
**Sub-category:**
Phase I Studies

**Category:**
Developmental Therapeutics - Clinical Pharmacology and Immunotherapy

**Meeting:**
2010 ASCO Annual Meeting

**Session Type and Session Title:**
Poster Discussion Session, Developmental Therapeutics - Clinical Pharmacology and Immunotherapy

**Abstract No:**
2528

**Citation:**
J Clin Oncol 28:15s, 2010 (suppl; abstr 2528)

**Author(s):**
T. A. Samuel, C. Sessa, C. Britten, K. S. Milligan, M. M. Mita, U. Banerji, T. J. Pluard, P. Stiegler, C. Quadt, G. Shapiro; Medical College of Georgia, Augusta, GA; Oncology Institute of Southern Switzerland, Ospedale Regionale Bellinzona e Valli, Bellinzona, Switzerland; University of California, Los Angeles Clinical Research Unit, Los Angeles, CA; National Cancer Institute, Las Vegas, NV; Cancer Therapy and Research Center, San Antonio, TX Drug Development Unit, Royal Marsden Hospital, Sutton, United Kingdom; Division of Medical Oncology, Washington University School of Medicine, Saint Louis, MO; Novartis Pharmaceuticals, East Hanover, NJ; Novartis Pharmaceuticals, Basel, Switzerland; Dana-Farber Cancer Institute, Boston, MA

**Abstract Disclosures**

**Faculty & Discussant Disclosures**

**Annual Meeting Planning Committee Disclosures**

**Abstract:**

**Background:** AUY922, a novel isoxazole-based HSP90 inhibitor, causes the degradation of multiple oncogenic cellular proteins and preclinical data suggest broad antitumor activity. **Methods:** Single agent AUY922 was administered as IV infusion over 1h, once weekly, to patients (pts) with advanced solid tumors to determine the maximum tolerated dose (MTD) in a phase I study. Dose escalation was guided by a Bayesian logistic regression model with overdose control. Endpoints included safety, tolerability, preliminary activity, PK, and PD. **Results:** 96 pts received AUY922 at doses of 2-70 mg/m$^2$ (23 pts at 70 mg/m$^2$). Pt characteristics: median age 57 yrs, 96% WHO performance status 0 or 1, 41% male, and 82% Caucasian. The most frequently reported adverse events possibly related to AUY922 were diarrhea in 53 pts (55%), nausea in 34 pts (35%), fatigue in 31 pts (32%), night blindness in 19 pts (20%), and vomiting in 18 pts (19%). Visual symptoms (mainly grade 1-2 and mostly reversible) including blurred vision, flashing, and delayed dark/light accommodation were reported starting at 40 mg/m$^2$, and increased in frequency or severity with dose. Dose limiting toxicities, all grade 3, included atrial flutter (22 mg/m$^2$), anorexia, fatigue, and diarrhea (40 mg/m$^2$), asthenia and diarrhea (54 mg/m$^2$) and diarrhea and darkening of vision (70 mg/m$^2$). The MTD was 70 mg/m$^2$. Median duration of exposure was 7.0 weeks (range; 1, 80). Disease stabilization was reported in 16 pts and 9 pts reported partial metabolic response in FDG-PET scans. AUY922 blood concentration followed a bi-exponential decline with a fast a phase ($t_{1/2} < 10$ min) and a slow $\beta$ phase ($t_{1/2} ~60$h). Dose-related induction of HSP70, indicating inhibition of HSP90, was seen. A phase II expansion study in pts with advanced breast cancer (HER2+ and ER+) has begun. **Conclusions:** Weekly IV infusion of single agent AUY922 was well tolerated at the MTD of 70 mg/m$^2$. Disease stabilization was seen in a subset of pts receiving AUY922.
Associated Presentation(s):

   
   Meeting: 2010 ASCO Annual Meeting
   Presenter: Thomas A. Samuel
   Session: Developmental Therapeutics - Clinical Pharmacology and Immunotherapy (Poster Discussion Session)

Other Abstracts in this Sub-Category:

1. Use of a human ribonuclease variant, QBI-139, for the treatment of cancer.
   
   Meeting: 2010 ASCO Annual Meeting  Abstract No: TPS162  First Author: L. E. Strong
   Category: Developmental Therapeutics - Clinical Pharmacology and Immunotherapy - Phase I Studies

2. Phase I study of dasatinib in combination with bevacizumab in advanced solid tumors.
   
   Meeting: 2010 ASCO Annual Meeting  Abstract No: TPS163  First Author: G. Kim
   Category: Developmental Therapeutics - Clinical Pharmacology and Immunotherapy - Phase I Studies

3. A multicenter, open-label phase Ib/II study to assess the safety and clinical activity of intravenous combretastatin A1 diphosphate (OXi4503) as monotherapy in subjects with primary or secondary hepatic tumor burden.
   
   Meeting: 2010 ASCO Annual Meeting  Abstract No: TPS164  First Author: P. N. Mainwaring
   Category: Developmental Therapeutics - Clinical Pharmacology and Immunotherapy - Phase I Studies

Abstracts by T. A. Samuel:

1. Effects of simvastatin and docetaxel on different pathways in the regulation of prostate and breast cancer cell survival.
   
   Meeting: 2011 ASCO Annual Meeting  Abstract No: e13545  First Author: S. T. Kochuparambil
   Category: Developmental Therapeutics - Experimental Therapeutics - DNA Repair and Apoptosis

2. Overall survival effect of lower chemotherapy dosing in extremely obese (BMI ≥ 35) patients with breast cancer based on adjusted BSA.
   
   Meeting: 2011 ASCO Annual Meeting  Abstract No: 1047  First Author: P. Sharma
   Category: Breast Cancer - Triple-Negative/Cytotoxics/Local Therapy - Cytotoxic Chemotherapy

   
   Meeting: 2010 ASCO Annual Meeting  Abstract No: 2528  First Author: T. A. Samuel
Presentations by T. A. Samuel:


Meeting: 2010 ASCO Annual Meeting
Presenter: Thomas A. Samuel, MD
Session: Developmental Therapeutics - Clinical Pharmacology and Immunotherapy (Poster Discussion Session)

More...

Educational Book Manuscripts by T. A. Samuel:

No items found.