

Abstract # 3083

A Phase 1 dose-escalation study of the Hsp90 inhibitor STA-9090 administered twice weekly in patients with solid tumors.

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Background: STA-9090 is a potent, next-generation Hsp90 inhibitor that is structurally unrelated to the first-generation ansamycin class of Hsp90 inhibitors, such as 17-AAG and IPI-504, and has shown superior activity and an improved safety profile relative to these agents in preclinical studies.

Methods: Patients with solid tumor malignancies who have exhausted standard of care treatment options are eligible. Patients receive STA-9090 as a 1-hr infusion twice weekly for 3 weeks of a 28-day cycle. Serial PK samples are obtained on days 1 and 15 of cycle 1. Safety assessments included the number and grade of AEs, changes from baseline in laboratory parameters, and ECG changes.

Results: Data are presented for the first 29 patients (13 M, 16 F; median age 55 yrs, range 32-81; ECOG status range 0-2) treated at dose levels ranging from 2 mg/m² to 25 mg/m². The AEs reported in >20% of patients were fatigue, nausea, anemia, diarrhea, vomiting, anorexia, and headache; the majority of these AEs were mild to moderate in severity. A DLT of elevated LFTs was reported in the 10 mg/m² cohort. STA-9090 shows linear pharmacokinetics, exhibits rapid distribution, has a mean terminal phase half life of 10-14 hours and no accumulation in plasma. The MTD has not been reached, and dose escalation continues with a total of 32 patients enrolled at doses up to 50 mg/m². Preliminary signs of clinical activity have been observed and include a durable PR in a patient with melanoma and tumor shrinkage with prolonged SD in several patients with different tumor types, including melanoma and NSCLC.

Conclusions: STA-9090 has been well tolerated at dose levels up to 25 mg/m² administered twice weekly. Preliminary safety profile and activity signals warrant continued evaluation of STA-9090 using a twice weekly dosing regimen.