SUPPLEMENTARY MATERIAL

Lower risk of severe checkpoint inhibitor toxicity in more advanced disease

Results of the prospective Dutch Melanoma Treatment Registry

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Supplementary table 1: Determinants of severe immune related adverse events in first-line anti-PD1 treated patients using both univariable and multivariable Poisson regression

	Univariable analysis			Multivariable analysis		
	RR	**95% CI**	**p-value**	**RR$_{adj}$**	**95% CI$_{adj}$**	**p-value**
Age (years)	1.00	0.99-1.02	0.710	1.00	0.98-1.03	0.665
Sex						
Male	ref			ref		
Female	1.01	0.64-1.59	0.947	1.02	0.65-1.62	0.923
WHO performance status						
0	ref			ref		
1	0.87	0.51-1.44	0.610	1.01	0.60-1.69	0.976
≥2	1.20	0.36-2.95	0.723	1.37	0.48-3.95	0.555
Number of comorbidities						
0	ref			ref		
1-2	1.08	0.66-1.82	0.763	0.98	0.56-1.74	0.955
≥3	0.97	0.48-1.87	0.929	0.89	0.41-1.93	0.775
Stage of disease						
Unresectable stage III/ M1a/ M1b	ref			ref		
M1c/ M1d	0.69	0.44-1.09	0.108	0.73	0.45-1.18	0.196
Number of metastatic sites						
<3	ref			ref		
≥3	0.91	0.50-1.55	0.733	1.09	0.64-1.85	0.761
LDH						
≤ ULN	ref			ref		
1-2x ULN	0.96	0.57-1.57	0.879	1.06	0.63-1.78	0.840
>2x ULN	0.52	0.09-1.69	0.372	0.71	0.17-3.00	0.636

RR: risk ratio; RR$_{adj}$: adjusted risk ratio; CI: confidence interval; CI$_{adj}$: adjusted confidence interval; WHO: World Health Organisation; LDH: lactate dehydrogenase; ULN: upper limit of normal (defined as 250U/L); the multivariable analysis was additionally adjusted for follow-up time.

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