine faculty, staff, and students at the University of Minnesota as part of the Grand Rounds seminar series on December 1, 2022 (virtual presentation).

**Report to Grant Sponsor from Investigator:**

We have screened 58 dogs for the study. None of the dogs were enrolled due to the detection of metastatic disease during the screening process. Two other dogs were not screened due to the prior use of Yunnan Baiyao beyond the 24-hour limit allowed, and another owner cancelled the morning of the screening for unknown reasons. We have enrolled 19 dogs to date, bringing enrollment to 95% of the dogs proposed for the study. We have recorded an adverse event (2-3 episodes of fainting/collapse) attributed to propranolol in one dog (MN02), which developed approximately 6 months into the treatment protocol. The issue was resolved by reducing the dose of propranolol to 1.0 mg/kg. We are continuing to enroll dogs in the highest dose cohort (1.3 mg/kg) as this adverse event fell outside of the 21-day assessment period used to define the dose escalation criteria. Our goal is to enroll the final dog in the study in the next few months.

For the PK studies in Milestone 2, we have completed the propranolol and doxorubicin PK analysis for all dogs enrolled to date.

Overall, five dogs enrolled in the study have lived more than nine months (26%), and four dogs have survived more than one year (21%). Of the 4 dogs that have survived for more than one year, two of these dogs have survived for over three years, one dog has survived for just over two year, and the other just under two years.