# RESEARCH PROGRESS REPORT SUMMARY

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

**Principal Investigators:** Erin Dickerson, PhD and Antonella Borgatti, DVM, MS

**Research Institution:** University of Minnesota

*Co-investigators:* David R. Brown, PhD; University of Minnesota, Michael O. Childress, DVM, MS; Purdue University, Jennifer Mahoney, DVM and Pascale Salah; University of Pennsylvania

**Grant Amount:** $334,306

**Start Date:** 7/1/2019 **End Date:** 6/30/2022

**Progress Report:** Mid-Year 2

**Report Due:** 12/31/2020 **Report Received:** 12/30/2020

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**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:** None at this time.

**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

**Report to Grant Sponsor from Investigator:**

During the first 18 months of the trial, we have made progress toward our objectives. The project goals have not been modified.

Our overall objective is to determine a clinically optimal dose and estimate the efficacy of propranolol in dogs with hemangiosarcoma when given as an adjunct to chemotherapy. Specifically:

*Objective 1:* We will confirm the tolerability and estimate the clinical benefit of propranolol in combination with doxorubicin.

*Objective 2:* We will assess levels of propranolol in the bloodstream after long-term administration to dogs with hemangiosarcoma to determine if there is a correlation between drug levels in blood and treatment effect. We will also determine if propranolol alters the blood levels (exposure) of doxorubicin in dogs receiving propranolol and compare these levels to those found in the published literature for dogs receiving doxorubicin. Collection of these data will allow us to better understand how these drugs may be working together.

We opened the trial on July 1, 2019. As of December 31, 2020, we have enrolled eight dogs in the study and no dose limiting toxicities have been observed. Based on these results, we are continuing to enroll dogs at the highest dose of propranolol (1.3 mg/kg) being tested.

Propranolol and doxorubicin levels in the blood from six of the dogs have been analyzed, and analysis of samples from the seventh and eighth dogs is pending.

The study was been delayed by approximately four months due to the COVID-19 pandemic. Enrollment was halted at all three study sites (University of Minnesota, University of Pennsylvania, Purdue University) in early to mid-March. Enrollment resumed at all three sites in late June/early July.
Our plans are to continue to screen and enroll dogs into the study with the goal of enrolling another 8-10 dogs within the next 6-9 months. We also plan to complete the initial analysis of drug levels in the blood samples.