Prospective comparison of invasive circulating tumor cells (iCTCs) vs PSA and mPFS in prostate cancer (PC) treated with SM-88.

Authors:

Wen-Tien Chen, Terence W. Friedlander, Huang Dong, Qiang Zhao, Giuseppe Del Priore; Stony Brook University, Stony Brook, NY; University of California San Francisco Medical Center, San Francisco, CA; Vitatex Inc., Stony Brook, NY, US; Tyme Technologies Inc., New York, NY

Background:

SM-88 is a relatively non-toxic novel combination of dysfunctional tyrosine and repurposed agents (CYP3a4 inducer, mTOR, oxidative stress catalyst) with activity in PC. PSA, mPFS and iCTCs were assessed in a Phase Ib/II trial.

Methods:

Blood from men treated with SM-88 for biochemically recurrent non-metastatic PC (nmPC) was prospectively examined for iCTCs and PSA at each cycle. A cell adhesion matrix (CAM)-based platform, Vita-AssayTM plate (two-step) and Vita-CapTM tube (single-step), were used to enrich metastasis-initiating cells from blood. Isolated cells were identified and enumerated by flow cytometry using tumor progenitor and epithelial markers plus negative hematopoietic lineage markers to identify iCTCs. Serial changes in iCTCs and PSA were measured in 124 blood and 305 serum samples, respectively, from 13 PC patients to assess their concordance and relationship with radiographic or metastasis progression free survival (mPFS).

Results:

Among 13 subjects with Vita-AssayTM iCTC results, there were 11/13 with reduction within the 1st cycle (28 days). Thereafter all 11 had continued reduction of iCTCs with median of 6 wks to nadir, and 5 having undetectable levels a median of 7 wks on treatment. Two of 124 iCTC assays had high background red cell due to microclots in transit. Correlation of the iCTC assays enriched by Vita-AssayTM vs Vita-CapTM was r2= 0.78 ($P < 0.0001$). 83% (10/12 subjects with ≥ 3 cycles of treatment) had an

improvement in PSA velocity and at least one decrease in PSA. There were 2 biochemical progressions (PCWG3 criteria), one of which also had radiographic progression. iCTC results matched PSA PD and local PD was confirmed by CT 12 wks later. The other progression was predicted 8 wks earlier by iCTCs than PSA (iCTC sensitivity and specificity for PD = 100%). Other biomarkers (LDH, uNTX, neutrophil:lymphocyte, bsAlkP) did not predict mPFS or PSA rise.

Conclusions:

Treatment with SM-88 in patients with nmPC in a phase Ib/II cohort was associated with iCTC reduction, and PSA stability. iCTCs prospectively correlate with prolonged mPFS despite equivocal PSA results, and predicted both biochemical and radiographic progression. Clinical trial information: NCT02796898