

Abstract # 2529

A Phase 1 dose-escalation study of the Hsp90 inhibitor STA-9090 administered once 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: In a standard 3 + 3 dose escalation trial, advanced cancer patients received STA-9090 as a 1-hr infusion once weekly for 3 weeks of a 28-day cycle. Blood samples for PK and biomarker analyses were collected in cycle 1. Safety assessments included the number and grade of AEs, changes from baseline in laboratory parameters, and ECG changes.

Results: 35 patients (17 M, 18 F; median age 61 yrs, range 37-87; ECOG status range 0-2) received doses ranging from 7-259 mg/m² once weekly. There have been 3 DLTs: 1 at 150 mg/m² (grade 3 amylase elevation) and 2 at 259 mg/m² (grade 4 fatigue and grade 3 diarrhea). The MTD is 216 mg/m². AEs reported in ≥ 20% of patients were diarrhea, anemia, fatigue, abdominal pain, nausea, elevated alk phos, constipation and dyspnea; most of these AEs were mild to moderate in severity. STA-9090 shows linear PK and has a mean terminal half life of 5-13 hours with no accumulation. Preliminary signs of clinical activity have been observed including a durable PR in a patient with rectal carcinoma, as well as several cases of tumor shrinkage and prolonged SD in patients with tumors including NSCLC, renal cell carcinoma and GIST, who were treated for 16 to 48 weeks.

Conclusions: STA-9090 has been well tolerated up to dose levels of 216 mg/m² given once weekly, without significant liver toxicity. Preliminary safety and activity signals warrant continued evaluation of single-agent STA-9090 using once weekly dosing.