AUBURN UNIVERSITY

COLLEGE OF VETERINARY MEDICINE

DEPARTMENT OF CLINICAL SCIENCES

# CLIENT INFORMED CONSENT FORM

**Title:** Efficacy of vinblastine as front line therapy for canine patients with multicentric lymphoma

1. **Why is the study being performed?**
This study is designed to investigate the effectiveness of a chemotherapeutic drug, vinblastine, in the treatment of lymphoma in dogs. Chemotherapy protocols used to treat lymphoma patients typically incorporate a similar drug called vincristine. While these drugs are very similar and share the same mechanism of action they do not have the same effectiveness against varying tumor types. The severity of side effects associated with vincristine and vinblastine are also different. At the most commonly used dosages, vincristine is associated with more frequent gastrointestinal side effects (i.e. decreased appetite and vomiting) compared to vinblastine. On occasion these side effects are significant enough to warrant discontinuation of the drug from the chemotherapy protocol. In such situations some oncologists have substituted vinblastine for vincristine; however, at this time there are no published studies evaluating the effectiveness of vinblastine in canine patients with lymphoma. The ultimate goal of this study is to evaluate the effectiveness of vinblastine against lymphoma in dogs in order to determine if vinblastine is a reasonable drug to incorporate into lymphoma chemotherapy protocols.

2. **Which animals / patients can participate in the study?**
Dogs that have been diagnosed with multicentric lymphoma that have not received any prior chemotherapy (including prednisone) in the treatment of their lymphoma are eligible for this study. All patients must have enlarged lymph nodes (at least 2cm in longest diameter) to be enrolled in the study. All stages, substages, and immunophenotypes of lymphoma are eligible for enrollment.

3. **Why might my animal NOT be able to participate in the study?**
Following the initial work-up the following patients may not participate in this study. Dogs that are breeds known to have MDR1 mutations are required to be tested for the mutation prior to being entered into the study. Dogs that test negative for the mutation (normal/normal) can be enrolled in the study, but dogs that are found to be positive for the mutation cannot be enrolled. Testing for a pet's MDR status involves sending a blood sample to Washington State University Veterinary Clinical Pharmacology Lab. Test results are typically available within 1 week following sample submission.

   Patients that have received prior chemotherapy (including prednisone) will not be eligible for enrolment in the study.

   If the clinician caring for your pet feels that your pet is not a good candidate for vinblastine administration, then your pet will not be eligible for the study. For example, patients that have liver and kidney dysfunction could have increased risk of side effects in which case the clinician in charge may not recommend this study.

4. **What will be happening to my animal if we participate in the study?**
Regardless of the planned chemotherapy protocol, all patients enrolled in the study will receive as initial treatment an intravenous (IV) injection of vinblastine at the standard dose of 2 mg/m2. The IV injection involves first isolation of a vein on your dog's limb followed by insertion of a needle attached to syringe into the vein. The vinblastine will be injected into the vein and then the needle will be removed. A light soft wrap will be placed following the injection, which should be removed 1 hour following injection. Prior to drug administration all patients will undergo a physical exam, lymph node measurements, and blood collection for initial complete blood count (CBC) and serum chemistry tests. All patients will be rechecked at Auburn University by the Oncology department seven

# CLIENT INFORMED CONSENT FORM

days following vinblastine administration to assess response to treatment and side effects. At this recheck appointment, a physical exam, lymph node measurements, a CBC, and any other tests that are recommended by the clinician caring for your pet will be performed following this study. Your pet will then start the chosen chemotherapy protocol.

Recommendations for continued treatment of your pet's lymphoma will be determined by the clinician caring for your pet; however, patients are not required to continue chemotherapy to be enrolled in the study.

5. **Are there any benefits from the study for my animal?**
While lymphoma is not curable in our canine patient, your pet could experience a partial or complete remission (resolution of clinically detectable disease) of their lymphoma following the administration of the vinblastine. The fees for vinblastine administration and 7 day recheck examination and CBC will be covered by the study. In general, Vinblastine has fewer gastrointestinal side effects than some of the other chemotherapy agents commonly used to treat lymphoma.

6. **Will there be any risks or discomforts for my animal?**
The administration of the vinblastine will not affect the administration of future chemotherapy agents for your pet. The discomfort from the administration of the vinblastine is expected to be comparable to what is experienced by a simple blood draw. If vinblastine escapes out of the vessel during the administration process, the drug can cause a wound to develop at the site of administration. These wounds typically resolve with conservative wound management and time. Other side effects from vinblastine administration are rare, but the most common side effects include bone marrow suppression and gastrointestinal upset. Both bone marrow suppression and gastrointestinal signs typically resolve within 2-3 days.

As with other chemotherapeutic agents, vinblastine is excreted in small amounts in the urine, feces, and saliva, it is important that all people and animals that are in contact with the pet avoid contact with these excrements for the first 48 hours following administration. If contact occurs thorough washing of the area with soap and water should be performed.

7. **Unforeseen adverse events**
A very rare side effect of vinblastine is a peripheral neuropathy, which manifests as generalized weakness. This is a very infrequent side effect and is mainly observed with significantly higher doses of vinblastine. Another rare side effect of chemotherapy administration in lymphoma patients in general, is "acute tumor lysis syndrome". It is a life-threatening condition that occurs when a large volume of tumor (i.e. lymphoma cells) die quickly resulting in electrolyte abnormalities and requires immediate veterinary care and hospitalization.

8. **Are there other treatment options other than participating in the study?**
There are other well established chemotherapy options for the treatment of multicentric lymphoma.

9. **Owner responsibilities**
You are responsible for paying for all diagnostics and treatments performed at the initial oncology consultation with the exception of the vinblastine and chemotherapy administration fees. These initial tests, including MDR1 mutation testing, must be performed the day of vinblastine administration and are your financial responsibility. If your pet qualifies for enrollment in the study, you will be asked to fill out an initial "Adverse Events Form" to get a baseline idea of how you pet is doing prior to vinblastine administration.

You are also responsible for bringing your pet to Auburn University seven days following the vinblastine

# CLIENT INFORMED CONSENT FORM

administration. At this time you will be asked to fill out an "Adverse Events Form" to describe how your pet has been doing over the 7 day period following vinblastine. The recheck examination and complete blood count charges will be the responsibility of the study, but charges for any other diagnostics or treatments performed at this time will be your financial responsibility.

10. **Participant dismissal**
Your pet will be removed from the study if they do not return for their 7 day recheck examination. Your pet will also be dismissed from the study if they are found to be taking any medications that were not approved by the primary investigators of the study.

11. **Financial obligations of all parties**
You will be responsible for the following fees:
    1. The initial oncology consultation and all initial diagnostics and treatments except for vinblastine administration.
    2. If indicated, MDR1 mutation testing and shipping.
    3. Treatment and diagnostics beyond $500 related to any complication following vinblastine administration.

    ***If you fail to return for the 7 day recheck exam, you will be billed for the expenses of the chemotherapy and the administration fee.

    The study will cover the following fees:
    1. Vinblastine and chemotherapy administration (including IV catheter if used)
    2. Recheck examination and CBC
    3. If your pet requires additional care due to vinblastine induced side effects, a maximum of $500 will be provided by the study for supportive care (anti-nausea and anti-diarrheal medications, fluid support, pain medications) and hospitalization. Any charges beyond $500 will be the responsibility of the owner.

12. **Access to study information**
You will have access to results from all blood work on the day that it is performed (CBC and chemistry panels). You will also receive information about your pet's individual response to treatment at the time of the seven day recheck. If you desire, the general conclusions based on this study will be made available to you. Please make this request by contacting the principle investigator, Dr. Stephanie Schleis (see below for contact information).

13. **Confidentiality**
The identity of you or your pet will remain confidential. If publication results from this study, identification methods will be used that prevent your pet's true identity from being determined.

14. **Contact persons regarding this study**
Participants may contact any of these individuals with questions about this study.
    **Dr. Noelle Bergman,** Department of Clinical Sciences, College of Veterinary Medicine, Auburn University. (334)844-4690.
    **Dr. Stephanie Schleis,** Department of Clinical Sciences, College of Veterinary Medicine, Auburn University. (334)844-4690.
    **Dr. Annette Smith**, Department of Clinical Sciences, College of Veterinary Medicine, Auburn University. (334)844-4690.

# CLIENT INFORMED CONSENT FORM

15. Hospital review contact person

Participants with concerns about any research study at the AU College of Veterinary Medicine may also contact:

**Doug Allen, DVM, MS, DACVS.** Director, Veterinary Teaching Hospital. College of Veterinary Medicine, Auburn University. (334) 844-4690.

**Frank F. "Skip" Bartol, PhD.** Associate Dean of Research and Graduate Studies. College of Veterinary Medicine; Auburn University. (334) 844-3700.

16. Owner acknowledgements:

As legal owner of (or agent for) this animal, I understand and acknowledge the following:

a. **I am agreeing to participate in a research study at the AU College of Veterinary Medicine.**
b. **I am free to withdraw my consent and to discontinue participation in the study at any time.**
c. **The decision for my animal to participate in this study is mine alone and *participation is voluntary.***
d. **The decision to withdraw from the study or to disregard the recommendations of the veterinarians involved in the study, relieves the investigators of current and future obligations (both medical and financial) to the pet and/or owner covered by this study.**
e. **Non-study treatment protocols have been discussed and I understand the relative benefits of those treatments.**
f. **I am responsible for decisions and financial obligations related to treatment(s) sought or required for my animal at AU-VTH or at any other veterinary facility that are NOT specified in this document. This would include treatment for disease progression or for medical complications - related or unrelated to the study.**
g. **If I withdraw my animal from the study, I may be responsible for medical, diagnostic and treatment costs incurred even if these were originally covered by the study.**
h. **Any decision to discontinue participation in this study, whether to pursue other therapies or to have my animal euthanized, does not entitle me to any financial reimbursement for costs incurred during participation.**
i. **I have discussed the procedures / benefits and risks of study participation and had the chance to have my questions about the study answered.**

_____ _____

Owner signature Date

17. Investigator assurances

a. I have explained the study details and answered questions to the best of my ability.
b. If the animal is a patient in the Auburn University Veterinary Teaching Hospital, I have discussed enrolling the patient into this study with the senior faculty member responsible for this patient's care.

_____ _____

Primary Investigator Date

_____ _____

Witness Date

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# CLIENT INFORMED CONSENT FORM

This study has been reviewed and approved by the Clinical Research Review Committee of the College of Veterinary Medicine (CRRC) and the Auburn University Institutional Animal Care and Use Committee (IACUC). (Effective date – Feb 2010)