

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 participants 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

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 844.308.2578.

Terms of the Study

PetCure Oncology is interested in better defining the role of SRS in the treatment of dogs with incompletely resected soft tissue sarcomas. Currently, there are no controlled, prospective studies in the veterinary literature that define the risks and benefits of SRS for incompletely resected sarcomas. To facilitate case accrual, PetCure Oncology will:

1. Provide an SRS video consult free of charge
2. Provide treatment at a subsidized cost - subsidy of \$3,500 for main trial
3. Provide the 6- and 18-month follow-up CT free of charge
4. Absorb the cost of having an autopsy performed for animals that die after study enrollment, if deemed necessary by PetCure Oncology

Eligibility Criteria

Any dog with a microscopically incompletely resected soft tissue sarcoma is potentially eligible for study entry provided they meet all 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. Biopsy slides used to confirm the diagnosis must be reviewed by a single pathologist to determine eligibility based on grade
3. Study subjects must have a simple (linear) resection scar <15cm in length. **Large, complex scars following reconstructive surgery are exclusionary**
4. Complete reference lab bloodwork with concurrent urinalysis must be available and less than four weeks old at the time of SRS treatment
5. Diagnostic CT scan of the thorax, or 3-view thoracic radiograph, 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 animal's ability to tolerate/survive multiple anesthetic events are exclusionary. Whether or not a particular abnormality constitutes a "significant co-morbidity" will be determined by PetCure Oncology**
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 an autopsy for any animal that dies following enrollment in the study, if deemed necessary by PetCure Oncology

Background and Rationale

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

CFRT is delivered in 15-21 small 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 is accompanied by an anesthetic event, leading some families to forgo post-operative radiation. Unfortunately, a large percentage of these animals will experience regrowth of their cancer. In one study, this occurred at a median of approximately seven months after the original surgery.²

Hypofractionated protocols have been used to treat marginally resected tumors with a good expectation of local control.^{3,4} Stereotactically delivered radiation should, in theory, improve this local control rate even further by delivering a higher, more precisely targeted 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 consistent with stereotactic radiosurgery. In fact, SRS has been used to treat resection sites in people with brain metastases. This strategy has resulted in improved local control with minimal radiation-induced morbidity, and supports the use of SRS to treat marginally resected disease, even when it is embedded in a critical normal structure such as brain.⁵⁻⁸

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 two months of stable, reproducible tissue marking that is visible on CT scan.^{9,10} Prior to the launch of this study, PetCure Oncology conducted a pilot study of 20

dogs whose treatment plans were created using the PetXMark liquid fiducial marker. No acute toxicities, local failures, or geographic misses were observed.

Hypothesis

Injection of PetXMark liquid fiducial 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 animals 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 animal 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 animals with incompletely resected grade 2 soft tissue sarcoma will respond to SRS. PetCure Oncology believes that the treatment will be safe and effective, and this study is designed to test this hypothesis.

Contact Information

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

Brandy Banks, RT(R)(T)

Clinical Trials Coordinator, PetCure Oncology

ClinicalTrials@PetCureOncology.com

844.308.2578

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

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References

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9. Acknowledgement: Data obtained from clinical investigation no. 310-01 "Proof of concept study evaluating safety and performance of a gel marker (PetXMark®) used for image guidance in deep inspiration breath- hold radiotherapy (DIBH IGRT) in patients with locally advanced non-small cell lung cancer (NSCLC)". Rigshospitalet, Copenhagen, Denmark. Principle Investigator: Prof. Lena Specht, MD.
10. 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/Province:

Zip/Postal Code:

Country:

Client Information

Patient name:

Breed:

Date of birth:

Gender:

Client name:

INTACT MALE

INTACT FEMALE

NEUTERED MALE

SPAYED FEMALE

Client email address:

Client phone number:

Questions About your Patient's Diagnosis

Has your patient been recently diagnosed with a histologically confirmed, incompletely resected grade 2 soft tissue sarcoma? YES NO

Has your patient had bloodwork and urinalysis done within the last four weeks? YES NO

Has your patient had a diagnostic thoracic CT or three-view thoracic radiographs performed? YES NO

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

Does your patient have any co-morbidities? YES NO

If yes, please describe co-morbidities below: