

	All	Low TMB						High TMB						Low TMB	High TMB
		Wildtype			Altered			Wildtype			Altered				
		STK11/KEAP1/EGFR	STK11 alt	KEAP1 alt	EGFR alt	STK11/KEAP1/EGFR	Altered STK11/KEAP1/EGFR	STK11/KEAP1/EGFR	STK11 alt	KEAP1 alt	EGFR alt	STK11/KEAP1/EGFR	Altered STK11/KEAP1/EGFR		
Patients (n)	75	31 (41.3)	9 (12.0)	7 (9.3)	3 (4.0)	15 (20.0)	16 (21.3)	9 (12.0)	5 (6.7)	1 (1.3)	13 (17.3)				
Age (mean [SD])	62.6 (9.9)	64.4 (9.9)	64.7 (8.8)	60.9 (5.9)	68.0 (12.2)	64.7 (8.5)	61.2 (8.5)	56.6 (13.2)	63.2 (6.9)	50.0	57.4 (11.9)		P=0.91		
Gender (%)															
Male	39 (52.0)	21 (67.7)	2 (22.2)	4 (57.1)	2 (66.7)	7 (46.7)	5 (31.2)	4 (44.4)	2 (40.0)	1.0 (100.0)	6 (46.2)		P=0.21		
Female	36 (48.0)	10 (32.3)	7 (77.8)	3 (42.9)	1 (33.3)	8 (53.3)	11 (68.8)	5 (55.6)	3 (60.0)	0.0 (0.0)	7 (53.8)				
Smoking status (n [%])															
Current/former	57 (76.0)	29 (74.2)	8.0 (88.9)	5.0 (71.4)	0.0 (0.0)	10 (66.7)	14 (87.5)	6.0 (66.7)	5.0 (100.0)	1.0 (100.0)	10.0 (76.9)		P=1.00		
Never	7 (9.3)	4 (12.9)	0.0 (0.0)	0.0 (0.0)	2.0 (66.7)	2 (13.3)	1 (6.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
Unavailable	11 (14.7)	4 (12.9)	1.0 (11.1)	2.0 (28.6)	1.0 (33.3)	3 (20.0)	1 (6.2)	3.0 (33.3)	0.0 (0.0)	0.0 (0.0)	3.0 (23.1)				
Pack years (mean [SD])	29.1 (19.3)	25.5 (15.9)	23.8 (16.9)	23.0 (8.5)	0.0 (0.0)	18.8 (16.6)	33.5 (16.6)	31.2 (11.1)	49.0 (32.9)	18.0	39.5 (25.1)		P=0.31		
ECOG (%)															
0	18 (24.0)	11.0 (35.5)	0.0 (0.0)	0.0 (0.0)	1.0 (33.3)	1.0 (6.7)	5.0 (31.2)	1.0 (11.1)	1.0 (20.0)	0.0 (0.0)	1.0 (7.7)		P=0.11		
1	40 (53.3)	13.0 (41.9)	7.0 (77.8)	5.0 (71.4)	1.0 (33.3)	10.0 (66.7)	9.0 (56.2)	5.0 (55.6)	3.0 (60.0)	1.0 (100.0)	8.0 (61.5)				
2	9 (12.0)	4.0 (12.9)	2.0 (22.2)	1.0 (14.3)	0.0 (0.0)	2.0 (13.3)	1.0 (6.2)	1.0 (11.1)	1.0 (20.0)	0.0 (0.0)	2.0 (15.4)				
>2	1 (1.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.0 (6.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
Unavailable	7 (9.3)	3.0 (9.7)	0.0 (0.0)	1.0 (14.3)	1.0 (33.3)	2.0 (13.3)	0.0 (0.0)	2.0 (22.2)	0.0 (0.0)	0.0 (0.0)	2.0 (15.4)				
Treatment (n [%])															
Nivolumab	48 (64.0)	21 (67.7)	7.0 (77.8)	5.0 (71.4)	1.0 (33.3)	10.0 (66.7)	9.0 (56.2)	5.0 (55.6)	3.0 (60.0)	1.0 (100.0)	8.0 (61.5)		P=0.76		
Pembrolizumab	24 (32.0)	8 (25.8)	2.0 (22.2)	2.0 (28.6)	2.0 (66.7)	5.0 (33.3)	7.0 (43.8)	3.0 (33.3)	2.0 (40.0)	0.0 (0.0)	4.0 (30.8)				
Atezolizumab	1 (1.3)	1 (3.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
Durvalumab	2 (2.7)	1 (3.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.0 (11.1)	0.0 (0.0)	0.0 (0.0)	1.0 (7.7)				
Treatment line (n [%])															
1	13 (17.6)	4.0 (12.9)	1.0 (11.1)	0.0 (0.0)	0.0 (0.0)	1.0 (6.7)	5.0 (31.2)	2.0 (25.0)	2.0 (40.0)	0.0 (0.0)	3.0 (25.0)		P=0.62		
2	54 (73.0)	22.0 (71.0)	7.0 (77.8)	7.0 (100.0)	3.0 (100.0)	13.0 (86.7)	11.0 (68.8)	6.0 (75.0)	3.0 (60.0)	0.0 (0.0)	8.0 (66.7)				
3	5 (6.8)	3.0 (9.7)	1.0 (11.1)	0.0 (0.0)	0.0 (0.0)	1.0 (6.7)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.0 (100.0)	1.0 (8.3)				
4	2 (2.7)	2.0 (6.5)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
5	0 (0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
Histology (n [%])															
Adenocarcinoma	47 (62.7)	16 (59.3)	6.0 (75.0)	4.0 (57.1)	3.0 (100.0)	10.0 (71.4)	8.0 (57.1)	7.0 (100.0)	4.0 (100.0)	1.0 (100.0)	11.0 (100.0)		P=0.51		
Squamous cell carcinoma	13 (17.3)	5 (18.5)	0.0 (0.0)	1.0 (14.3)	0.0 (0.0)	1.0 (7.1)	3.0 (21.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				
NOS	13 (17.3)	4 (14.8)	2.0 (25.0)	2.0 (28.6)	0.0 (0.0)	3.0 (21.4)	3.0 (21.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)				

Other	2 (2.7)	2 (7.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)		
PD-L1 expression status (n [%])												
<1%	27 (36.0)	12 (38.7)	4.0 (44.4)	2 (28.6)	1.0 (33.3)	6 (40.0)	5 (31.2)	2.0 (22.2)	1.0 (20.0)	1.0 (100.0)	4.0 (30.8)	P=0.99
1-50%	16 (21.3)	7 (22.6)	2.0 (22.2)	1 (14.3)	2.0 (66.7)	4 (26.7)	5 (31.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	P=0.10
>50%	14 (18.7)	4 (12.9)	0.0 (0.0)	2 (28.6)	0.0 (0.0)	2 (13.3)	4 (25.0)	3.0 (33.3)	2.0 (40.0)	0.0 (0.0)	4.0 (30.8)	
Unavailable	18 (24.0)	8 (25.8)	3.0 (33.3)	2 (28.6)	0.0 (0.0)	3 (20.0)	2 (12.5)	4.0 (44.4)	2.0 (40.0)	0.0 (0.0)	5.0 (38.5)	
BOR (n [%])												
PD	43 (57.3)	20.0 (64.5)	9.0 (100.0)	7.0 (100.0)	3.0 (100.0)	15.0 (100.0)	7.0 (43.8)	1.0 (11.1)	0.0 (0.0)	0.0 (0.0)	1.0 (7.7)	P=0.030
SD	16 (21.3)	7.0 (22.6)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	3.0 (18.8)	6.0 (66.7)	2.0 (40.0)	0.0 (0.0)	6.0 (46.2)	
PR	16 (21.3)	4.0 (12.9)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	6.0 (37.5)	2.0 (22.2)	3.0 (60.0)	1.0 (100.0)	6.0 (46.2)	
CR	0 (0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	
DCB (n [%])												
NO	47 (62.7)	22 (71.0)	9.0 (100.0)	7.0 (100.0)	3.0 (100.0)	15.0 (100.0)	8 (50.0)	2 (22.2)	0.0 (0.0)	0.0 (0.0)	2 (15.4)	P=0.021
YES	28 (37.3)	9 (29.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	8 (50.0)	7 (77.8)	5.0 (100.0)	1.0 (100.0)	11 (84.6)	P=0.11

Table S3. Baseline characteristics of patients in the discovery cohort, stratified by the TMB and *STK11/KEAP1/EGFR* alteration status.

Two-sided P-values are shown for between-cohort comparisons of available data and were calculated with Wilcoxon rank-sum test (continuous variables), Fisher's exact test (dichotomous variables), or χ^2 test (discrete variables with >2 levels).