

## EVALUATION OF THE ORAL ANTIMITOTIC, ABT-751, ALONE AND IN COMBINATION AN ANTIANGIOGENIC PEPTIDE OF THROMBOSPONDIN-1, ABT-510, IN DOGS WITH LYMPHOMA

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**Introduction:** Previous studies defined the MTD of ABT-751 in dogs with lymphoma to be 350 mg/m<sup>2</sup>. Dose limiting toxicities (DLT) were gastrointestinal, including vomiting and diarrhea. Early evidence of clinical activity was observed at this dose. ABT-510, an oral antiangiogenic agent has resulted in efficacy in open-label treatment of dogs with a variety of cancers, including lymphoma.

**Methods:** Prospective studies of single-agent ABT-751 or in combination with ABT-510 were undertaken in dogs with lymphoma, most of whom had received previous chemotherapy. The dose of ABT-751 was 350mg/m<sup>2</sup> PO QD for 7 days, then EOD. ABT-510 was given at 0.5mg/kg SQ BID starting 24 hours after the first dose of ABT-751. Primary endpoints included response rate, response duration, time to progression, and toxicity. Secondary endpoints included pharmacokinetics and changes in circulating endothelial cells.

**Results:** Treatment with single agent ABT-751 resulted DLT in 4/19 (21.0%) dogs. DLT was observed in 9/25 (36.0%) dogs treated with combination therapy. Cytopenias were observed in 3 dogs treated with combination therapy. No cytopenias were observed in dogs treated with ABT-751 alone. In the treatment-received population, which included dogs on study for at least 7 days, clinical responses were seen in 3/15 (20.0%) treated with ABT751 and 8/20 (40.0%) treated with ABT-751 and ABT-510. Response duration ranged from 8-111 days.

**Conclusion:** Though small study numbers were evaluated, response rate was higher for combination ABT-751 and ABT-510 versus ABT-751 alone. Toxicity profiles were similar for combination therapy and single-agent ABT-751. No previous toxicity has been observed in over 300 dogs treated with ABT-510; thus, toxicities seen with combination therapy are attributed to ABT-751.