Abstract No. 9100

Interim results of viagenpumatucel-L (HS-110) plus nivolumab in previously treated patients with advanced non-small cell lung cancer in two treatment settings

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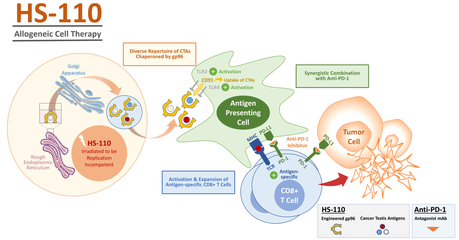
BACKGROUND

- Viagenpumatucel-L (HS-110) is an allogeneic, off-the-shelf, cell-based immunotherapy engineered from a human lung adenocarcinoma cell line that expresses a diverse repertoire of cancer testis antigens (CTAs) and a secretory form of heat shock protein gp96
- HS-110 is designed to utilize gp96 to (1) chaperone multiple CTAs for effective uptake by antigen-presenting cells via CD91; (2) activate antigen presenting cells via stimulation of toll-like receptor (TLR)-2 and TLR-4; and (3) activate and expand antigen-specific CD8+ cytotoxic T cells (**Figure 1**)
- Synergistic antitumor activities of HS-110 in combination with an anti-programmed cell death 1 (PD-1) monoclonal antibody have been demonstrated in a B16 melanoma mouse model[1]
- HS-110 is being evaluated in a multi-arm phase 2 trial for the treatment of patients with unresectable or metastatic non-small cell lung cancer (NSCLC) (NCT02439450) in multiple therapeutic settings. This trial has completed enrollment
  - Here, we present interim findings of HS-110 in combination with nivolumab (NIVO) in previously treated patients with NSCLC who were checkpoint inhibitor (CPI) therapy naïve and patients who progressed on or after prior CPI therapy (CPI progressors)

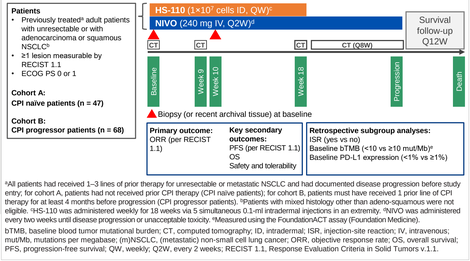
Figure 1. MOA of HS-110 in combination with an anti–PD-1 inhibitor



mAb, monoclonal antibody; MHC, major histocompatibility complex; MOA, mechanism of action; PD-L1, programmed death ligand 1; TLR, toll-like receptor.

METHODS

Figure 2. Study design



[a]All patients had received 1–3 lines of prior therapy for unresectable or metastatic NSCLC and had documented disease progression before study entry; for cohort A, patients had not received prior CPI therapy (CPI naïve patients); for cohort B, patients must have received 1 prior line of CPI therapy for at least 4 months before progression (CPI progressor patients). [b]Patients with mixed histology other than adeno-squamous were not eligible. [c]HS-110 was administered weekly for 18 weeks via 5 simultaneous 0.1-ml intradermal injections in an extremity. [d]NIVO was administered every two weeks until disease progression or unacceptable toxicity. [e]Measured using the FoundationACT assay (Foundation Medicine).

bTMB, baseline blood tumor mutational burden; CT, computed tomography; ID, intradermal; ISR, injection-site reaction; IV, intravenous; mut/Mb, mutations per megabase; (m)NSCLC, (metastatic) non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; Q2W, every 2 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumors v.1.1.

METHODS (cont'd)

Study Endpoints

- Primary endpoint was objective response rate (ORR) by RECIST 1.1; secondary endpoints included progression-free survival (PFS) by RECIST 1.1, overall survival (OS), safety, and tolerability

Statistical Analyses

- Safety analyses were conducted using data from all patients who received at least 1 dose of HS-110 (safety population)
- PFS and OS data were analyzed using Kaplan–Meier methodology; ORR data are presented as counts and percentages for each cohort
- Retrospective subgroup analyses were conducted by
  - Injection site reaction (ISR): yes (+) or no (–)
  - Baseline blood tumor mutational burden (bTMB): low (bTMB-L, <10 mutations/megabase [mut/Mb]) or high (bTMB-H, ≥10 mut/Mb)
  - Baseline tumor PD-L1 expression: negative (<1%) or positive (≥1%)
- The data cutoff date for this pre-specified interim analysis was November 2020

RESULTS

- In total, 115 patients were enrolled: 47 patients to cohort A and 68 to cohort B

Table 1. Baseline characteristics

Baseline characteristics	Cohort A n = 47	Cohort B n = 68
Age (years), median (range)	65 (37–87)	67 (46–84)
Sex, female, n (%)	26 (55.3)	37 (54.4)
Race, n (%)		
Asian	1 (2.1)	1 (1.5)
Black	4 (8.5)	11 (16.2)
White	42 (89.4)	54 (79.4)
Other	0	1 (1.5)
Unknown	0	1 (1.5)
ECOG PS, n (%)		
0	16 (34.0)	25 (36.8)
1	31 (66.0)	43 (63.2)
Histology, n (%)		
Adenocarcinoma	44 (93.6)	55 (80.9)
Adenosquamous	0	1 (1.5)
Squamous cell carcinoma	3 (6.4)	12 (17.6)
Smoking status, n (%)		
Current/former	39 (83.0)	57 (83.8)
Never	8 (17.0)	11 (16.2)
Tumor driver mutations, n (%)		
EGFR positive	6 (12.8)	3 (4.4)
ALK positive	0	1 (1.5)
KRAS positive	7 (14.9)	16 (23.5)
Prior line(s) of treatment, n (%)		
1	33 (70.2)	26 (38.2)
2	6 (12.8)	21 (30.9)
≥3	8 (17.0)	21 (30.8)
PD-L1 status, n (%)		
<1%	22 (46.8)	29 (42.6)
≥1%	9 (19.1)	23 (33.8)
Not evaluable	16 (34.0)	16 (23.5)
TMB status, n (%)		
Low (<10 mut/mb)	2 (4.3)	32 (47.1)
High (≥10 mut/mb)	2 (4.3)	11 (16.2)
Unknown	43 (91.5)	25 (36.8)

ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; KRAS, Kirsten rat sarcoma viral oncogene homolog.

RESULTS (cont'd)

Safety and Tolerability

- Combination of HS-110 and NIVO was well tolerated
- No safety concerns were identified based on a review of immune-related adverse events
- TEAEs related to HS-110 were reported in 21 (44.7%) patients in cohort A and 18 (26.5%) patients in cohort B (**Table 2**)
  - TEAEs occurring with a prevalence of >5% of patients included fatigue, maculopapular rash, nausea, diarrhea, and pruritus
- Few TEAEs related to HS-110 led to discontinuation of treatment
  - Cohort A, 5 patients (10.6%); cohort B, 3 patients (4.4%)
- No SAEs or deaths were considered to be related to HS-110

Table 2. Summary of TEAEs and SAEs

Events, n (%)	Cohort A n = 47	Cohort B n = 68
Any TEAEs	47 (100)	66 (97.1)
Any TEAE grade ≥3	16 (34.0)	17 (25.0)
Most common TEAEs (≥15%)		
Fatigue	13 (27.7)	23 (33.8)
Nausea	7 (14.9)	12 (17.6)
Dyspnea	5 (10.6)	12 (17.6)
Diarrhea	7 (14.9)	11 (16.2)
Decreased appetite	6 (12.8)	11 (16.2)
Pruritus	5 (10.6)	11 (16.2)
Any treatment-emergent SAE	13 (27.7)	16 (23.5)
TEAEs leading to discontinuation of HS-110	5 (10.6)	3 (4.4)
TEAEs leading to discontinuation of NIVO	4 (8.5)	3 (4.4)
TEAEs leading to death	2 (4.3)	0
HS-110–related TEAEs	21 (44.7)	18 (26.5)
HS-110–related TEAE grade 3[a]	2 (4.3)	0
HS-110–related TEAE leading to death	0	0
Most common HS-110–related TEAEs (≥5%)		
Fatigue	2 (4.3)	6 (8.8)
Pruritus	2 (4.3)	4 (5.9)
Diarrhea	3 (6.4)	2 (2.9)
Maculopapular rash	3 (6.4)	0

[a]No grade 4 or grade 5 HS-110-related TEAEs had been reported as of November 2020 data cutoff.

Efficacy

Cohort A: Previously treated, CPI naïve patients with unresectable or mNSCLC

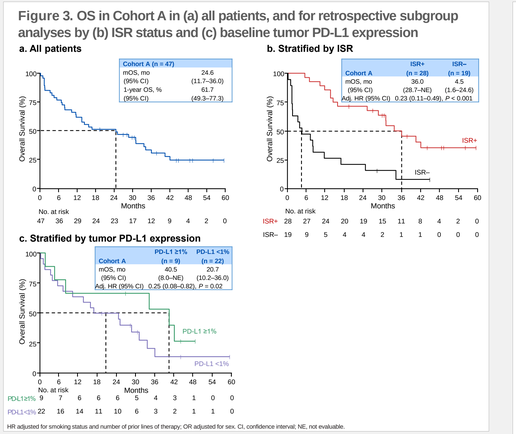
- Median OS was 24.6 months for all patients in cohort A at a median follow-up time of 19.4 months (**Table 3, Figure 3**)
  - Significantly longer PFS and OS were observed in ISR+ patients ($P = 0.01$ and $P < 0.001$, respectively)
  - Patients with tumor PD-L1 expression ≥1% had significantly improved ORR and OS ($P = 0.04$ and $P = 0.02$, respectively)

Table 3. Summary of outcomes for Cohort A including retrospective subgroup analyses

	All	ISR+	ISR–	Adj. HR or OR[a]; *P*	PD-L1 ≥1%	PD-L1 <1%	Adj. HR or OR[a]; *P*
n	47	28	19	–	9	22	–
ORR, %	21.3	28.6	10.5	3.91[b]; 0.12	44.4	9.1	8.10[b]; 0.04
mPFS, mo	1.8	5.4	1.5	0.43[c]; 0.01	4.8	1.8	0.46[c]; 0.11
mOS, mo	24.6	36.0	4.5	0.23[c]; <0.001	40.5	20.7	0.25[c]; 0.02

[a]HR adjusted for smoking status and number of prior lines of therapy; OR adjusted for sex. [b]Adjusted OR. [c]Adjusted HR.
Adj., adjusted; HR, hazard ratio; mPFS, median PFS; mOS, median OS; OR, odds ratio.

Figure 3. OS in Cohort A in (a) all patients, and for retrospective subgroup analyses by (b) ISR status and (c) baseline tumor PD-L1 expression



HR adjusted for smoking status and number of prior lines of therapy; OR adjusted for sex. CI, confidence interval; NE, not evaluable.

Cohort B: CPI progressor patients with unresectable or mNSCLC

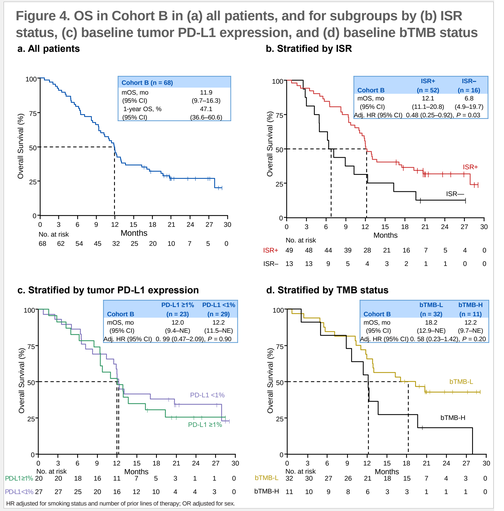
- Median OS was 11.9 months for all patients in cohort B at a median follow-up time of 11.9 months (**Table 3, Figure 4**)
  - Significantly longer OS was observed in ISR+ patients ($P = 0.03$)
  - A trend toward longer OS was observed in bTMB-L patients ($P = 0.20$)
  - Survival was independent of tumor PD-L1 expression

Table 4. Summary of outcomes for Cohort B including retrospective subgroup analyses

	All	ISR+	ISR–	Adj. HR or OR[a]; *P*	bTMB-L	bTMB-H	Adj. HR or OR[a]; *P*	PD-L1 ≥1%	PD-L1 <1%	Adj. HR or OR[a]; *P*
n	68	52	16	–	32	11	–	23	29	–
ORR, %	10.3	11.5	6.3	1.99[b]; 0.60	15.6	9.1	2.25[b]; 0.50	13.0	10.3	1.27[b]; 0.80
mPFS, mo	2.8	3.0	1.7	0.63[c]; 0.14	3.7	2.7	0.94[c]; 0.90	3.2	2.9	1.11[c]; 0.80
mOS, mo	11.9	12.1	6.8	0.48[c]; 0.03	18.2	12.2	0.58[c]; 0.20	12.0	12.2	0.99[c]; >0.90

[a]HR adjusted for smoking status and number of prior lines of therapy; OR adjusted for sex. [b]Adjusted OR. [c]Adjusted HR.

Figure 4. OS in Cohort B in (a) all patients, and for subgroups by (b) ISR status, (c) baseline tumor PD-L1 expression, and (d) baseline bTMB status



HR adjusted for smoking status and number of prior lines of therapy; OR adjusted for sex.

CONCLUSIONS

1. In previously treated patients with unresectable or mNSCLC, HS-110 in combination with NIVO was well tolerated and demonstrated potential signs of efficacy:
   - In cohort A (CPI naïve patients)
     - OS was significantly longer in PD-L1 ≥1% versus PD-L1 <1% patients
     - Data support evaluating HS-110 in combination with CPI-containing frontline regimens
   - In cohort B (CPI progressor patients)
     - Survival was independent of tumor PD-L1 status
     - A trend of improved OS was observed in bTMB-L versus bTMB-H patients
2. ISR could potentially be utilized to identify patients who may derive a therapeutic benefit from HS-110
   - Significantly longer OS was observed in ISR+ versus ISR– patients in both cohorts A and B
3. Taken together, these results support future clinical evaluation of HS-110 in combination with a PD-1 inhibitor

REFERENCE

1. Morgensztern D, et al. Treating advanced non-small lung cancer patients after checkpoint inhibitor treatment failure with a novel combination of viagenpumatucel-L (HS-110) plus nivolumab. Poster presented at: The Society for Immunotherapy of Cancer (SITC) 34th Annual Meeting; November 6–10, 2019; National Harbor, MD.

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