AUBURN
UNIVERSITY

ATTN:11/10/2014

COLLEGE OF VETERINARY MEDICINE

DEPARTMENT OF CLINICAL SCIENCES

CLIENT INFORMED CONSENT FORM

Title: A randomized, masked, placebo controlled field study to determine efficacy and safety of Paccal Vet® in dogs with non resectable (or unresected) mammary carcinoma of stage III-V

1. **Why is the study being performed?**

Paclitaxel is one of the most commonly used drugs in human cancer treatment. Previously, it was not safe for use in dogs due to allergic reactions to the formulation. A new formulation of the drug (Paccal Vet®) has eliminated this concern. Since paclitaxel is used in women with breast (mammary) cancer with favorable results, this chemotherapy drug may be useful in dogs, as well. Good treatment options beyond surgery for dogs with this commonly occurring cancer have not been available. Previous research in dogs has determined a reasonably safe dose of Paccal Vet®, as well as shown some response in mammary cancer in dogs (about 60% of patients treated had tumor shrinkage). This study is being performed to better document the response of mammary cancer in dogs to this drug, in pursuit of FDA (Food & Drug Administration) approval.

2. **Which animals / patients can participate in the study?**

Female dogs of any size or breed that have mammary carcinoma that cannot be removed with surgery, or you have declined surgery, may participate. The tumor must be at least 1 cm with lymph node metastasis (tumor spread), or more than 5 cm without lymph node metastasis. Dogs with tumor spread to other organs are also eligible, although their life expectancy must be more than one month.

3. **Why might my animal NOT be able to participate in the study?**

Dogs that are pregnant, nursing, or intended for breeding during the study period may not participate. Any dog with blood abnormalities including a neutrophil count < 2500, platelets < 100,000, total bilirubin of twice the upper limit of normal (ULN), alanine aminotransferase (ALT) or alkaline phosphatase (ALP) quadruple the ULN, or creatinine greater than the ULN are not eligible. Any previous treatment for the current tumor, including radiation, chemotherapy, hormones, or biologics will disqualify the patient. Your pet may not be enrolled in any other clinical treatment trial. Dogs with active infections or other systemic organ dysfunction that would result in a life expectancy of less than three months may not participate. No dogs owned by the investigator, staff of the Auburn University College of Veterinary Medicine, or family members are eligible.

4. **What will be happening to my animal if we participate in the study?**

This is a randomized, blinded, placebo-controlled trial of one year's duration. Your dog will be randomly assigned to receive the drug or a placebo (inactive drug). Neither you nor your clinicians will be aware of whether your pet is receiving drug or placebo. Two out of three patients (67%) will be receiving active drug. The drug is given in the vein through a catheter over approximately 20 minutes every three weeks for four total treatments. Your dog will return multiple times

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(see calendar below) for evaluation, including blood sampling, imaging (x-rays and ultrasound), lymph node sampling, and tumor measurement. Approximately weekly visits will occur during the first 3 months, then monthly for one year. These visits including blood and urine sampling, as well as imaging, are similar to any patient receiving chemotherapy. If your pet's tumor progresses within the first 12 weeks and your dog is removed from the study, you may contact the sponsor for coverage of the costs of additional treatment at a facility of your choice.

	Screening	Drug administration	Monitoring			
	Min of 10 days prior to admission to study	Days: 0, 21, 42, 63	Days: 4, 11, 25, 32,46, 53, 67, 74	Month: 3	Months: 4, 6, 8, 10, 12	Months: 5, 7, 9, 11
Examination and quality of life determination	X	X	X	X	X	X
Tumor biopsy	X					
Lymph node aspirate	X					
Abdominal Ultrasound and aspirates as needed	X			X	X	
3 view chest radiographs	X			X	X	

5. **Are there any benefits from the study for my animal?**

Potential benefits for your pet as a result of response to the chemotherapy would include shrinkage or stabilization of the tumor, and prevention or treatment of tumor spread with extension of your pet's comfort and life. The costs of drug treatment and monitoring for one year will be covered by the sponsor. The usual costs of this treatment and veterinary visits would average $15,000.

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6. **Are there any risks or discomforts for my animal?**

As with all chemotherapy treatments, there are potential side effects, including death. The most common side effects seen with this drug in previous studies include a drop in the white blood cell count (increases infection risk), nausea, loss of appetite, diarrhea, and hair loss. These side effects are similar to that seen with other chemotherapy treatments and are usually manageable with concurrent medications that will be provided for you.

Since this study includes placebos in one out of three patients, your dog may not receive active drug. The tumor may progress without treatment. Even if your dog is receiving active drug, the tumor may not respond.

Minor risks associated with the drawing of blood or urine and sampling of the lymph node or other organs include bleeding or bruising at the site.

7. **Unforeseen adverse events**

A dose that is deemed reasonably safe has been determined previously in dogs. However, as with any chemotherapy drug, unforeseen events can occur, including illness or death.

8. **Are there other treatment options other than participating in the study?**

Mammary tumors in dogs may be treated with surgery, radiation, chemotherapy, or some combination, depending on the location, grade (aggressiveness) of the tumor, presence of tumor spread (metastasis), overall general health of the patient, and a client's expectations. All potential treatment options, including this study, will be presented. You may decline treatment, or choose a different treatment regimen for your pet. Declining participation will not negatively affect any further care your pet receives at our hospital.

9. **Owner responsibilities**

You must bring your dog back for scheduled monitoring and treatment according to the calendar. As the primary caregiver of your pet, you will play an active role in monitoring for and promptly reporting any problems you observe in your pet. If your pet dies during treatment, a necropsy (autopsy) will need to be performed to determine the cause of death. Your pet's body may be returned to you, at your request.

10. **Participant dismissal**

A patient may be removed from the study at the owner's request at any time. Lack of compliance with the scheduled monitoring and treatment will result in dismissal from the study. If your dog has significant side effects (determined by you or the clinician) associated with treatment that cannot be controlled with routine supportive care, or the tumor progresses (grows by 20% in size or new lesions occur), your dog will be dismissed from the study and other treatment options will be presented. Dismissal may occur if any other anti-tumor treatment (including NSAIDs or steroids, supplements, etc.) is initiated, so all new medications should be discussed with the study clinician prior to initiating treatment. If your pet is dismissed as a result of removal by your request, lack of compliance with scheduled treatment and monitoring, or initiation of other treatments without prior approval, there will be no further financial compensation from that point.

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11. **Financial obligations of all parties**

Costs of Paccal Vet® treatment and monitoring related to the mammary tumor in this study are covered by the sponsor. If side effects related to treatment occur, these costs will be covered by the sponsor. A prepaid card will be provided to you by the sponsor at each scheduled clinic visit ($160 for each 3-week treatment cycle, and $65 for each monthly follow-up visit). During the initial 12 weeks of active drug administration, if your dog's tumor progresses and your pet is dismissed from the study, you may contact the sponsor for coverage of costs of further treatment at the clinic of your choice. You are responsible for the costs of any further treatments chosen after the study period has ended or dismissal from the study.

12. **Access to study information**

Information from this study will not be distributed to you as an individual but may be available through scientific publications.

13. **Confidentiality**

Information, case materials, photos and generic patient information gathered in this study may be used for scientific presentations and publications. Confidentiality of personal information (client and animal) will be maintained to the extent of the law.

14. **Contact persons regarding this study**

Participants may contact any of these individuals with questions about this study.

Annette N. Smith, DVM, MS, DACVIM (Oncology & Small Animal IM)	334-844-4690 smith30@auburn.edu
Stephanie Schleis, DVM, DACVIM (Oncology)	334-844-4690 ses0034@auburn.edu
Jennifer Spooner, LVT	334-844-4690 jsh0014@auburn.edu

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.**

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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

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)