VIRGINIA TECH
ANIMAL CANCER CARE AND RESEARCH CENTER

AIM: Ablative Immune Modification with Nanopulse Stimulation prior to treatment with doxorubicin in dogs with diffuse large B-cell lymphoma

Purpose

To evaluate if treatment with NPS alters immune markers and impacts treatment outcome when combined with standard chemotherapy

Background

Large cell lymphoma affecting the peripheral lymph nodes (multicentric) is one of the most common cancers diagnosed in dogs, and diffuse large B-cell lymphoma (DLBCL) is the most common subtype. DLBCL in dogs is clinically and genetically similar to DLBCL in people; clinical trials in dogs are helping to identify new treatments to benefit both dogs and people diagnosed with this cancer. One of cancer's strategies is to evade the immune system by suppressing immune cell recognition and the ability of these immune cells to kill cancer cells. Treatments that address this by using drugs, antibodies, or directly training a patient's immune system, are becoming common in people, but we are far from curing lymphoma in dogs or people. The use of local ablative strategies to modify the immune system (AIM, or ablative immune modification) and shift it from a suppressed to an active environment has been shown to be effective in rodent models and people with other cancer types.

The purposes of this study are 1.) to evaluate the impact on the number and types of immune cells and their gene expression following a single treatment to a lymph node in dogs with DLBCL, and 2.) whether NPS pre-treatment prolongs the remission time when treated with standard chemotherapy with doxorubicin.

This study is funded by the iTHRIV Scholars program.

Eligibility

- Confirmed diagnosis of multi-centric diffuse large B-cell lymphoma
- At least 1 year old and weighing at least 10kg / 22lbs.
- Your dog cannot have received any treatment for lymphoma, including prednisone.
- Lab work showing adequate organ and bone marrow function to safely receive treatment with chemotherapy. A consultation with a cardiologist may be required at the time of screening to determine whether your dog can safely receive doxorubicin.
- Owner willingness to comply with study requirements

Exclusion Criteria

- Dog cannot have received cancer-directed therapy including prednisone
- Stage 5 lymphoma (i.e. bone marrow, lung, kidney, eye, gastrointestinal tract, skin, or other non-lymphoid organ involvement)
- Dog must be expected to live for at least 4 weeks even if s/he were to receive no treatment or only supportive, palliative care
- Significant heart dysfunction (arrhythmia or weak pumping)

Study Design

This study takes place at the Animal Cancer Care and Research Center (ACCRC) in Roanoke, VA.

This is a prospective, single-blind, randomized, proof-of-principle clinical trial. Dogs will be randomized to either AIM (treatment with NPS), or placebo. Only the investigation team will know whether your dog has received AIM (NPS). Blood and lymph node needle biopsies will be obtained periodically throughout the study to monitor the immune response. All dogs will undergo standard chemotherapy treatment with doxorubicin following AIM (NPS) or placebo. Chemotherapy will be given under the direct supervision of a board-certified veterinary medical oncologist at the ACCRC. If you agree to participate in the study, we will perform the following procedures:

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(a) Pretreatment evaluation (screening, prior to enrollment)

Before beginning treatment, your dog must undergo the following tests to determine if s/he is a good candidate to enroll in the study.

1. Complete physical exam
2. Lab work
3. Biopsy or fine needle aspirate of a lymph node read by a pathologist
4. Special testing to identify whether the lymphoma is B-cell or T-cell (immunophenotyping by flow cytometry)
5. Thoracic and abdominal imaging

(b) Treatment

Once your dog is enrolled in the study, there are (13) protocol clinic visits which include (1) NPS or placebo treatment under general anesthesia or heavy sedation, (5) chemotherapy treatments, (2) imaging visits, (13) blood draws, and (8) fine needle aspirates (needle biopsy) of a lymph node. Please see the study visit summary below. Upon completion of the chemotherapy protocol, monthly exams are required to monitor for remaining in complete remission: the number of these visits will vary. Nanopulse stimulation is short bursts of electrical fields applied directly to the lymph node. It is considered painless in humans and does not generate heat. NPS treatment is expected to take 30-45 minutes.

Study visit summary (*PD = progression of disease, or relapse, of the lymphoma)

Procedures by day	**-7**	**0**	**3**	**7**	**14**	**28**	**35**	**49**	**56**	**70**	**77**	**91**	**98**	**PD***
Diagnosis	x													x
Immunophenotype	x													
Thoracic radiographs, abdominal ultrasound	x							x						x
CBC	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Chemistry panel	x			x		x		x		x		x		x
Urinalysis	x			x		x		x		x		x		x
NPS or placebo		x												
Doxorubicin i.v.				x		x		x		x		x		
Blood and fine needle aspirate of lymph node		x	x	x		x		x		x		x		x

Compensation

The study covers the sedation and NPS (or placebo) treatment, the collection and analysis of blood and lymph node samples for determining immune response, and $250 per chemotherapy treatment visit. **The total compensation per patient enrolled is $1,430.** All other costs associated with screening, the chemotherapy treatment and monitoring visits, required imaging exams at day 49, and any medications or hospital visits necessary for managing side effects are out-of-pocket. All diagnostics or procedures not covered by the study are standard, and would be performed in any pet dog undergoing evaluation and treatment for lymphoma with chemotherapy. The out-of-pocket costs may vary during the study period. As of July 1, 2021, the screening costs are estimated to be $1000-1200, the costs of imaging are estimated to be $500-700. The cost of treatments vary based on your dog's weight, and management of side effects also greatly varies. Estimates of treatment visits will be calculated specifically for your dog and provided at the time of screening.

Contact

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