

Pilot Study for a New Quasiorganelle Therapy in Dogs with Histiocytic Sarcoma

Purpose of the study:

Histiocytic sarcoma is an aggressive cancer in dogs that often does not respond well to standard treatments like chemotherapy or radiation. While some dogs experience benefit, these treatments affect many cells at once and cannot adapt as a tumor changes. New research shows that cancer closely interacts with the immune system and surrounding tissues, suggesting that better treatments may need to work inside cells, not just target them from the outside. Quasiorganelle therapy is an experimental approach that aims to do this by using weakened, non-disease-causing bacteria derived from *Listeria monocytogenes* to deliver helpful genetic instructions directly into immune and tumor cells, with the goal of improving how the body recognizes and responds to cancer.

The aim of this study is to determine whether quasiorganelle therapy can be given safely to dogs with histiocytic sarcoma and to determine an appropriate dosing schedule. The treatment has been tested in laboratory and preclinical studies but not yet in dogs with naturally occurring cancer. Because animals with cancer may respond differently than healthy animals, this study also looks for early biological or clinical signs that the therapy may be beneficial.

Eligibility criteria:

Inclusion criteria:

- Confirmed diagnosis of histiocytic sarcoma, including hemophagocytic histiocytic sarcoma, as determined by immune marker expression.
- Visible tumor at the time of enrollment.
 - Up to 5 lesions
 - Sum of the longest lesion dimensions <15cm
- Adequate organ function indicated by standard laboratory tests.
- Minimum weight requirement of 20 kg (44 lbs).
- VCOG performance status up to 2.

Exclusion criteria:

- Concurrent diseases such as: diabetes mellitus, Addison's disease (hypoadrenocorticism), Cushing's disease (hyperadrenocorticism), kidney disease
- Active wounds.
- Concurrent medications such as: immunosuppressants (including corticosteroids, cyclosporine, azathioprine, mycophenolate) or systemic antibiotics within 14 days.
- Neutropenia, immunodeficiency, or immune-mediated disease
- Prior anti-cancer treatment
 - Corticosteroid (prednisone) within 7 days.
 - Chemotherapy within 14 days.
 - Radiation therapy within 30 days.

Treatment:

The first group (8 dogs) will receive quasiorganelle therapy alone. Their tumor will be measured and they will receive the quasiorganelle infusion. They will then be observed for up to 4 days at the MSU Veterinary Medical Center and blood and fecal samples will be taken at set timepoints. The

dogs will return for treatment once weekly for 4 doses followed by 2 weeks off. This schedule will then be repeated two more times for a total of 16 weeks of treatment. Imaging to determine alterations in tumor size will be repeated at the end of each 4 week treatment period.

The second group (8 dogs) will receive quasiorganelle therapy that includes gene therapy. Their treatment and monitoring schedule will be identical to that of the first group.

Following the 16 week treatment period, dogs will return for evaluation every 4 weeks or until progressive disease is documented.

Please note: While enrolled, dogs should not live with anyone who is pregnant or planning to become pregnant.

Compensation:

- This is a funded trial. All tests and treatments associated with the trial will be covered once a dog is enrolled.
- Complications associated with the trial will be covered. Clients are financially responsible for all treatments and diagnostics that are unrelated to the trial. Association between complications and trial treatment will be determined by the overseeing clinician and investigators.
- Initial evaluation appointments will be charged.
- Quasiorganelle therapy (with or without gene therapy) will be administered free of cost. Hospitalization immediately following administration and associated treatments will be free of cost. Blood and fecal sampling and imaging studies associated with the trial will be free of cost.

Contact information: Please feel free to contact our **Medical Oncology Team at (517) 353-5420** or **cvm.oncoinfo@msu.edu** to refer a patient or for any additional information. Referring veterinarian and client calls are welcome.