

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 patients for a clinical trial evaluating the effectiveness of stereotactic radiosurgery (SRS) for the treatment of post-surgical, grade 2 soft tissue sarcoma in dogs using a liquid fiducial marker.

Historically, stereotactic radiation (SRS/SRT) has not been an available treatment option for pet patients who have undergone surgery to remove a malignant tumor. This is due to the lack of an appropriate treatment target, among other factors.

A liquid fiducial marker can be injected along a surgical incision or painted into a resection cavity for later imaging. This allows for the creation of an artificial target 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. 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 evaluating the use of a liquid fiducial in the treatment of post-surgery soft tissue sarcomas in canine patients. Additionally, other tumors of the skin and subcutaneous tissues can be treated with the fiducial in a secondary protocol setting. Aside from this clinical study, there are no controlled, prospective studies in veterinary literature designed to truly define the risks and benefits of this kind of radiation therapy for incompletely resected tumors.

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 dog with soft tissue sarcoma that has residual cancer following surgery is potentially eligible for study entry provided they meet all of 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. 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) surgical scar less than 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 radiation (SRS/SRT) is not possible unless the cancer presents an identifiable target that can be used to create a treatment plan. In cases where patients have had their tumor surgically removed with microscopic disease remaining, 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 anesthesia, leading many families to forgo additional radiation after surgery. A large percentage of these patients may 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 of the cancer 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 the 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 trial, 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 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 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

References

1. Jølcck RI, Binderup T, Hansen AE, et al. Injectable Colloidal Gold in a Sucrose Acetate Isobutyrate Gelating Matrix with Potential Use in Radiation Therapy. 2014:1680-1687. doi:10.1002/adhm.201300668.
2. 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
3. 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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5. Hypofractionated Stereotactic Radiosurgery and Radiotherapy to Large Resection Cavity of Metastatic Brain Tumors. Lima LC, Sharim J, Levin-Epstein R, Tenn S, Teles AR, Kaprealian T, Pouratian N. World Neurosurg. 2017 Jan;97:571-579. doi: 10.1016/j.wneu.2016.10.076. PMID: 27777153
6. 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
7. Intentional marginal excision of canine limb soft tissue sarcomas followed by radiotherapy. Demetriou JL, Brearley MJ, Constantino-Casas F, Addington C, Dobson J. J Small Anim Pract. 2012 Mar;53(3):174-81. doi: 10.1111/j.1748-5827.2011.01186.x. PMID: 22931399
8. 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.
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.

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 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?

YES

NO

If yes, please detail them below:

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