

## ONGOING EVALUATION OF SINGLE AGENT THALIDOMIDE IN DOGS WITH MEASURABLE CANCER.

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### INTRODUCTION

Angiogenesis is essential for cancer progression and metastasis. Inhibition of angiogenesis may be an effective treatment for cancers. The anticancer activity of thalidomide has been demonstrated in early human clinical trials. The objectives of this study are: 1) to determine the safety and efficacy of oral thalidomide against measurable canine cancers, 2) to define an optimal biological dose for thalidomide in dogs, and 3) to define tumor types sensitive to antiangiogenic therapy with thalidomide.

### METHODS

This is a single agent, phase I/II clinical study. Entry requirements include measurable and histologically confirmed disease, body weight > 10 kg, no chemotherapy within 10 days of treatment, and informed owner consent. Three escalating dose cohorts (30 cases/cohort) have been defined: 3.3-6.5, 6.6-13, and 13.3-26 mg/kg QD. Physical examinations, CBC, serum biochemistry, and tumor response will be evaluated at day 0 and every 30 days thereafter. Urine and plasma samples collected before and during thalidomide therapy will be assayed for markers of antiangiogenic activity including, basic fibroblast growth factor, vascular endothelial growth factor and interleukin-8.

### RESULTS

Six cases to date have been evaluated. All dogs had progressive disease prior to study entry. No side effects to thalidomide have been noted in the first dose cohort.

Histology	TNM Stage	Measurable Lesion	Prior Treatment	Treatment Length	Outcome
Malignant pericardial mesothelioma	TsxM1pulmonary (possible CNS)	Pulmonary	Surgery, Chemotherapy, Immunotherapy	116 days	SD x 90 days then PD
Nasal carcinoma	T3N2mandibular, prescapular M0	Lymph nodes, Orbital proptosis	Radiation therapy, Chemotherapy	80 days	SD x 77 days then PD
Rib osteosarcoma	T2M1 pulmonary	Pulmonary, local recurrence	Surgery, Chemotherapy	33 days	PD
Carcinomatosis abdomen		Liver	None	27 days	PD
Hepatocellular, carcinoma		Liver	Surgery	36 days	PD
Osteosarcoma	T2M1 pulmonary	Pulmonary	Surgery, Chemotherapy	9 days	PD

SD -Stable Disease; PD - Progressive Disease

### DISCUSSION

Thalidomide appears to be well tolerated in the current dose cohort. No objective tumor responses have been documented at this time. Additional entry of cases with smaller tumor burden may allow antiangiogenic activity to be exerted before disease progression. Surrogate markers of systemic antiangiogenic activity, measured in plasma and urine, may be helpful in defining optimal biologic dose.