Study #3

Veterinary Clinical Trials in Canine and Feline Patients Using Combination Novel Therapeutics, Devices, and Data Collection Techniques

***Study objective**: To evaluate the local and systemic immune effects of calreticulin nanoparticle (CRT-NP)–based immunotherapy in combination with high-intensity focused ultrasound (HIFU) histotripsy, with or without anti-PD-L1 therapy in dogs with advanced, naturally occurring melanoma. Intratumoral CRT-NP, which promotes immunogenic cancer cell death and upregulates PD-L1 on cancer cell membrane, may synergize with HIFU to enhance antigen presentation and immune activation at the treated tumor and distant, untreated tumors. Anti-PD-L1 addition to CRT-NP and HIFU treatments may further amplify T cell-mediated responses, promoting antitumor immunity and overcoming treatment resistance in melanoma patients and other "cold" tumors.*

Treatments

Arm 1

- CRT-NP given to tumor by injection weekly for 4-8 weeks
- HIFU (histotripsy) treatments given weekly, 24-48 hours after CRT-NP to same tumor for 4-8 weeks

Arm 2

- CRT-NP given to tumor by injection weekly for 4-8 weeks
- HIFU (histotripsy) treatments given weekly, 24-48 hours after CRT-NP to same tumor for 4-8 weeks
- Anti-PDL1 (Gilvetmab) given on the same day as CRT-NP through the veins; given every other week for length of CRT-NP and HIFU treatments

Treatment Timeline

Referring vet or client contacts VROC and sends patient's medical records.

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VROC clinicians review patient's medical records and decide if they may be eligible for a clinical trial.

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Potentially eligible patients are scheduled for a consultation and consented to the Master protocol for tissue and data collection to confirm cancer and assess their health.

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After consultation, clinicians review the patient's case and determine which treatment arm, if any, they qualify for.

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The clinician will discuss treatment options with owner and owner can consent to start determined treatment plan for the patient's cancer.

Tumor Types Enrolling

- Melanomas

Inclusion Criteria

- Must have a confirmed active melanoma tumor diagnosis
- Must have at least one primary and one distant tumor

Exclusion Criteria

- Prior immunotherapy treatments
- Severe chronic diseases (e.g. some cardiovascular diseases, history of anesthetic complications) that increase the risk for anesthetic or treatment complications
- Tumor is not accessible for injectable treatments

Procedures

- Questionnaire before consultation, weekly questionnaires during treatment, and questionnaires at each post-treatment visit (at least at 3, 6, and 12 weeks)
- Physical exams at consultation, treatment, and post-treatment visits
- Sample collection (e.g. blood, urine, feces, etc.) and possible imaging (MRI, CT, X-ray, ultrasound, etc.) at consultation, treatment, and post-treatment visits. A CT or ultrasound will be taken at 3 months post-treatment
- Patients will be evaluated for extended monitoring after 3 months post-treatment appointment.
- Optional biopsy/aspirate may be performed at 4 months post-treatment.

**Clinicians may decide that your pet is in need of additional samples/diagnostics at any time throughout the study based on their current health condition. Post-treatment follow-up visits for 3 months are mandatory for on-study pets.*

This study will be fully paid for by owners. However, possible subsidies may be presented.