Tumor antigen expression and survival of patients with previously-treated advanced non-small cell lung cancer (NSCLC) receiving viagenpumatucel-L (HS-110) plus nivolumab

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Background:
Viagenpumatucel-L (HS-110) is an allogeneic cellular vaccine derived from a human lung adenocarcinoma cell line transfected with gp96-Ig fusion protein. Gp96-Ig functions as an antigen chaperone for dendritic cell activation and direct CD8+T cell expansion via cross presentation. DURGA is a multi-cohort study evaluating HS-110 plus anti-PD-1 mAbs in patients (pts) with advanced NSCLC. We report on Cohort A, which enrolled previously-treated pts who had not received an anti-PD(L)1 prior to study entry.

Methods:
Primary objectives were safety and objective response rate (ORR). Overall Survival (OS) was a secondary endpoint. Pts received 1 X 10^7 HS-110 cells intradermally every week for 18 wks and nivolumab until tumor progression. To determine cancer testis antigen (CTA) overexpression from baseline pt tumor samples, hybrid-capture RNA-seq libraries were prepared from macrodissected formalin fixed paraffin embedded tumor tissue and sequenced on an Illumina NovaSeq 6000. Gene-level transcripts were quantified using the Salmon software package.

Results:
47 pts were enrolled into Cohort A. ORR and clinical benefit rate (CR + PR + SD) were 21% and 43%, respectively, with a 17.2 month median duration of response. Median OS was 28.7 months (mos), with a median follow up of 15.7 mos. One and 2-year survival were 57% and 36%, respectively. A prespecified exploratory analysis of CTA expression level in baseline pt tumor tissue was performed. 50% of pts shared at least 8 of the 39 total antigens overexpressed by HS110. Although there was no difference in ORR between these groups, mOS was higher in pts with tumors that shared ≥ 8 antigens with HS-110 (not reached (NR) [95%CI: 10.3 mos, NR] vs 6.7 mos [95%CI: 1.4 mos, NR]), p=0.028. Pts whose tumors expressed the ZNF492 antigen also had improved OS (NR [95%CI: 11.6 mos, NR] vs 7.2 mos [95%CI: 1.6 mos, NR]), p=0.03. All pts experienced at least one adverse event (AE), and the most common AEs were fatigue (28%), arthralgia (19%) and cough (17%). There were 2 grade 5 AEs not related to treatment.

Conclusions:
The combination of HS-110 and nivolumab appears safe and well tolerated. OS was improved in pts whose tumors express ≥ 8 shared antigens with HS110, as well as in those who specifically expressed ZNF492. Further exploration of antigen expression as a predictor for treatment outcome with HS110 plus nivolumab is ongoing.