

MP14-02 The impact of zygosity and supertypes of HLA genotypes on the clinical outcomes of patients with genitourinary cancers treated with anti-PD-1 drugs

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We assessed the impact of zygosity for and the supertypes of HLA-I genotype on the clinical outcomes of patients with genitourinary cancers treated with anti-programmed cell death protein 1 (PD-1) drugs in Japan.

Germline HLA variation in all patients

Germline HLA variation		RCC (n = 26)	%	UC (n = 26)	%	
Homozygosity	HLA A (Allele)	9	34.6	2	7.7	
	HLA A (Sero)	9	34.6	7	26.9	
	HLAB (Allele)	2	7.7	0	0.0	
	HLA B (Sero)	4	15.4	2	7.7	
	HLAC (Allele)	3	11.5	5	19.2	
	HLA C (Sero)	4	15.4	5	19.2	
	HLA A+B (Allele)	11	42.3	2	7.7	
	HLA A+B (Sero)	13	50.0	9	34.6	
	HLA A+B+C (Allele)	12	46.2	6	23.1	
	HLA A+B+C (Sero)	15	57.7	13	50.0	
	HLA C KIR ligand	19	73.1	20	76.9	
	Supertype	A01	6	23.1	6	23.1
		A02	13	50.0	17	65.4
		A03	2	7.7	11	42.3
A01A03		1	3.8	0	0.0	
A24		21	80.8	11	42.3	
B07		16	61.5	15	57.7	
B27		4	15.4	4	15.4	
B44		11	42.3	15	57.7	
B62		10	38.5	9	34.6	
Unclassified		3	11.5	1	3.8	

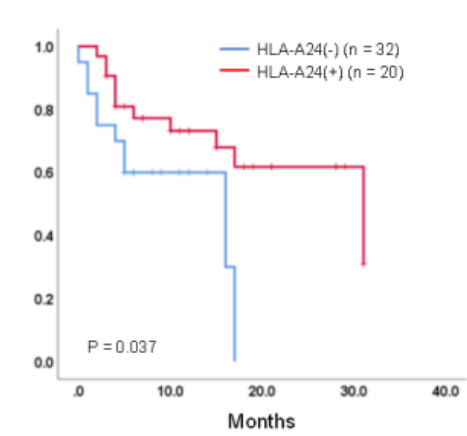
Radiographic response and HLA status of patients with RCC and UC

Cohort 1:RCC		CR	PR	SD	PD	p value	CR+PR	SD+PD	p value	CR+PR+SD	PD	p value
HLA ABC (Sero)	Heterozygous	2	1	6	2	0.145	3	8	0.188	9	2	0.040
	Homozygous	1	0	5	9		1	14		6	9	
HLA AB (Sero)	Heterozygous	2	1	6	4	0.524	3	10	0.297	9	4	0.214
	Homozygous	1	0	5	7		1	12		6	7	
Cohort 2: UC*		CR	PR	SD	PD	p value	CR+PR	SD+PD	p value	CR+PR+SD	PD	p value
HLA ABC (Sero)	Heterozygous	0	5	0	7	0.312	5	7	0.286	5	7	0.596
	Homozygous	0	3	2	8		3	10		5	8	
HLA AB (Sero)	Heterozygous	0	5	0	11	0.191	5	11	0.626	5	11	0.222
	Homozygous	0	3	2	4		3	6		5	4	

Univariate and multivariable analyses of risk factors for RFS in patients with RCC treated with nivolumab

			Univariate			Multivariable		
			HR	95% CI	p value	HR	95% CI	p value
Age	Continuous		1.05	1.00–1.10	0.050	1.01	0.96–1.07	0.663
Sex	Female vs. male		1.15	0.48–1.74	0.476			
ECOG-PS	≥1 vs. 0		1.21	0.48–3.07	0.690			
Histology	Non-clear vs. clear		1.58	0.21–11.92	0.659			
IMDC risk classification	Poor vs. favorable and intermediate		1.19	0.39–3.61	0.763			
Neutrophil level	High vs. low		7.39	1.83–29.79	0.005	4.93	1.11–21.84	0.036
Anemia	Low vs. high		2.21	0.64–7.60	0.210			
Number of treatment line	Multiple vs. one		2.65	1.01–6.99	0.049	2.27	0.84–6.07	0.103
HLA zygosity	Homogyzous at HLA-ABC		1.99	0.75–5.25	0.166			
	Homogyzous at HLA-AB		1.79	0.71–4.52	0.219			
	Homogyzous at HLA-C KIR ligand		0.78	0.28–2.17	0.629			
HLA supertype	A01	Yes vs. no	2.33	0.82–6.66	0.115			
	A02	Yes vs. no	0.40	0.16–1.02	0.055	0.62	0.18–2.09	0.438
	A24	Yes vs. no	0.76	0.22–2.66	0.665			
	B07	Yes vs. no	1.51	0.57–3.99	0.404			
	B44	Yes vs. no	1.22	0.49–3.05	0.675			
	B62	Yes vs. no	0.68	0.26–1.79	0.435			

Kaplan–Meier curve of OS in patients with genitourinary cancers according to HLA-A24



Univariate analyses of risk factors for RFS in patients with UC treated with pembrolizumab

			Univariate		
			HR	95% CI	p value
Age	Continuous		1.00	0.96–1.04	0.984
Sex	Female vs. male		0.83	0.30–2.33	0.727
Primary site	Upper tract vs. others		0.61	0.24–1.57	0.304
ECOG-PS	0 vs. ≥1		1.12	0.44–2.84	0.819
Bullmunt risk	≤1 vs. ≥2		0.96	0.38–2.40	0.925
Lymph node only	Yes vs. No		0.73	0.26–2.05	0.554
Liver metastasis	Yes vs. No		1.47	0.52–4.06	0.484
Hemoglobin	Low vs. high		1.20	0.48–3.01	0.693
Prior chemotehrapy line	Multiple vs. one		1.57	0.54–4.53	0.409
Time from chemotheapy	<3m vs. >3m		2.03	0.79–5.26	0.144
Radiation therapy	Yes vs. no		1.58	0.63–3.97	0.333
HLA zygosity	Homogyzous at HLA-ABC		1.28	0.52–3.19	0.591
	Homogyzous at HLA-AB		0.89	0.34–2.35	0.813
	Homogyzous at HLA-C KIR ligand		0.94	0.31–2.85	0.918
HLA supertype	A01	yes vs. no	0.88	0.29–2.67	0.827
	A02	yes vs. no	1.15	0.45–2.93	0.774
	A24	yes vs. no	1.15	0.47–2.84	0.761
	B07	yes vs. no	0.57	0.22–1.43	0.230
	B44	yes vs. no	1.28	0.50–3.26	0.613
	B62	yes vs. no	1.32	0.50–3.50	0.582

Conclusion

- Germline HLA status may be associated with clinical outcomes in genitourinary cancer treated with anti-PD-1 drug. However, its impact might depend on the cancer type.
- Homozygosity for and the HLA-A2 supertype of the HLA-I loci may be associated with treatment response in patients with metastatic RCC treated with nivolumab, and the germline HLA-A24 supertype may be a prognostic factor in patients with genitourinary cancer treated with immuno-oncology drugs.
- Now we perform a multicenter validation study with a larger number of patients.