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Abstract # **1282**

Phase I evaluation of STA-1474, a pro-drug of the novel HSP90 inhibitor STA-9090, in dogs with spontaneous cancer.

Cheryl A. London[1], Misty D. Bear[1], Jennifer McCleese[1], Kevin P. Foley[2], Reji Paalangara[2], Takayo Inoue[2], Weiwen Ying[2], James Barsoum[2].

[1] Ohio State University, Columbus, OH
[2] Synta Pharmaceuticals Corp., Lexington, MA

Purpose: The novel water soluble compound STA-1474 is metabolized to STA-9090, a potent HSP90 inhibitor previously shown to kill canine tumor cell lines *in vitro* and inhibit tumor growth in the setting of murine xenografts. The purpose of the following study was to extend these observations and investigate the safety and efficacy of STA-1474 in dogs with spontaneous tumors.

Experimental Design: This was a Phase 1 trial in which dogs with spontaneous tumors received STA-1474 under one of three different dosing schemes. Pharmacokinetics, toxicities, biomarker changes, and tumor responses were assessed.

Results: Twenty-five dogs with a variety of cancers were enrolled. Toxicities were primarily gastrointestinal in nature consisting of diarrhea, vomiting, inappetence and lethargy. Upregulation of HSP70 protein expression was noted in both tumor specimens and PBMCs within 7 hours following drug administration. Measurable objective responses were observed in dogs with malignant mast cell disease (n=3), osteosarcoma (n=1), melanoma (n=1) and thyroid carcinoma (n=1), for a response rate of 24% (6/25). Stable disease (>10 weeks) was seen in 3 dogs, for a resultant overall biological activity of 36% (9/25).

Conclusions: This study provides evidence that the STA-1474 exhibits biologic activity in a relevant large animal model of cancer. Given the similarities of canine and human cancers with respect to tumor biology and HSP90 activation, it is likely that STA-1474 and STA-9090 will demonstrate comparable anti-cancer activity in human patients.