

**COTC008:** Evaluation of the mTOR inhibitor Rapamycin in Dogs with Metastatic Osteosarcoma

**Sponsor:** Morris Animal Foundation and The Center for Cancer Research, NCI. Scientific endorsement from the Children's Oncology Group and the Sarcoma Alliance for Research through Cooperation (SARC).

**Purpose:** Signaling through the mTOR pathway has been recently shown to contribute to the growth, progression and chemo resistance of several cancers. Accordingly, agents that act against this pathway, namely Rapamycin and its analogs (Rapalogs), have been developed as potentially valuable therapeutics for cancer, with a particular emphasis on sarcomas and osteosarcoma. However the use of mTOR inhibitors requires optimization of dose and regimen. This study seeks to define and compare three schedules for chronic delivery of Rapamycin using endpoints of tolerability, blood Rapamycin levels, modulation of mTOR targets in the blood and anti-tumor activity against pulmonary metastatic disease. Dogs will receive intramuscular injections at home on varying schedules (sometimes daily) and return weekly to their COTC site for evaluation and serial blood collections. Tumor burden will be assessed monthly.

**Participating Sites:** University of Tennessee, Colorado State University, University of Missouri, University of Pennsylvania, University of Wisconsin, Ohio State University, University of Illinois, Tufts University, University of California-Davis, Cornell University, University of Florida, University of Georgia, North Carolina State University, Purdue University

**Study Numbers:** 24-30 dogs anticipated (8 per schedule arm)

**Eligibility Requirements:**

- Radiographically measurable osteosarcoma pulmonary metastases (may be presumed based on clinical history)
- Pulmonary metastatic burden < 15 metastatic lesions; no lesion greater than 5 cm diameter. Concurrent organ metastatic sites are permissible.
- Rapamycin as the sole therapy (NSAIDs allowed if on for 30 days)
- Favorable performance status and life expectancy of at least 60 days
- Informed owner consent
- No 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