Supplementary Figure 9

Baseline	- OS
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Variable		N	Hazard ratio	р
CSM	Above median	36	Reference	
	Below median	38	0.58 (0.33,	1.02) 0.061
cohort	A: Head & Neck	15	Reference	
	B: Breast	18	0.92 (0.43,	1.99) 0.834
	C: Ovarian	18	0.48 (0.21,	1.09) 0.080
	D: Melanoma	11	0.18 (0.05,	0.74) 0.017
	E: Other	12	0.38 (0.16,	0.90) 0.028
PD-L1 fraction		74	0.22 (0.08,	0.61) 0.004
log TMB		74	0.98 (0.67,	1.42) 0.902

Baseline - PFS

Variable		N	Hazard ratio		р
CSM	Above median	36	•	Reference	
	Below median	38		0.61 (0.35, 1.06)	0.08
cohort	A: Head & Neck	15		Reference	
	B: Breast	18		2.78 (1.27, 6.07)	0.01
	C: Ovarian	18		1.38 (0.64, 2.96)	0.42
	D: Melanoma	11	·	0.37 (0.10, 1.33)	0.13
	E: Other	12		0.49 (0.21, 1.18)	0.11
PD-L1 fraction		74	·	0.29 (0.11, 0.80)	0.02
log TMB		74		0.79 (0.55, 1.15)	0.22

Cycle 3 - OS

Variable		N	Hazard ratio		р
CSM	Above median	26	•	Reference	
	Below median	27		0.51 (0.23, 1.17)	0.11
cohort	A: Head & Neck	12		Reference	
	B: Breast	10		0.69 (0.27, 1.72)	0.42
	C: Ovarian	10		0.37 (0.12, 1.12)	0.08
	D: Melanoma	10	·	0.11 (0.02, 0.60)	0.01
	E: Other	11	·	0.35 (0.14, 0.89)	0.03
PD-L1 fraction		53		0.26 (0.08, 0.81)	0.02
log TMB		53		1.17 (0.78, 1.78)	0.45

Cycle 3 - PFS

Variable		Ν	Hazard ratio		р
CSM	Above median	26	.	Reference	
	Below median	26		0.49 (0.24, 1.01)	0.05
cohort	A: Head & Neck	12		Reference	
	B: Breast	10	—	2.41 (0.97, 6.03)	0.06
	C: Ovarian	10	·	1.28 (0.49, 3.38)	0.61
	D: Melanoma	9	·	0.17 (0.03, 0.98)	0.05
	E: Other	11		0.47 (0.19, 1.18)	0.11
PD-L1 fraction		52		0.39 (0.13, 1.16)	0.09
log TMB		52		0.93 (0.62, 1.41)	0.73
			0.05 0.1 0.2 0.5 1 2 5		

Supplementary Figure 9. Multivariable analysis of survival using cancer-specific methylation (CSM) scores at baseline and cycle 3 of pembrolizumab. We computed CSM scores across the trial cohort. At both baseline and cycle 3, patients were split into above- or below-median groups. Survival outcomes are shown in a multivariable analysis including cohort, PD-L1 expression, and tumor mutation burden (TMB).