

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

Study Summary

PetCure Oncology™ is currently recruiting participants for a clinical trial evaluating the effectiveness of stereotactic radiosurgery (SRS) combined with a liquid fiducial marker for the treatment of incompletely resected, grade 2 soft tissue sarcoma in dogs.

Historically, stereotactic radiation (SRS/SRT) has not been recommended for pets that have undergone surgery to remove a malignant tumor, primarily because there is no clearly definable treatment target. PetXMark, a liquid fiducial marker, can be injected along a surgical incision or painted into a resection cavity and will be visible on subsequent imaging. This allows an artificial target to be created that can then be treated with SRS in a single fraction, rather than the 19-21 fractions typically recommended for the treatment of an incompletely resected soft tissue sarcoma with conventionally fractionated radiation therapy (CFRT).

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 866.753.5083.

Terms of the Study

PetCure Oncology is interested in evaluating the use of a liquid fiducial in the treatment of post-surgery soft tissue sarcomas with SRS in dogs. Additionally, other tumors of the skin and subcutaneous tissues can be treated with the fiducial in a secondary protocol setting. No controlled, prospective studies currently exist in the veterinary literature that define the risks and benefits of SRS for microscopic residual disease in this population.

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 soft tissue sarcoma that has microscopic residual cancer following surgery is potentially eligible for study entry provided they meet all the following requirements:

1. The type of cancer 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) surgical scar less than 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 radiation (SRS/SRT) is not possible unless the cancer is large enough to provide an identifiable target that can be used to create a treatment plan. In cases where a tumor has been almost completely surgically removed, leaving only microscopic disease and no clear target behind, the typical recommendation has been to initiate a course of conventionally fractionated radiation therapy (CFRT).

CFRT is delivered in 15-21 small fractions of radiation 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 anesthesia. The prospect of a prolonged course of radiation including numerous anesthetic events leads some families to forgo post-operative radiation for their pets. 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.¹

Hypofractionated protocols, where a smaller number of large radiation fractions are delivered, have been used to treat dogs with marginally resected tumors and have a good expectation of local control.^{2,3}

Stereotactically delivered radiation should, in theory, improve this local control rate even further by delivering a higher dose of very precisely targeted 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 of the cancer with minimal radiation side effects and supports the use of SRS in the treatment of marginally resected cancer, even when it is embedded in a critical normal structure such as the brain.⁴⁻⁷

PetXMark is a liquid fiducial marker that can be injected along a surgical incision or painted into a resection cavity for later imaging.⁸ 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 trial, PetCure Oncology conducted a pilot study of 20 dogs 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 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 dogs 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(RT

Clinical Trials Coordinator, PetCure Oncology

ClinicalTrials@PetCureOncology.com

866.753.5083

References

1. Elmslie RE, Glawe P and Dow SW. Metronomic therapy with cyclophosphamide and piroxicam effectively delays tumor recurrence in dogs with incompletely resected soft tissue sarcoma. *J Vet Intern Med*, 2008; 22:1373-1379.
2. Hypofractionated radiation therapy for the treatment of microscopic canine soft tissue sarcoma. Kung MB, Poirier VJ, Dennis MM, Vail DM, Straw RC. *Vet Comp Oncol*. 2014 Nov 13. doi: 10.1111/vco.12121. [Epub ahead of print] PMID: 25393921
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4. Survival was Significantly Better with Surgical/Medical/Radiation Co-interventions in a Single-Institution Practice Audit of Frameless Stereotactic Radiosurgery. Taggar A, MacKenzie J, Li H, Lau H, Lim G, Nordal R, Hudson A, Khan R, Spencer D, Voroney JP. *Cureus*. 2016 May 17;8(5):e612. doi: 10.7759/cureus.612. PMID: 27335717215
5. Postoperative Stereotactic Radiosurgery Using 5-Gy × 5 Sessions in the Management of Brain Metastases. Abuodeh Y, Ahmed KA, Naghavi AO, Venkat PS, Sarangkasiri S, Johnstone PA, Etame AB, Yu HH. *World Neurosurg*. 2016 Jun;90:58-65. doi: 10.1016/j.wneu.2016.02.007. PMID: 26921701
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8. Rydhög JS, Mortensen SR, Larsen KR, Clementsen P, Jølkck RI, Josipovic M, Aznar M, Specht L, Andresen TL, Rosenschöld PM, Persson GF: Liquid fiducial marker performance during radiotherapy of locally advanced non small cell lung cancer, *Radiotherapy and Oncology* (2016); Volume 121, Issue 1, Pages 64–69.
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.

Pet Parent Clinical Fiducial Trial Enrollment Form

Pet Parent Information

Your name:

Your phone number:

Your email address:

Preferred method of contact:

PHONE

EMAIL

Pet Information

Pet name:

Pet date of birth:

Breed:

Gender:

MALE

FEMALE

Your Veterinarian's Information

Veterinarian's name:

Veterinarian's practice:

Veterinarian phone number:

Veterinarian email address:

Do you authorize PetCure Oncology to contact your veterinarian in order to acquire medical history, imaging, or other pertinent information related to the health of your dog?

YES

NO

Questions About your Pet's Diagnosis

Has your dog been diagnosed with a grade 2 soft tissue sarcoma?

YES

NO

I'M NOT SURE

Has your dog had bloodwork and urinalysis done within the last four weeks?

YES

NO

I'M NOT SURE

Has your dog had a CT scan or other form of imaging performed on their chest (between neck and abdomen)?

YES

NO

I'M NOT SURE

If yes, are you in possession of the imaging?

YES

NO

Outside of the soft tissue sarcoma, does your dog have any other medical conditions? If yes, please detail them below:

YES

NO

Anything else you would like to share with us? Let us know here: