

Supplementary Tables

Supplementary Table 1. Demographic and clinical characteristics by *CDKN2A* deletion status

		1st line mono-IO			1st line chemo-IO		
		<i>CDKN2A</i> del+ (n=71)	<i>CDKN2A</i> del- (n=371)	P- value ¹	<i>CDKN2A</i> del+ (n=177)	<i>CDKN2A</i> del- (n=738)	P- value ¹
Age at treatment start, years, median (range)		74 (40, 85)	72 (38, 85)	0.03	69 (36, 85)	68 (33, 85)	0.8
Gender, n (%)				0.3			0.01
	Female	36 (51)	215 (58)		67 (38)	360 (49)	
	Male	35 (49)	156 (42)		110 (62)	378 (51)	
Race, n (%)				0.7			0.06
	Asian	<5	<5		<5	7 (1)	
	Black or African American	<5	18 (5)		13 (7)	47 (6)	
	Other	11 (15)	54 (15)		17 (10)	127 (17)	
	White	52 (73)	270 (73)		121 (68)	489 (66)	
	Missing	6 (8)	25 (7)		22 (12)	68 (9)	
Smoking history, n (%)				1.0			0.6
	Yes	67 (94)	351 (95)		152 (86)	670 (91)	
	No	4 (6)	20 (5)		25 (14)	68 (9)	
Practice type, n (%)				0.6			0.8
	Academic	6 (8)	25 (7)		11 (6)	39 (5)	
	Community	65 (92)	346 (93)		166 (94)	699 (95)	
Advanced stage at diagnosis², n (%)				0.2			0.9
	Yes	53 (75)	239 (64)		148 (84)	606 (82)	
	No	17 (24)	126 (34)		27 (15)	123 (17)	
	Not reported	1 (1)	6 (2)		2 (1)	9 (1)	
ECOG performance status³, n (%)				0.6			0.07
	0	10 (14)	78 (21)		48 (27)	203 (28)	

1	29 (41)	134 (36)			59 (33)	273 (37)	
2+	19 (27)	88 (24)			39 (22)	105 (14)	
Missing	13 (18)	71 (19)			31 (18)	157 (21)	
Disease type, n (%)			0.01				0.5
Lung adenocarcinoma	48 (68)	298 (80)			150 (85)	623 (84)	
Lung non-small cell lung carcinoma (nsclc) (nos)	12 (17)	52 (14)			15 (8)	78 (11)	
Other	11 (15)	21 (6)			12 (7)	37 (5)	
Tissue of origin, n (%)			0.2				0.007
Lung	26 (37)	185 (50)			66 (37)	360 (49)	
Lymph node	10 (14)	50 (13)			21 (12)	104 (14)	
Brain	9 (13)	28 (8)			13 (7)	39 (5)	
Bone	2 (3)	17 (5)			18 (10)	37 (5)	
Other/unknown	24 (34)	91 (25)			59 (33)	198 (27)	
TMB, n (%)			1.0				1.0
Low (<10 mut/Mb)	36 (51)	191 (51)			112 (63)	471 (64)	
High (≥10 mut/Mb)	35 (49)	180 (49)			65 (37)	267 (36)	
PD-L1 expression, n (%)			0.5				0.2
No (<1% TPS)	1 (2)	15 (8)			44 (46)	140 (37)	
Low (1-49% TPS)	7 (16)	26 (14)			29 (31)	141 (37)	
High (≥50% TPS)	35 (81)	139 (77)			22 (23)	102 (27)	
Missing	28	191			82	355	
Total number of lines of therapy received, n (%)			0.9				1.0
1	50 (70)	269 (73)			124 (70)	520 (70)	
2	14 (20)	71 (19)			33 (19)	138 (19)	
3+	7 (10)	31 (8)			20 (11)	80 (11)	
Class of 2nd line therapy received, n (%)			1.0				0.06

Chemotherapy alone	8 (38)	40 (39)			15 (28)	63 (29)	
IO-Chemo combination	4 (19)	19 (19)			9 (17)	14 (6)	
Immunotherapy alone	4 (19)	17 (17)			1 (2)	17 (8)	
Other	5 (24)	26 (25)			28 (53)	124 (57)	

¹Characteristics were compared between cohorts using a Wilcoxon rank-sum test for continuous measures and a chi-squared test or Fisher's exact test for categorical measures.

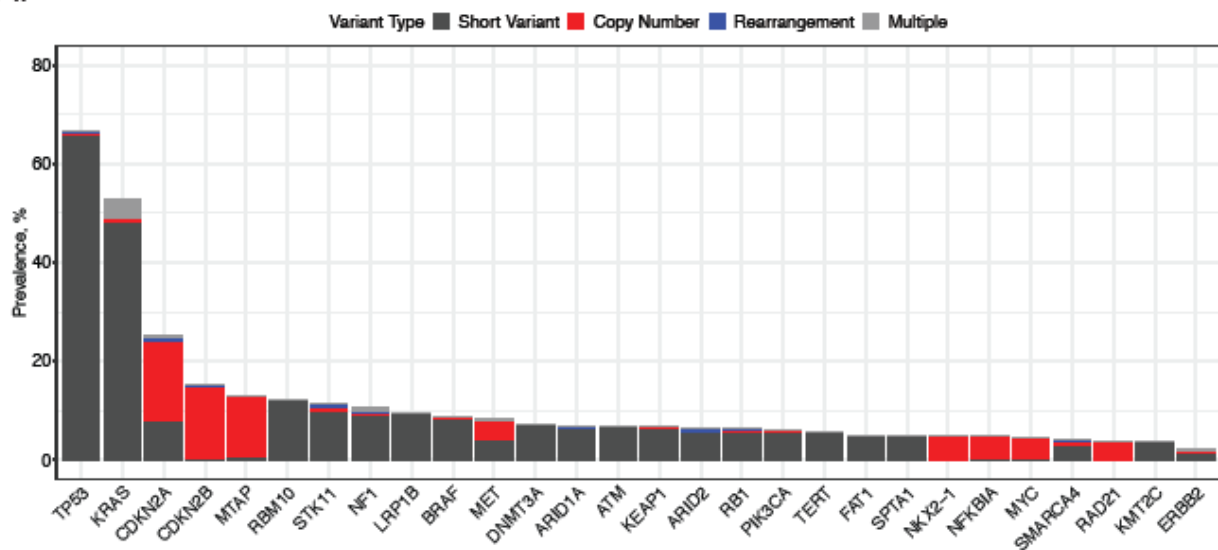
²Includes stages IIIB, IIIC, IV, IVA, IVB.

³Assessed on or up to 30 days before treatment start date.

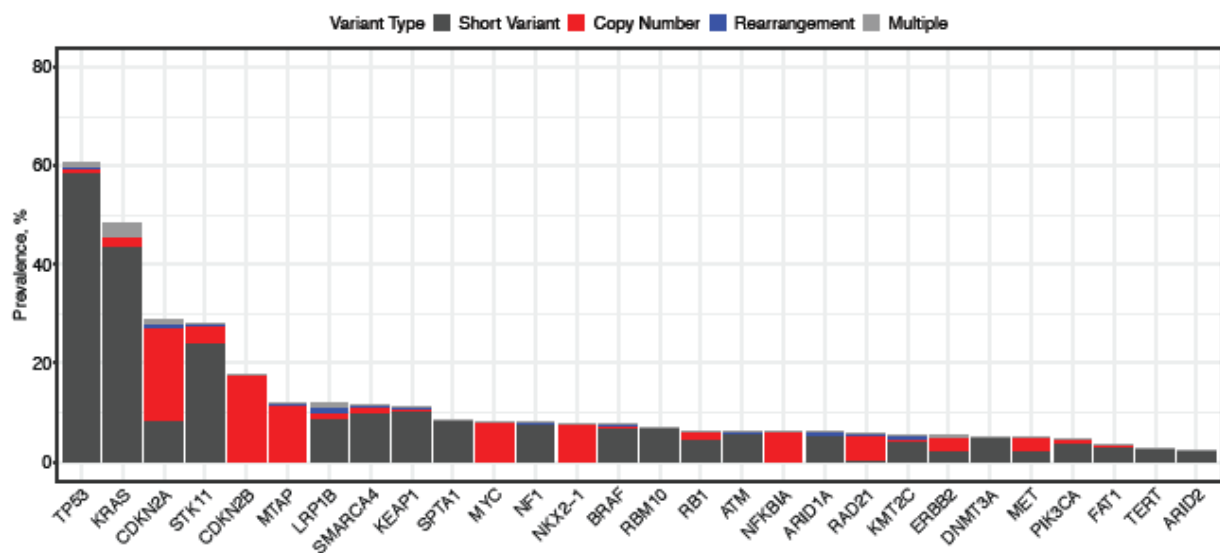
Supplementary Figures

Supplementary Figure 1. Genomic characterization of the clinical cohort. (a-b) Bar chart of the prevalence of gene alterations by alteration type for patients in the (a) mono-IO and (b) chemo-IO cohort. (c) Oncoprint plot of prevalent genomic alterations in the mono-IO and chemo-IO cohort.

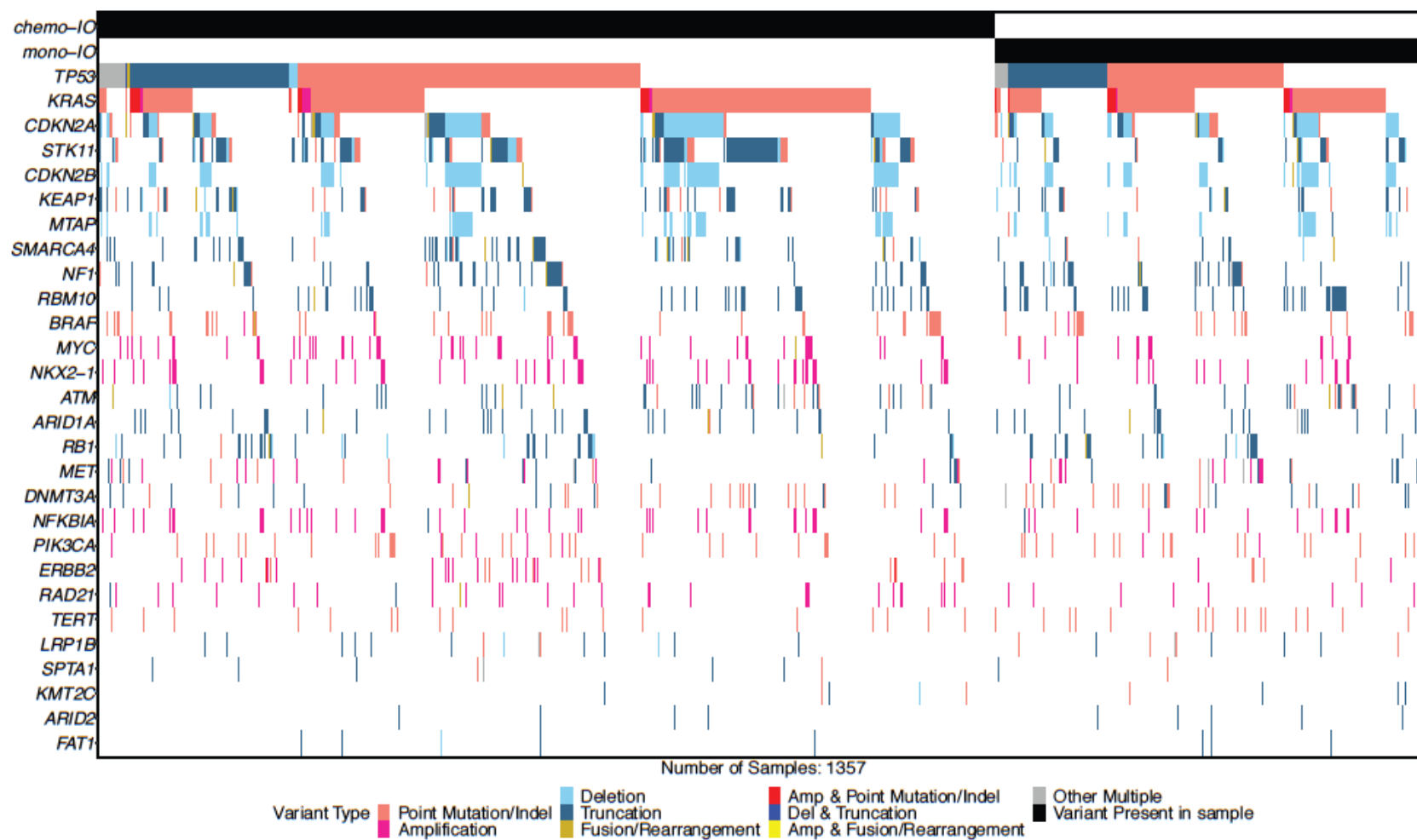
A.



B.



C.



Supplementary Figure 2. *CDKN2A* deletion is associated with lower time to next treatment (TTNT) after first-line immunotherapy. Kaplan-Meier plot of TTNT for mono-IO (left) and chemo-IO (right) treated patients according to *CDKN2A* deletion status.

