GRANT PROGRESS REPORT SUMMARY

Grant: 01426: c-Kit Mutation and Localization Status as Response Predictors in Canine Mast Cell Tumors Treated with Toceranib or Vinblastine: A Response-Adaptive Randomized Trial

Principal Investigator: Dr. Douglas H Thamm, VMD
Research Institution: Colorado State University
Grant Amount: $90,000.00
Start Date: 1/1/2011  End Date: 6/30/2013
Progress Report: End-Year 2
Report Due: 12/31/2012  Report Received: 12/18/2012

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. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

While surgery remains the mainstay of treatment for canine mast cell tumors (MCT), surgery alone is not curative in some cases, and not possible in other cases. Medical therapy remains an important component of MCT therapy. New drugs that affect signaling through the KIT growth factor receptor are showing considerable promise for the treatment of canine MCT, and MCT with mutations in the KIT protein that make it constantly active may be more sensitive to KIT inhibitors. The drug combination vinblastine and prednisone has roughly the same effectiveness as KIT inhibition against canine MCT; however, the two treatments have not been compared head-to-head, and it is not clear whether vinblastine or KIT inhibitors are more appropriate for the treatment of MCT without KIT mutations. We have recently developed a rapid test, which can be performed on fine-needle aspirates, to determine whether MCT possess KIT mutations or not. We intend to investigate the predictive value of KIT mutation status using this rapid genotyping assay, as well as KIT staining on biopsy sections, in dogs with measurable MCT randomized to receive either vinblastine or the KIT inhibitor toceranib (Palladia®). Randomization will utilize a novel adaptive statistical strategy that makes use of the KIT assay results. The results of this study will clarify whether KIT mutation testing is a useful decision-making tool for the selection of the best possible medical therapy for dogs with MCT.
Grant Objectives:

Hypothesis: KIT-mutant MCT will have a superior response to toceranib, but an inferior response to vinblastine (VBL).

Objective 1: To determine the predictive value of rapid PCR-based KIT genotyping and immunohistochemical KIT localization in dogs with MCT treated with either toceranib or vinblastine.

Publications:

Report to Grant Sponsor from Investigator:

While surgery remains the mainstay of treatment for canine mast cell tumors (MCT), surgery alone is not curative in some cases, and not possible in other cases. Medical therapy remains an important component of MCT therapy. New drugs that affect signaling through the KIT growth factor receptor are showing considerable promise for the treatment of canine MCT, and MCT with mutations in the KIT protein that make it constantly active may be more sensitive to KIT inhibitors. The drug combination vinblastine and prednisone has roughly the same effectiveness as KIT inhibition against canine MCT; however, the two treatments have not been compared head-to-head, and it is not clear whether vinblastine or KIT inhibitors are more appropriate for the treatment of MCT without KIT mutations. We have recently developed a rapid test, which can be performed on fine-needle aspirates, to determine whether MCT possess KIT mutations or not. We are investigating the predictive value of KIT mutation status using this rapid genotyping assay, as well as KIT staining on biopsy sections, in dogs with measurable MCT randomized to receive either vinblastine or the KIT inhibitor toceranib (Palladia). Randomization utilizes a novel adaptive statistical strategy that makes use of the KIT assay results.