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## **Investigation of a Traditional Chinese Medicine Herbal Therapy protocol for Treatment of Dogs with Stage II Splenic Hemangiosarcoma after Splenectomy**

Hemangiosarcoma is a common cancer affecting the spleen of dogs. Most dogs diagnosed with this type of cancer are treated by removal of the spleen after the tumor has ruptured and bled, causing life-threatening blood loss. Survival time after surgery is short, with most dogs living only 2 months after surgery due to spread of the cancer to other organs. Because of the aggressive nature of this disease, chemotherapy is usually recommended after surgery in the hope of prolonging good quality life. However, the addition of chemotherapy only modestly prolongs survival. Most dogs still die of cancer spread within 3-4 months of diagnosis. New treatments are needed for this aggressive disease. The purpose of this study is to determine if treatment with a specific herbal therapy regimen is helpful in prolonging survival time after surgery in dogs with hemangiosarcoma of the spleen and no evidence of cancer spread.

### **Does my Dog Qualify for this study?**

Your veterinarian can help you determine if your dog qualifies as a study participant.

#### **Your dog may qualify if:**

- He/she has had a splenectomy (removal of the spleen) for a bleeding splenic tumor, biopsy was consistent with splenic hemangiosarcoma, and there is no evidence of cancer spread beyond the spleen
- Splenectomy was performed less than 3 weeks ago
- You are willing and able to bring your pet to the participating clinical trial center each month for evaluation
- You have declined chemotherapy

#### **Your dog does not qualify if:**

- Your dog had surgery for splenic hemangiosarcoma but did not have a ruptured spleen tumor
- Metastasis (spread of cancer beyond the spleen) is present
- They have a concurrent medical problem expected to limit life span to less than 6 months
- They are receiving any other supplements or treatment for cancer including chemotherapy, herbs, glandular, or homeopathic therapies

### **What are the benefits of participation?**

If your dog qualifies for enrollment and completes the study, the following will be provided free of charge:

- Herbal medications and supplements in the study protocol are provided at no cost to you
- Serum vitamin D, calcium, TK1 and CRP monitoring is provided every 2 months at no cost to you

**What procedures are required to determine eligibility and during the conduct of the study?**

- Prior to study inclusion, your dog must have blood chemistry panel, CBC, abdominal ultrasound and thoracic radiographs performed within 3 weeks of being enrolled in the study to determine general health as well as verify acceptability for enrollment in the study according to the inclusion criteria. Your dog will also receive a clinical examination that will require disclosure of complete medical history. Only after meeting all of the inclusion and none of the exclusion criteria will your dog be eligible to participate.
- During the initial evaluation, your dog will be evaluated to determine your dog's qualification for enrollment in the study.
- Your dog will be re-evaluated by one of the oncologists at the participating clinical trial centers every month. At these rechecks, your dog will be evaluated with a complete physical examination and every 2 months restaging (thoracic radiographs and abdominal ultrasound) and serum monitoring of vitamin D, calcium, TK1 and CRP will be performed.

## What are my responsibilities during the course of the study?

- You will be responsible for administering the study herbal medications and supplements (three herbal medications and one vitamin D3 supplement) regularly and as directed. The dosing of two of the two granular herbal medications is typically 3/4 tsp to 1 and 1/2 tsp twice daily (every 12 hours) or three times daily (every 8 hours), depending on the size of your dog. One of the herbal medications is in capsule form, usually 1-2 capsules twice daily. Vitamin D3 is administered once daily and is in liquid form.
- You will be required to transport your dog to the participating clinical trial center for monthly re-evaluation.
- You will be responsible for costs associated with restaging (thoracic radiographs and abdominal ultrasound) and office visits. You will also be responsible for cost of any other tests or treatments which may be recommended for medical management of your dog's condition.
- During the course of the study your dog may not receive any herbal supplements other than those prescribed by the Investigators.
- Your dog will continue to remain in the study for life, until the end of the study period or until your dog is unenrolled from the study by the Investigators or withdrawn from the study by you for any reason.
- You are required to continue administration of the herbal medications and supplements in the study protocol as directed during the entire time your dog is enrolled in the study.

## Is the study formula safe for my dog?

The main study formula ("HSA Compound") is a modification of a classical traditional Chinese Medicine formula which has been in use for centuries with no published reports of toxicity in humans or animals. Yun Zhi is a granular form of whole *Coreolus* Mushroom. In the experience of the clinical investigator, no toxicities have been seen other than transient diarrhea at high doses. Yunnan Pai Yao is an herbal formula used to decrease risk of bleeding. It is generally well tolerated with minimal risk of stomach upset. Possible adverse events with any herbal medication may include gastrointestinal toxicity (such as diarrhea, poor appetite or vomiting) and, with most Chinese herbal therapies, are typically related to gastrointestinal irritation and resolve with discontinuation of the formula or dose reduction.

Vitamin D3 supplementation at high doses can result in elevation in serum calcium (hypercalcemia). Toxicity has not been reported in the target serum vitamin D range (100-120 ng/mL) being used in this clinical study. Although the precise threshold of 25(OH)D<sub>3</sub> associated with hypercalcemia in animals has not been established, based on a number of animal studies the plasma vitamin D<sub>3</sub> concentrations associated with toxicity have all been in excess of 930 ng/mL. High doses of vitamin D3, either by accidental ingestion or administration of vitamin D3 outside of the prescribed dosage, could result in elevated serum calcium level that may be dangerous to your dog. Serum calcium will be monitored every 2 months during the course of the study.