Abstract # 1152P

Phase 1 study of HSP105-derived peptide vaccine for patients with advanced esophageal cancer/ colo-rectal cancer. (EPOC1411)

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Background

- The HSP105 protein has been identified in pancreatic cancer by the SEREX method, and this protein has also been reported to play a role in controlling apoptosis in cancer cells.
- HSP105 is highly expressed in various human cancers, including colorectal cancer, esophageal cancer, pharyngeal cancer, pancreatic cancer, breast cancer, and melanoma.
- We have therefore identified the respective HSP105-derived peptides that bind to HLA-A24 and HLA-A2 (EP1536006, JP5112615, JP5291641, US9,404,925).
- We investigated the safety and efficacy of HSP105-derived peptide vaccine for patients (pts) with advanced esophageal cancer (EC) / colo - rectal cancer (CRC).

Key Inclusion Criteria

- Histologically confirmed advanced or metastatic squamous cell carcinoma of the esophagus or adenocarcinoma of colon or rectum.
- Refractory or intolerant to standard chemotherapy.
- ECOG PS 0-1, age ≥ 20, with measurable lesion (RECIST v1.1)
- Adequate organ and bone marrow function
- Positive one either or more of HLA-A*24:02, 02:01, 02:06 , 02:07.

Study Treatment and Assessment

- HSP105-derived peptide vaccine is administered weekly by intradermal injection, for a maximum of 1 year.

Endpoints and Statistical Considerations

Primary endpoint:

- P1a: Proportion of dose limiting toxicity , P1b: Response rate

Secondary endpoint:

- Progression free survival, Treatment failure rate, Adverse events
- Immunological effects

Statistical consideration:

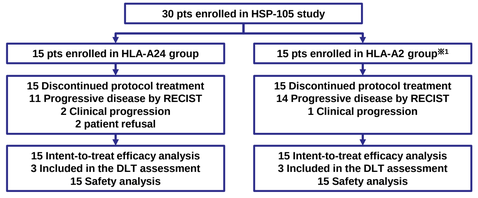
- The recommended dose is determined based on the incidence of dose limiting toxicity (DLT) during phase 1a (P1a).
- Pts will then be added in phase 1b (P1b) to investigate the safety and efficacy of the vaccine.

	Level	Administered Vaccine	Dosage
HLA-A24 group HLA-A*24:02	Level 1	HSP105 A24-1	3 mg
		HSP105 A24-7	3 mg
	Level 0	HSP105 A24-1	1 mg
		HSP105 A24-7	1 mg
HLA-A2 group HLA-A*02:01, A*02:06, A*02:07	Level 1	HSP105 A2-7	3 mg
		HSP105 A2-12	3 mg
	Level 0	HSP105 A2-7	1 mg
		HSP105 A2-12	1 mg

Methods and Results

- A total 30 pts (HLA-A24 group 15pts, HLA-A02 group 15 pts) were enrolled and grouped into level 1.
- No DLT occurred and no major safety problems were reported throughout the trial.

Figure 1. Patient flow diagram (N=30)



※1 Includes patients positive for either A*02:01, A*02:06 or A*02:07, and positive for HLA-A*24:02

Figure 2. Progression-free survival (N=30)

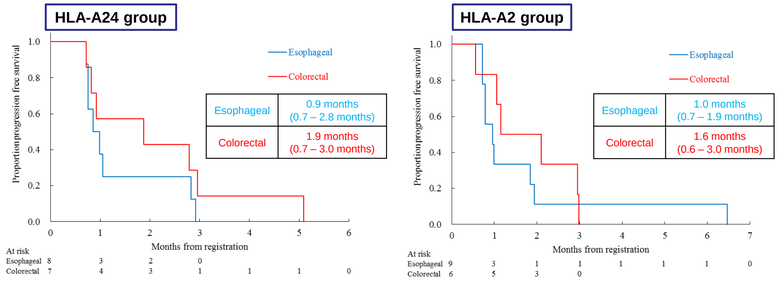


Table 1. Patients Characteristics (N=30)

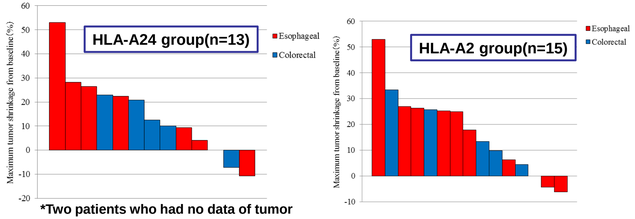
		HLA-A24 group		HLA-A2 group	
		EC (N=8)	CRC (N=7)	EC (N=9)	CRC (N=6)
Gender	Male	7	4	7	3
	Female	1	3	2	3
Age (years)	Median	66	61	69	50.5
Performance Status	0	6	6	5	6
	1	2	1	4	0
Previous Surgery	Yes	5	6	5	6
	No	3	1	4	0
Previous Radiotherapy	Yes	1	1	1	0
	No	7	6	8	6
No. of prior regimens	1	0	0	1	0
	2	4	0	4	1
	3	2	1	4	2
	≥ 4	2	6	0	3

Table 2. Treatment related Adverse Events (N=30)

	HLA-A24 group		HLA-A2 group	
	Any grade N (%)	Grade 3/4 N (%)	Any grade N (%)	Grade 3/4 N (%)
Cough	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site reaction	13 (86.7)	0 (0.0)	6 (40.0)	0 (0.0)
Malaise	1 (6.7)	0 (0.0)	1 (6.7)	0 (0.0)
Nausea	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonitis	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)
Fever	2 (13.3)	1 (6.7)	0 (0.0)	0 (0.0)
Rash maculo-papular	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)

No treatment-related deaths were observed.

Figure 3. Waterfall plot (N=30)



*Two patients who had no data of tumor diameter after the baseline.

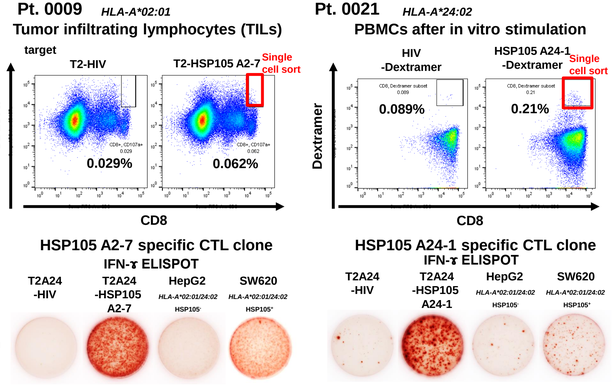
Table 3. Overall Response (N=30)

	HLA-A24 group		HLA-A2 group	
	N	%	N	%
Complete Response (CR)	0	0	0	0
Partial Response (PR)	0	0	0	0
Stable Disease (SD)	4	26.7	3	20.0
Progressive Disease (PD)	9	60.0	12	80.0
Not Evaluated (NE)	2	13.3	0	0
DCR (95% CI)	26.7 (7.8 to 55.1)		20.0 (4.3 to 48.1)	
RR (95% CI)	0.0 (0.0 to 21.8)		0.0 (0.0 to 21.8)	

Table 4. Immunological Response (N=30)

	HLA-A24 group		HLA-A2 group	
	N	%	N	%
HSP105 specific CTL response	7	46.7	8	53.3

Figure 4. Establishment of HSP105 peptide-specific CTL clones



Summary of the results

- A total 30 pts (HLA-A24 group 15pts, HLA-A2 group 15 pts) were enrolled and grouped into level 1 which received intradermally administration of peptide vaccine (emulsifying agent: Montanide ISA 51 VG) 3 mg/body.
- No DLT occurred and no major safety problems were reported throughout the trial. Although pts with objective clinical efficacy was not apparent, 7 pts (HLA-A24 of 4 and HLA-A2 of 3) showed stable disease 2 months after initiation of treatment.
- The HSP105-derived peptide vaccine induced HSP105-specific CTL response in 15 pts (50%) of 30 pts (HLA-A24 of 7 and HLA-A2 of 8).
- Additionally, we established several HSP105 peptide-specific CTL clones from PBMCs and tumor of pts vaccinated with HSP105 peptide by single cell sorting using Dextramer or anti-CD107a antibody.

Conclusions

- Although objective clinical efficacy was not apparent, HSP105 - derived peptide vaccine appears safe and well tolerated with minimal local toxicity.

Clinical trial information:UMIN000017809

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