Treating advanced non-small lung cancer (NSCLC) patients after checkpoint inhibitor treatment failure with a novel combination of Viagenpumatucel-L (HS-110) plus nivolumab

Daniel Morgensztern[1], Saiama N. Waqar[1], Lyudmila Bazhenova[2], Rachel E. Sanborn[3], Lori McDermott[4], Jeff Hutchins[4], Luis E. Raez[5], Corey J. Langer[6], Roger B. Cohen[6]

[1]Washington University School of Medicine, St. Louis, MO; [2]UC San Diego, Moores Cancer Center, La Jolla, CA; [3]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR; [4]Heat Biologics, Inc, Durham, NC; [5]Memorial Cancer Institute, Pembroke Pines, FL; [6]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

Background:
Viagenpumatucel-L (HS-110) is an allogeneic cellular vaccine derived from a human lung adenocarcinoma cell line transfected with the gp96-Ig fusion protein that functions as an antigen chaperone for cross presentation and dendritic cell activation. DURGA is a multi-cohort study evaluating the combination of HS-110 and anti-PD-1 monoclonal antibodies in patients with advanced NSCLC. We report on Cohort B, which enrolled patients with progressive disease (PD) after receiving a minimum of 4 months of treatment with a checkpoint inhibitor (CPI) at any time prior to study entry.

Methods:
Patients with previously treated NSCLC received weekly HS-110 (1 X 10^7 cells) intradermally for 18 consecutive weeks and nivolumab IV 240 mg every 2 weeks, followed by nivolumab maintenance until tumor progression or intolerable toxicity. Tissue was tested at baseline for PD-L1 expression (≥ 1% or < 1%) and tumor infiltrating lymphocytes (TILs). TIL high was defined as >10% CD8+ lymphocytes in the tumor stroma. The primary endpoint was objective response rate (ORR) by RECIST 1.1. Secondary endpoints included ORR and clinical benefit rate using iRECIST, progression-free survival (PFS), overall survival (OS) and adverse events (AEs).

Results:
As of March 2019, 56 patients were enrolled and evaluated for efficacy. The median number of prior treatment lines was 2 [range 1 to 6]. Seven patients (13%) achieved partial response and 26 patients (46%) had stable disease. Median PFS and median OS were 3.2 months and 11.8 months, respectively. Immune ORR and clinical benefit rate by iRECIST were 14% and 61%, respectively. Patients experiencing injection site reactions (ISR) had improved PFS (3.7 vs 1.8 months; HR 0.21, *p =0.0021*) and improved OS (12 vs 5 months; HR 0.16, *p=0.0005*) compared to those without ISR. 96% of patients experienced at least one adverse event, and 92% of all AEs were grade 1 or 2. The most common AEs were fatigue (34%), hypocalcemia (18%), cough (16%) and diarrhea and dyspnea (14% each). There were four grade 4 events: QTc prolongation, stroke, pericardial tamponade, and hyponatremia, none of which were deemed related to treatment. There were no grade 5 AEs.

Conclusions:
The combination of HS-110 and nivolumab is well tolerated, and does not appear to increase the incidence of immune-related AEs as compared to CPI monotherapy. Patients continue to be enrolled into this cohort. Data suggest that re-challenging the immune system with nivolumab and HS-110 after CPI treatment failure restores responsiveness and clinical benefit for some patients.