A biopsy will be collected from enrolled dogs prior to the first dose of drug (pre-treatment), on Day 8, Day 12, and possibly on Day 22 depending on how the dog has responded to therapy. Each biopsy will occur under anesthesia, either local (sedation with anesthetic) or general. Dogs will return to the Veterinary Medical Center on Days 8, 12, 15 and 22. Serial blood collections (5 time points) will occur on Day 1 of the study. Subsequent, single time point collections will occur on Days 8, 12, 15, and 22. Owners will be required to administer doses of TdCyd or Aza-TdC at home on Days 2, 3, 4, and 5 and on Days 9, 10, 11. The clinician will provide instructions on when and how to administer this medication to your dog.

This clinical trial led by the National Cancer Institute (NCI) assesses the safety and effectiveness of TdCyd and Aza-TdC, novel anticancer agents when given to dogs with cancer. Studies in dogs with cancer will complement currently open human trials designed to test new doses and effects of this agent.

**Client Compensation:**
Most costs associated with this study will be provided as part of participation. In the event, complications arise from study drug administration, the management will be covered by study funds up to $1250/per dog/event. This would include any unanticipated hospitalizations. Please discuss the study costs with the clinician. Additionally, support will be provided after the dog completes this study, a $1000 gift towards additional treatment for the dog's cancer at the Veterinary Medical Center.

**Potential Medical Benefits:**
The dog's cancer could respond well to the treatment they have been assigned. You will have the option to continue to give the same treatment to your dog for an additional 22 days in the event a response is detected. During that time, you will need to continue to regularly visit the Veterinary Medical Center for blood collection, as well as a biopsy of your dog's tumor. Please carefully discuss the full study calendar with the clinician.

**Potential Medical Risks:**
Cancer Progression: inappetence, pain, lameness/reluctance to walk or exercise, lethargy, coughing, respiratory impairment, gastrointestinal upset (vomiting, diarrhea, inappetence), evidence of metastatic spread of cancer cells to other parts of the body and subsequent organ failure.

Drug toxicities: fever, lethargy, gastrointestinal upset (vomiting, diarrhea, inappetence), cardiac arrhythmias, hyper/hypotension, impaired vision, low platelet counts (blood clotting cells), high or low white blood cell counts, anemia (low red blood cells), worsening kidney function, elevated liver enzymes, hypersensitivity/allergic reaction, rash, sepsis, fatality.

Research protocol: bruising, infection, bleeding at catheter site (if one is placed by the COTC site investigator); biopsy site infection, seroma (sterile fluid-filled swelling), pain, bruising, dehiscence.

It is hopeful that minimal adverse events will be seen and that they will be transient in nature. However, these are experimental therapies, so all potential adverse events are not known. Any sign of illness in enrolled dogs should be reported to the oncologist immediately and may require a return to the Veterinary Medical Center for evaluation.

# COTC027: Preclinical Comparison of Two Hypomethylating Nucleosides in Tumor-Bearing Dogs

Blue Buffalo Clinical Trials Office CVM-ClinicalTrials@osu.edu

**What qualifies my pet for enrollment?**

**Inclusion Criteria:**

Eligible patients (any breed of {species}) must meet all the following:

- Body weight ≥ 15 kg
- Histologically confirmed lymphoma or solid tumor (lymphoma may be confirmed by pre-treatment biopsy or cytology)
- Favorable performance status (grade 0 or 1)
- Both newly diagnosed dogs and those with recurrent/relapsed disease are eligible.

**Exclusion Criteria:**

- Dogs < 15 kg
- Histologic diagnosis of mast cell tumor (MCT), cutaneous hemangiosarcoma (cHSA), or soft tissue sarcoma.
- Dogs with a solid tumor or corresponding draining lymph node that is not readily accessible/amenable to serial biopsy/aspiration (respectively)
- No concurrent chemotherapy or radiation therapy. Dogs must be off all such therapy for 2 weeks prior to study enrollment (exception L-asparaginase).
- No corticosteroids or L-asparaginase for 7 days prior to study initiation (exclusive TdCyd and Aza-TdC administration required).
- Hypercalcemia causing illness.
- Significant co-morbid illness, which includes, but is not limited to, renal or hepatic failure, history of congestive heart failure or clinical coagulopathy.
- Creatinine > 3.0, Bilirubin > 2.0 or elevated bile acids, HCT < 25%, platelets < 50,000 any > grade 2 hematologic/biochemical abnormality

**Diagnosis/Condition Being Studied:** Canine lymphoma or solid tumor.

**Intervention:** TdCyd or Aza-TdC

**Primary Outcome:**
To identify a maximum tolerated dose (MTD) of TdCyd and Aza-TdC in dogs with the eligible tumor types.

**Primary Outcome Measure:**
Toxicity will be evaluated via dose escalation and assessment of dose-limiting toxicities (DLT). Evaluation of pharmacokinetics (drug exposure), and tumor pharmacodynamic modulation (global methylome assessment, DNMT1, DNMT3, p16 status; DDR/cell death/autophagy biomarker panels) will be assessed to define a dose-PD response relationship for TdCyd and Aza-TdC.

**Primary Outcome Endpoint:**
To define the safety, pharmacokinetics, and pharmacodynamic modulation of these investigational agents.

**Contact:**
Clinical Trials Office
Email: CVM-ClinicalTrials@osu.edu

Dr. William Kisseberth
Email: kisseberth.2@osu.edu

**If you believe your pet may be eligible for this study, please fill out a pre-screening questionnaire.**

**Pre-Screen HERE**