Clinical Trial Information Sheet & Enrollment Form:

Evaluation of a liquid fiducial marker for the creation of a planning target volume in dogs with post-resection soft tissue sarcomas

Statement of Intent

PetCure Oncology™ is currently recruiting patients for a prospective study evaluating the effectiveness of stereotactic radiosurgery (SRS) in the treatment of incompletely resected, grade 2 soft tissue sarcoma of the skin and subcutaneous tissues in dogs. Specifically, the study is intended to evaluate the utility of PetXMark, a liquid fiducial marker that incorporates sucrose acetate isobutyrate, X-SAIB (Iodinated sucrose acetate isobutyrate) and EtOH in the creation of a planning target volume.[1]

Prior to the launch of this study, PetCure Oncology conducted a pilot study of 20 canine patients whose treatment plans were created using the PetXMark liquid fiducial marker. The pilot study did not result in any acute toxicity, local failures, or geographic misses.

How to Enroll

Complete the Enrollment Form below or visit www.PetCureOncology.com/ClinicalTrials. Any additional inquiries may be directed to the Clinical Trials Coordinator, Brandy Banks RT(R)(T), at ClinicalTrials@PetCureOncology.com or 412.366.3400.

Terms of the Study

PetCure Oncology is interested in better defining the role of SRS in the treatment of canine patients with incompletely resected soft tissue sarcomas. Currently, there are no controlled, prospective studies in the veterinary literature that are designed to truly define the risks and benefits of this kind of radiation therapy for incompletely resected sarcomas. To facilitate case accrual in an appropriate manner, PetCure Oncology will:

1. Provide an SRS video consult free of charge
2. Treat the patient for the same costs associated with CFRT protocols
3. Provide the 6- and 18-month follow-up CT free of charge
4. Absorb the cost of having an autopsy performed for patients that die after study enrollment

Eligibility Criteria

Any canine patient with a post-resection soft tissue sarcoma is potentially eligible for study entry provided they meet all of the following requirements:

1. Histologically is confirmed as a grade 2 soft tissue sarcoma. This includes a diagnosis of:
    a. Fibrosarcoma

   b. Hemangiopericytoma
   c. Peripheral nerve sheath tumor
   d. Spindle cell sarcoma
2. All biopsy slides used to confirm the diagnosis were reviewed by a single pathologist to determine eligibility based on grade (cancer stage)
3. Simple (linear) resection scar <15cm in length. ***Large, complex scars following reconstructive surgery are exclusionary***
4. Complete reference lab bloodwork is available and less than four weeks old
5. Diagnostic CT scan of the thorax, or 3-view metastatic check, has been performed. ***Evidence of metastatic disease is exclusionary for this study, but alternative treatment paths may be available***
6. ***Significant co-morbidities that would impact the patient's ability to tolerate/survive multiple anesthetic events is exclusionary***
7. Caregiver has signed informed consent confirming that they understand this is an ongoing clinical study to better define the role of SRS in the treatment of incompletely resected soft tissue sarcomas in dogs
8. Caregiver agrees to follow the prescribed follow-up procedure, including repeat CT scans at 6- and 18-months post-treatment
9. Caregiver consents to a potential autopsy for any patient that dies following enrollment in the study

Background and Rationale

Traditional dogma in radiation therapy has held that stereotactic radiosurgery (SRS) fractionation (radiation exposure treatment) is not possible unless there is gross residual disease to target. In cases where patients have had their tumor resected down to microscopic residual disease, the current recommendation would be to initiate a course of conventionally fractionated radiation therapy (CFRT).

CFRT is delivered in 15-21 fractions on a M-F or M-W-F basis, depending on the protocol being used. For veterinary radiation therapy (RT) patients, each one of these fractions of radiation is accompanied by an anesthetic event, leading many families to forgo additional radiation after surgery. A large percentage of these patients will develop recurrent disease, typically within 9-18 months.

SRS has been used to treat resection sites in human patients with brain metastases. This strategy has resulted in improved local control with minimal radiation-induced morbidity in these patients, and supports the use of SRS to treat marginally resected disease, even embedded in a critical normal structure such as brain.[2-5]

Hypofractionated protocols have been used for marginally resected tumors with a good expectation of local control.[6,7] Stereotactically delivered radiation should, in theory, improve this local control rate by delivering a dose of radiation intended to cure in 1-3 consecutive day fractions. Integral to this is the ability to define a planning target volume and to deliver a dose of radiation to that target volume that meets the fractionation and target dose metrics associated with stereotactic radiosurgery.

PetXMark is a liquid fiducial marker that can be injected along a surgical incision or painted into a resection cavity for later imaging.[1] It is a stable and non-toxic compound, does not migrate after injection, and is intended to provide at least 2 months of stable, reproducible tissue marking.[8,9] Prior to

the launch of this study, PetCure Oncology conducted a pilot study of 20 canine patients whose treatment plans were created using the PetXMark liquid fiducial marker. The pilot study did not result in any acute toxicity, local failures, or geographic misses.

Hypothesis

Injection of PetXMark along the scar of a marginally resected soft tissue sarcoma will allow for the creation of an objectively based planning target volume (PTV) that can then be treated with single-fraction SRS, maximizing local control with minimal acute or delayed radiation toxicity.

Study Design

This is a prospective single arm clinical study. All patients are treated on protocol with a single 20Gy fraction. Clinical target volume (CTV) is delineated using PetXMark injected at 1cm intervals along the resection scar. The PTV will incorporate a 1cm margin applied to the PetXMark defined CTV. A 3mm skin sparing margin will be applied within the planning structure set, and the skin metrics will be within the limits established by the PetCure Oncology Scientific Advisory Board (DMax <26Gy, 10cc <23Gy). A Case Report Form (CRF) will be completed for each patient enrolled in the study. The CRF will be completed by the treating radiation oncologist, and will become part of the permanent medical record. A completed copy of the CRF will be provided to Nanovi for their records.

Our Commitment to You

This study is designed to research how veterinary patients with incompletely resected skin and subcutaneous tumors will respond to SRS. We believe that the treatment will be safe and effective, and this study is designed to answer those questions. We appreciate your willingness to participate in the study and commit to retreat your pet for free in the event of:

- Early Local Failure – Defined as recurrence within the treatment field within two years following SRS
- Geographic Miss – Defined as regrowth at the periphery of the treatment field

Contact Information

If you have questions about enrollment criteria or would like to refer a patient for evaluation/inclusion in the study, contact:

Brandy Banks, RT(R)(T)
Clinical Trials Coordinator, PetCure Oncology
ClinicalTrials@PetCureOncology.com
412.366.3400

If you have questions about the study design or the protocol for treatment, contact:

Dr. Neal Mauldin
Dipl. ACVIM (Internal Medicine and Oncology)

Dipl. ACVR (Radiation Oncology)
Director, PetCure Scientific Advisory Board
SAB@PetCureOncology.com
773.850.3400

References

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9. Acknowledgement: Data obtained from clinical investigation no. 310-02 ” Proof of concept study Evaluating safety and performance of a gel marker (PetXMark®) used for image guided radiotherapy (IGRT) of esophageal cancer”. Rigshospitalet, Copenhagen, Denmark. Principle Investigator: Prof. Lena Specht, MD.

Veterinary SRS Liquid Fiducial Trial Enrollment Form

Veterinarian Information

Veterinarian name:

Veterinarian phone number:

Veterinarian email address:

Are you a primary care or specialist veterinarian?

Practice name:

PRIMARY ◯ SPECIALIST ◯

Practice address:

Practice address 2:

City: State/Provence: Zip/Postal Code: Country:

Client Information

Patient name:

Breed:

Date of birth:

Gender:

Client name:

MALE ◯ FEMALE ◯

Client phone number:

Client email address:

Questions About your Patient's Diagnosis

Has your patient been recently histologically confirmed with a grade 2 soft tissue sarcoma? YES ◯ NO ◯ I'M NOT SURE ◯

Has your patient had bloodwork done within the last four weeks? YES ◯ NO ◯ I'M NOT SURE ◯

Has the patient had a diagnostic CT or three-view metastatic check of the thorax? YES ◯ NO ◯ I'M NOT SURE ◯

If yes, are you in possession of the imaging? YES ◯ NO ◯

Does the patient have any co-morbidities? YES ◯ NO ◯

If yes, please describe co-morbidities below: