VIAGENPUMATUCEL-L (HS-110) IN COMBINATION WITH NIVOLUMAB IN PREVIOUSLY-TREATED PATIENTS WITH ADVANCED NON-SMALL LUNG CANCER (NSCLC)

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Background

Viagenpumatucel-L (HS-110) is an allogeneic cellular immunotherapy that incorporates a broad range of tumor antigens that are known to be shared amongst a high proportion of patients with non-small cell lung cancer (NSCLC). This cell system contains gp96-Ig and is designed to enable the cell to express gp96 in secreted form. The secreted gp96 acts as a chaperone to induce cellular immune responses to the tumor antigens expressed by **Viagenpumatucel-L (HS-110)**. gp96 is a unique chaperone because it can activate MHC and up-regulate T-cell co-stimulation and deliver chaperoned antigens to an APC for display via MHC I, with the net result being CD8+ T-cell mediated immune responses[1-2].

The HS110-102 "Durga" Trial is an exploratory, multi-cohort master protocol evaluating HS-110 in combination with anti-PD1 mAbs in the treatment of advanced non-small lung cancer. Here we present top line data from Cohort A. This cohort is comprised of previously-treated patients who have not received a checkpoint inhibitor (CPI) prior to study entry. NCT Trial ID: **NCT02439450**

Mechanism of Action

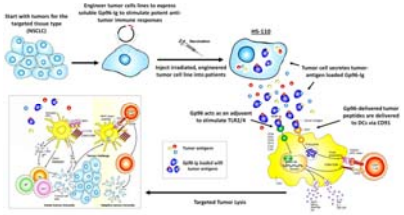


Figure 1: Viagenpumatucel-L (HS-110) Mechanism of Action and Pre-clinical Activity
HS-110 is derived from a lung adenocarcinoma cell line transfected with gp96-Ig, which acts as a chaperone protein for tumor associated antigens and is recognized by CD91 on APCs, resulting in cross-presentation of antigen to MHC I for the selection of antigen-specific CD8 cells. Gp96-Ig also binds to TLRs 2 and 4 leading to upregulation of co-stimulatory molecules, which include MHC II and secretion of cytokines and chemokines.

Study Schema

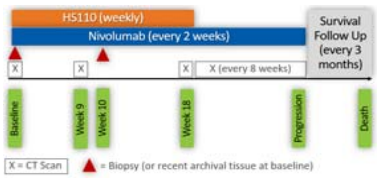


Figure 2: HS110-102 Study Schema
Patients receive weekly HS-110 (1 x 10^7 cells) intradermally for 18 weeks via 5 simultaneous injections of 0.1ml each, and biweekly nivolumab 240 mg IV until disease progression or unacceptable toxicity.

Patient Characteristics

		ITT (N = 46)
Median age (range)		65 (37 – 87)
Female gender		26 (57%)
Caucasian		41 (89%)
ECOG PS 1		32 (70%)
EGFR or ALK positive		6 (13%)
Histology	Adeno Squamous	43 (93%) 3 (7%)
Smoking status	Current/past Never	39 (85%) 7 (15%)
Prior lines of tx	1 2 3 or more	31 (67%) 7 (15%) 8 (18%)
PD-L1	< 1% ≥ 1% Unevaluable	21 (46%) 9 (19%) 16 (35%)

Table 1: Patient Characteristics
Baseline patient demographics of Intent-to-treat population (n=46).

Best Overall Response

	RECIST 1.1	iRECIST
ORR	**20% (9)**	**22% (10)**
PR	20% (9)	22% (10)
SD	26% (12)	26% (12)
Not Evaluable	7% (15)	7% (15)
DCR	**46% (21)**	**48% (22)**

Table 2: Objective Response Rates
ORR of the Intent-to-treat population (n=46) performed locally by study Investigators using RECIST 1.1. iRECIST shown as one patient achieved confirmed PR after initial radiographic PD.

T Cell Changes by Best Overall Response (BOR)

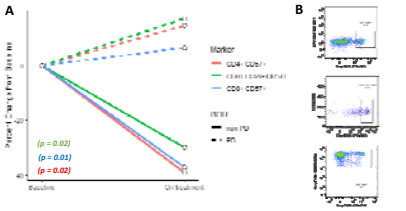


Figure 3: T Cell Subset Changes in Peripheral Blood Based on BOR
A. Mean flow cytometric measurements of T cell subset changes in 22 patients at baseline and on-treatment based on CD57+ (terminal differentiation) expressed on CD8+ (effector), CD8+CD28- (effector memory) and CD4+ (helper) cells according to the patient's BOR clinical outcome by RECIST 1.1: Progressive Disease (PD, n=9) or non-Progressive Disease (SD or PR, n=13). This downward trend is an indicator of effective immunity in an antigen driven population of effector cells. **B.** Representative flow cytometry histograms of peripheral blood T cell subpopulations for a study patient at baseline.

Overall Survival

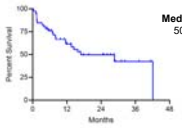
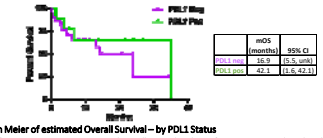
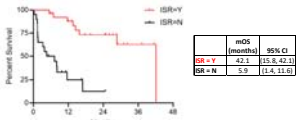


Figure 4: Kaplan Meier of estimated Overall Survival – ITT Population
Overall survival of ITT population (N=46). Twenty-three (23) patients censored. mOS is estimated by KM to be 16.9 months [95% CI; 11.6, 42.1].



	mOS (months)	95% CI
PDL1 neg	16.9	[5.5, unk]
PDL1 pos	42.1	[1.6, 42.1]

Figure 5: Kaplan Meier of estimated Overall Survival – by PDL1 Status
Using a cut-off of 1% PDL1 expression, estimated overall survival is shown for PDL1 negative (n=21) and PDL1 positive (n=9).



	mOS (months)	95% CI
ISR = Y	42.1	[15.8, 42.1]
ISR = N	5.9	[1.4, 11.6]

Figure 6: Kaplan Meier of estimated Overall Survival – by Injection Site Reaction
Using KM estimates of survival, patients who experienced at least one injection site reaction at any time during treatment (n=26) had statistically significant improved overall survival compared to patients who did not experience an injection site reaction (n=20). HR 0.14 [95% CI; 0.05, 0.36] *p<0.0001*

Best Target Lesion Response

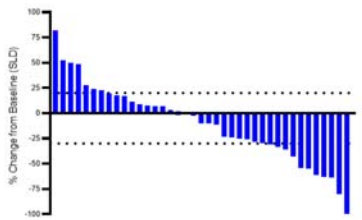


Figure 7: Best Target Lesion Response
Waterfall plot of evaluable ITT patients (N=39) using RECIST 1.1 Target Lesion Response. Post-baseline scans not available for 7 patients. Tumor shrinkage was observed in 21 (46%) of 46 ITT patients.

Progression Free Survival

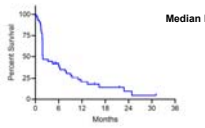
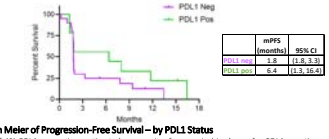
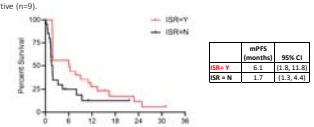


Figure 8: Kaplan Meier of Progression-Free Survival – ITT Population
Progression-free survival of ITT population (N=46). Seven (7) patients censored. mPFS is estimated by KM to be 1.9 months [95% CI; 1.8, 6.4].



	mPFS (months)	95% CI
PDL1 neg	1.8	[1.8, 3.3]
PDL1 pos	6.4	[1.3, 16.4]

Figure 9: Kaplan Meier of Progression-Free Survival – by PDL1 Status
Using a cut-off of 1% PDL1 expression, estimated progression-free survival is shown for PDL1 negative (n=21) and PDL1 positive (n=9).



	mPFS (months)	95% CI
ISR = Y	6.1	[1.8, 11.8]
ISR = N	1.7	[1.3, 4.4]

Figure 10: Kaplan Meier of Progression-free Survival – by Injection Site Reaction
Using KM estimates of survival, patients who experienced at least one injection site reaction at any time during treatment (n=26) had statistically significant improved progression-free survival compared to patients who did not experience an injection site reaction (n=20). HR 0.51 [95% CI; 0.26, 0.97] *p=0.0417*

Duration of Clinical Benefit

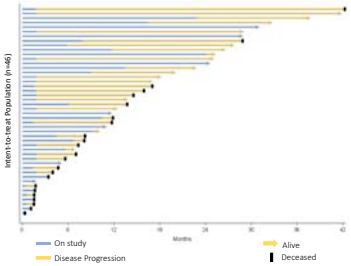


Figure 11: Duration of Clinical Benefit
Swimmer plot of time until disease progression and current survival status. With a median follow up time of 17 months, 23 (50%) patients remain alive and 7 (15%) did not experience disease progression.

Frequently Reported Adverse Events

Adverse Events	Cohort A (N=46)
Any Adverse Event	46 (100%)
Any event ≥ Grade 3	17 (37%)
Injection Site Reaction	26 (57%)
Fatigue	12 (26%)
Cough	8 (17%)
Arthralgia	8 (17%)
Constipation	7 (15%)
Diarrhea	7 (15%)
Decreased Appetite	7 (15%)

Table 3: Adverse Event Table
Most commonly reported treatment-emergent adverse events (regardless of attribution) occurring in the safety population. 63% of all AEs were Grade 1 or 2. There was one grade 4 event (hyponatremia) and two grade 5 events (Acute myocardial infarction and Pulmonary embolism due to disease progression) none of which were deemed related to study treatment.

Conclusions

HS-110 in combination with nivolumab is well tolerated.

The effect of HS-110 in combination with nivolumab is not dependent on baseline PDL1 expression.

Best Overall Response of SD or better is associated with on-treatment decreasing levels of terminally differentiated T cell subsets by flow cytometry.

The occurrence of dermal injection site reactions (any grade) is associated with improved progression-free survival and overall survival.

References

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2. Oizumi S, Strbo N, Pahwa S, Deyev V, and Podack ER. Molecular and cellular requirements for enhanced antigen cross-presentation to CD8 cytotoxic T lymphocytes. Journal of immunology 2007; 179, 2310-2317.

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