Veterinary Health Center
AT KANSAS STATE UNIVERSITY
TO DISCOVER. TO TEACH. TO HEAL.

Probiotic prevention of GI hyperpermeability and metabolome disturbances in dogs with multicentric lymphoma undergoing multi-drug chemotherapy

Purpose:

This study aims to evaluate the effects of probiotic administration on gastrointestinal (GI) toxicity in dogs with lymphoma receiving chemotherapy.

Dogs with chemotherapy-related GI toxicity commonly experience vomiting, diarrhea, and decreased appetite following treatment. Some dogs may also be at increased risk of bacterial GI translocation (bacteria moving from the intestines into the blood) due to damage to the GI tract. The side-effects may be due to changes in the normal bacteria found in the GI tract and changes in the normal products that the bacteria make (e.g. bile acids and short chain fatty acids). None of the traditionally prescribed anti-nausea drugs or antibiotics reliably prevent these side-effects. In humans, giving probiotics with chemotherapy decreases episodes of severe diarrhea and decreases the need for antibiotics. If our study shows that probiotics prevent changes to bacterial by-products and GI permeability in dogs receiving chemotherapy, we may allow them to better tolerate their cancer treatment and decrease the need for hospitalization due to side-effects.

Prior to entry into this study, your dog must have a diagnosis of non-gastrointestinal lymphoma, based on either cytology or biopsies, abdominal ultrasound, initial screening blood work, and lack of historical GI signs. He/she must also be considered a good candidate for CHOP-based chemotherapy and start this chemotherapy protocol at the time of study enrollment.

Explanation:

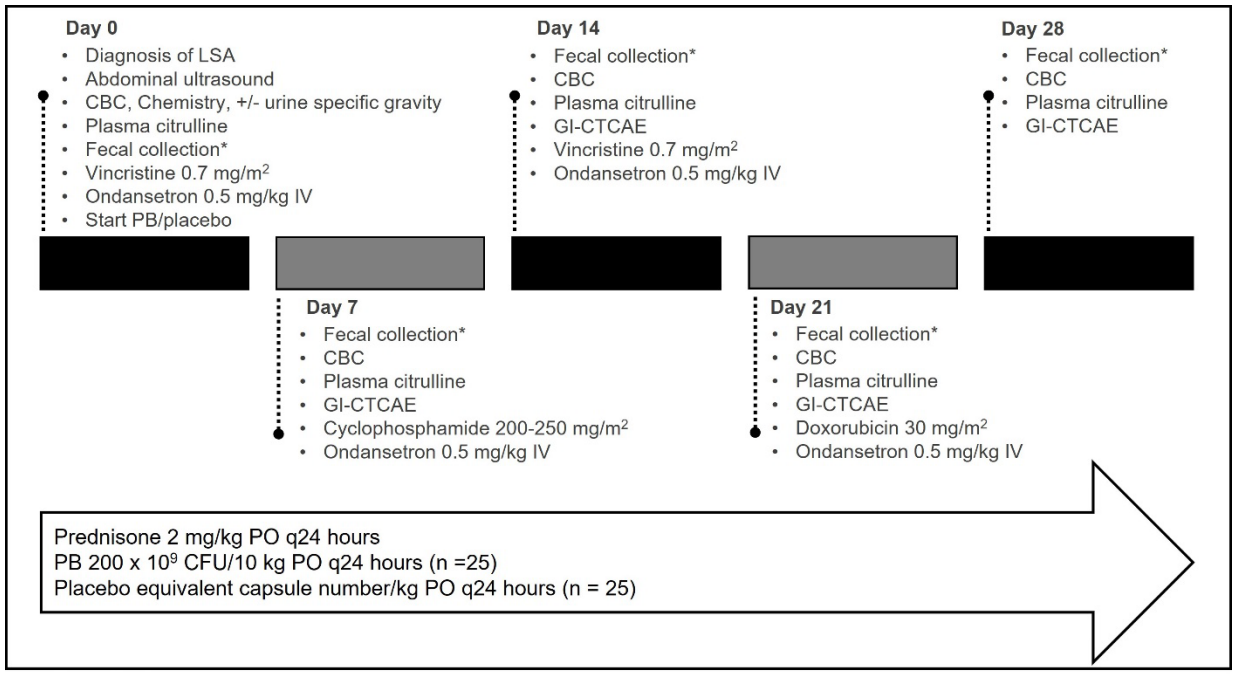
If your dog takes part in the study, he/she will have blood drawn for measurement of red and white blood cell counts (CBC) prior to chemotherapy and on each subsequent day of chemotherapy for the first month of treatment (Days 0, 7, 14, 21, 28); if your dog has a chemotherapy treatment delay, rechecks will be performed on the next day of chemotherapy and study timeline extended accordingly. A CBC would already be performed as part of your dog's standard chemotherapy protocol. We will also collect fecal samples on the day of enrollment prior to chemotherapy and days 7, 14, 21, 28 to look for changes in bacterial populations and fecal bile acids; *if your dog defecates at home the morning of his/her recheck appointments, we will ask you to bring a stool sample with you*. We will also ask that you take a picture of your dog's stool daily and email to mjugan@vet.k-state.edu. We will also take a blood sample to test for GI permeability (blood citrulline concentrations). *Please note that all fecal tests, as well as tests for GI permeability, are performed in bulk at study completion and results will not be immediately available.*

Your dog will receive either a daily probiotic medication or placebo for the 28 days of the study, or through the week after his/her first dose of doxorubicin if your dog has a treatment delay. We will also ask you to complete a survey about your dog's clinical signs, stool quality, as well as his/her current diet and other medications. We also request that, as long as your dog continues to eat its normal food well, you do not change your dog's diet during the study.

Please note this is a double-blinded study, meaning that neither you nor the oncologist treating your dog will know which treatment your dog receives.

Your dog will receive a single antinausea injection prior to chemotherapy at each of the study appointments but will not be prescribed anti-nausea drugs or antibiotics to give at home for GI side-effect prevention after chemotherapy. However, for dogs experiencing severe side-effects from their treatment, these may be prescribed following consultation with your dog's veterinarian.

Timeline



*Fecal testing:
Fecal scores, dysbiosis index,
Illumina 16S rRNA V4 analysis, bile acids

Investigators:
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Rachel Uyehara, DVM, MS

Eligibility:
Inclusion criteria:

- Dogs with a confirmed diagnosis of non-gastrointestinal lymphoma, whose owners have elected for chemotherapy treatment using the CHOP protocol
- Abdominal ultrasound screening within 2 weeks prior to starting chemotherapy
- Owner must be willing/able to administer a daily oral powder on their dog's food or mixed with water in a syringe if your dog is unwilling to eat mixed with food.
- Owner must be willing/able to return for rechecks at each day of chemotherapy for the first round of CHOP (Day 0- vincristine, Day 7- cyclophosphamide, Day 14- vincristine, Day 21- Doxorubicin, Day 28- Post-doxorubicin check)
- Owner must be willing/able to complete and return the daily clinical signs journal.

Exclusion criteria:

- Dogs with chronic GI clinical signs (vomiting, diarrhea, novel antigen/ hydrolyzed diet or medications (e.g. prednisone) to control historical GI disease, intestinal thickening or layering loss on ultrasound).
- Dogs with an MDR1 mutation** The Oncologist will likely recommend testing for this mutation if you own a dog breed that is at-risk for this mutation.
- Dogs who have received IV or oral antibiotics or probiotics in the last month.
- Dogs who have received IV or oral anti-emetics in the last week.
- Dogs who have previously received chemotherapy in the last year.
- Dogs who have received greater than one week treatment with steroids or anti-acids (omeprazole/Prilosec) within the last month.

Fees for Services: For enrolled dogs (those meeting initial eligibility based on CBC, chemistry panel, abdominal imaging, and commitment to administer the study drug for the first round of CHOP chemotherapy), the study will cover the cost of the CBC at initial visit and the 4 rechecks noted above. A chemistry profile to look for other diseases (e.g. kidney disease) will be covered at the initial appointment. The study will also cover the initial screening abdominal ultrasound. At the 4 rechecks noted above, the study will cover the cost of the Oncology recheck examination. It will cover an antinausea injection prior to chemotherapy at each of the study appointments. The study also covers the costs of the probiotic/placebo product, all fecal testing (microbiome analysis, bile acids), and GI permeability testing (plasma citrulline).

No direct compensation is provided, and the owner is responsible for additional testing, hospitalization, or changes in chemotherapy treatment, as well as other supportive medications (e.g. appetite stimulants) as recommended by the attending clinician. Changes in chemotherapy protocol (i.e. switching to a different drug type) or stopping chemotherapy will exclude your dog from further participation in the study.

Owner Responsibilities: Your dog will need to return to the Veterinary Health Center for chemotherapy, blood draw, and fecal sample collection on days 7, 14, 21, and 28 after his/her first dose of chemotherapy. You will need to provide us with a stool sample at each of the rechecks if your dog defecates the morning of the appointment, as well as daily picture of your dog's stool via email. We will also ask you to complete a survey about your dog's clinical signs and stool quality. You will need to administer the study drug once daily during the course of the study.

For questions or concerns regarding this study, please contact:
Dr. Maria Jugan at 785-532-5690