

Supplementary

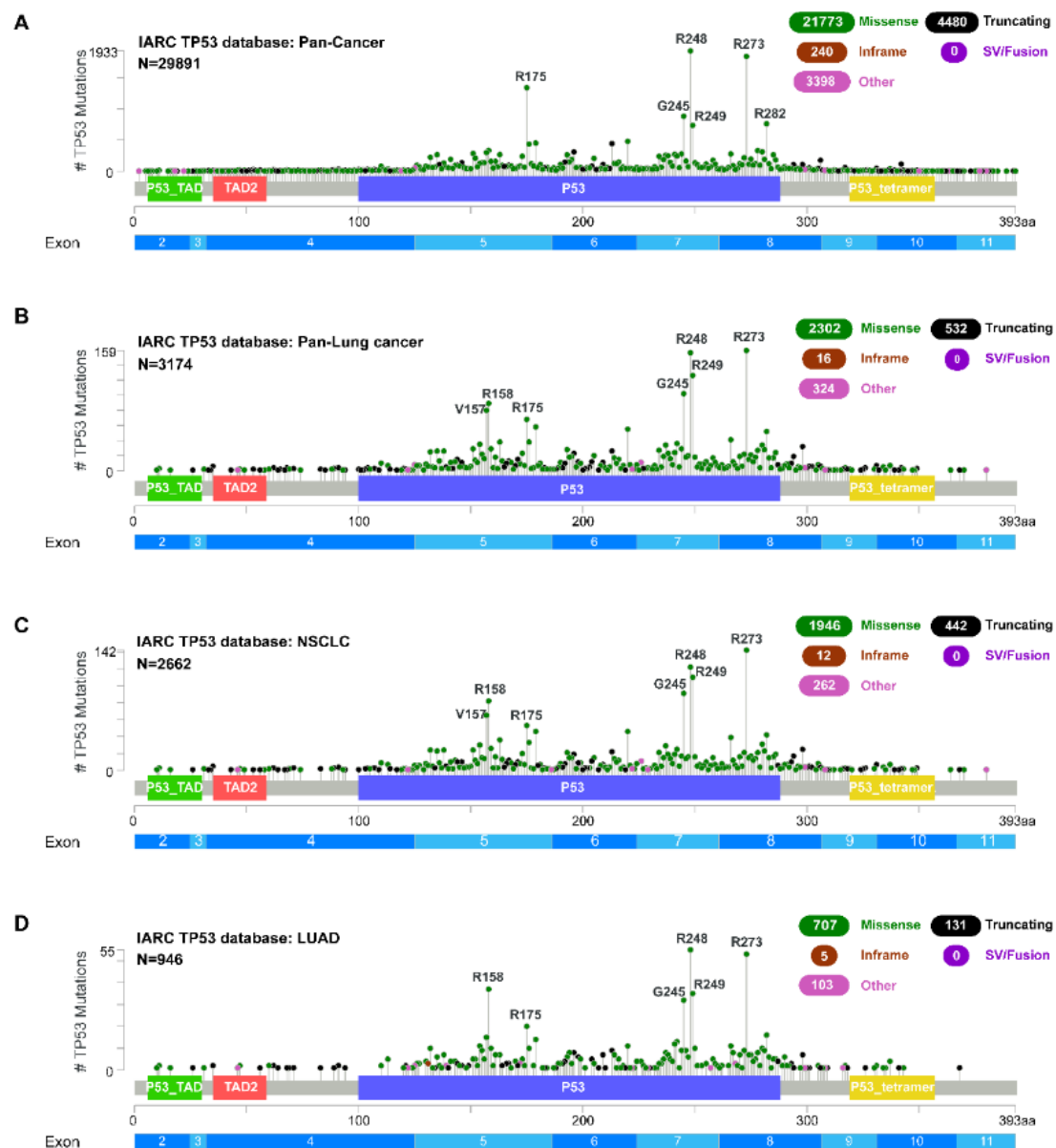


Figure S1 Distributions of *TP53* mutations in IARC *TP53* Database (R20, July 2019, <https://tp53.isb-cgc.org>). (A) Distributions of *TP53* mutations in Pan-Cancer. (B) Distributions of *TP53* mutations in Pan-Lung cancer. (C) Distributions of *TP53* mutations in NSCLC. (D) Distributions of *TP53* mutations in LUAD. LUAD, lung adenocarcinoma; NSCLC, non-small-cell lung cancer.

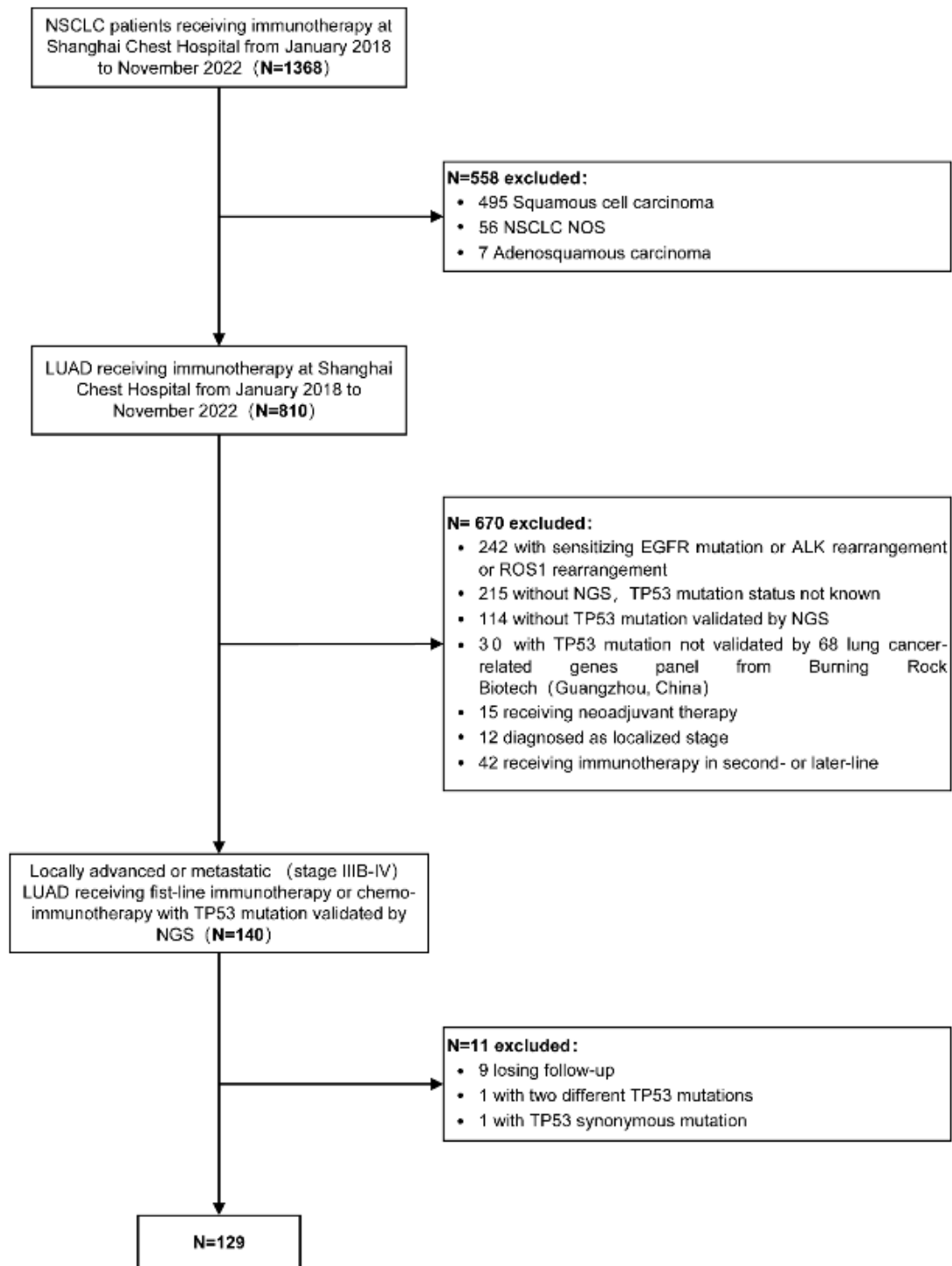


Figure S2 Flow diagram visualizing the inclusion and exclusion of patients in our cohort. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; LUAD, lung adenocarcinoma; NGS, next-generation sequencing; NOS, not otherwise specified; NSCLC, non-small-cell lung cancer; ROS1, c ROS proto-oncogene 1.

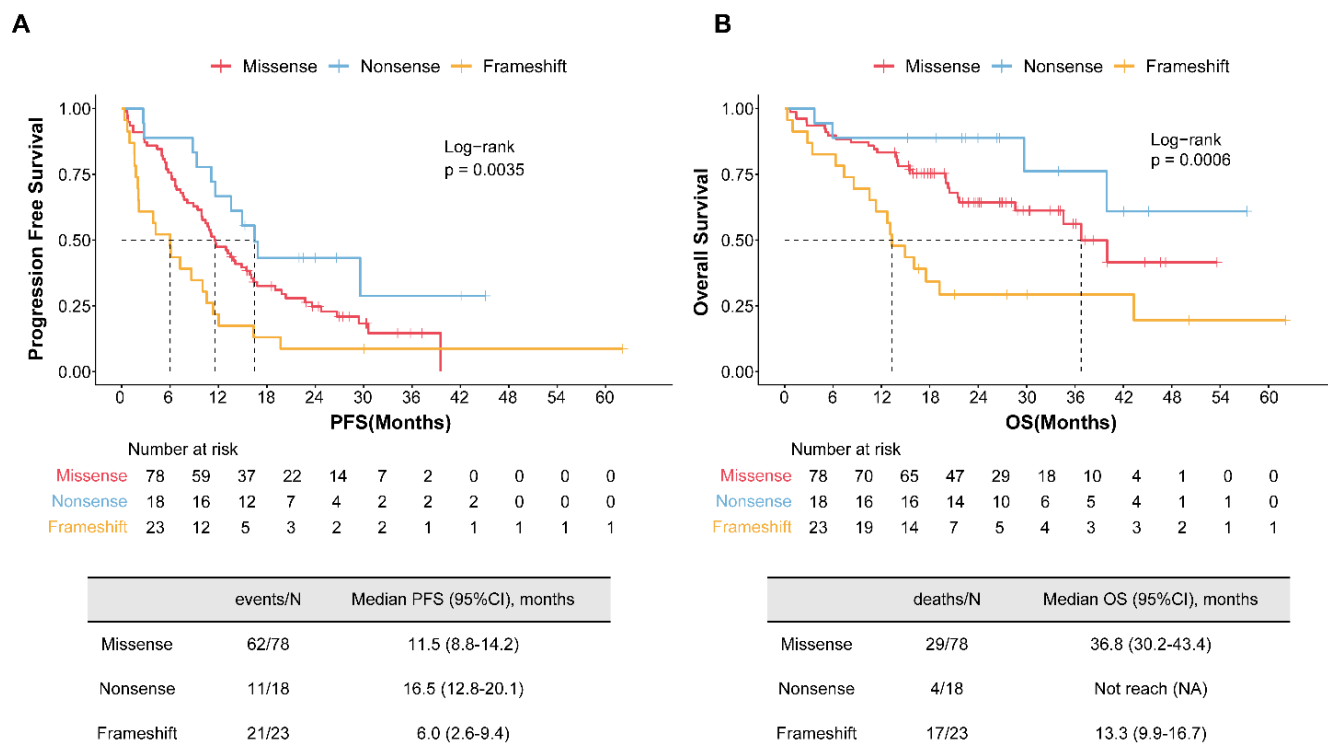


Figure S3 Sensitivity analysis of PFS and OS according to *TP53* mutation subtypes after excluding patients with other rare variants. (A) Kaplan–Meier curves for PFS according to *TP53* mutation subtypes after excluding patients harboring other rare variants. (B) Kaplan–Meier curves for OS according to *TP53* mutation subtypes after excluding patients harboring other rare variants. CI, confidence interval; OS, overall survival; PFS, progression-free survival.

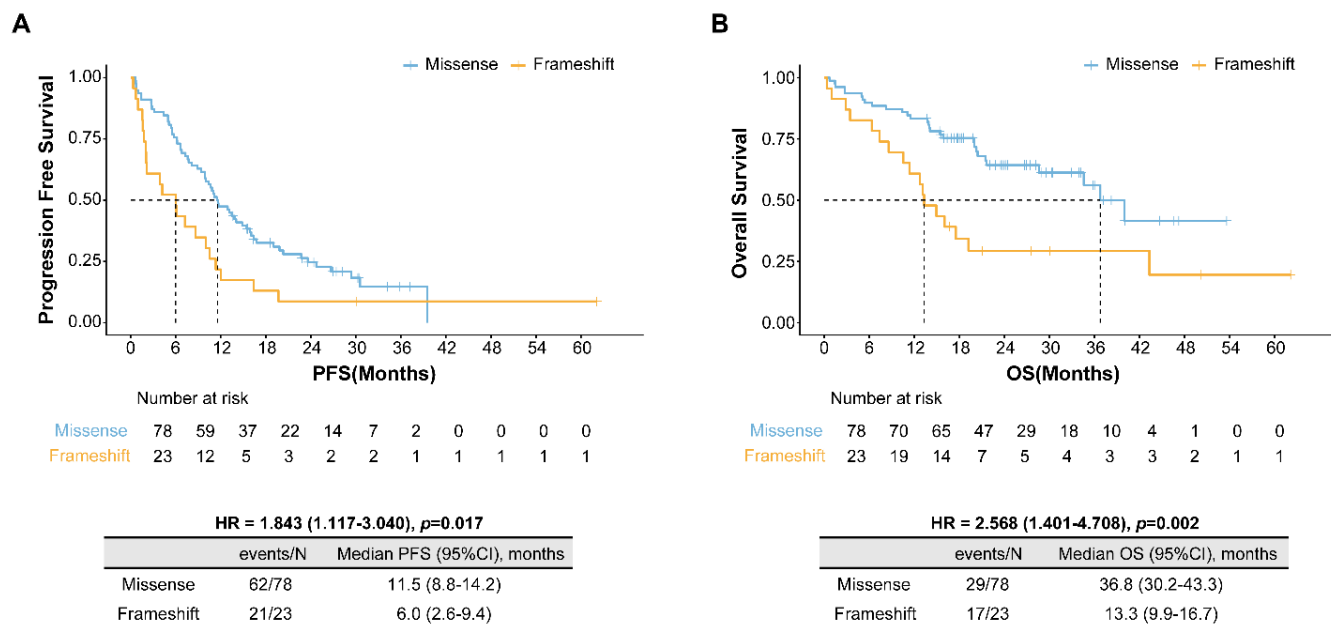


Figure S4 Kaplan–Meier analysis of PFS and OS in patients with *TP53* frameshift versus missense mutations. (A) PFS of *TP53* frameshift mutation group versus missense mutation group. (B) OS of *TP53* frameshift mutation group versus missense mutation group. CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

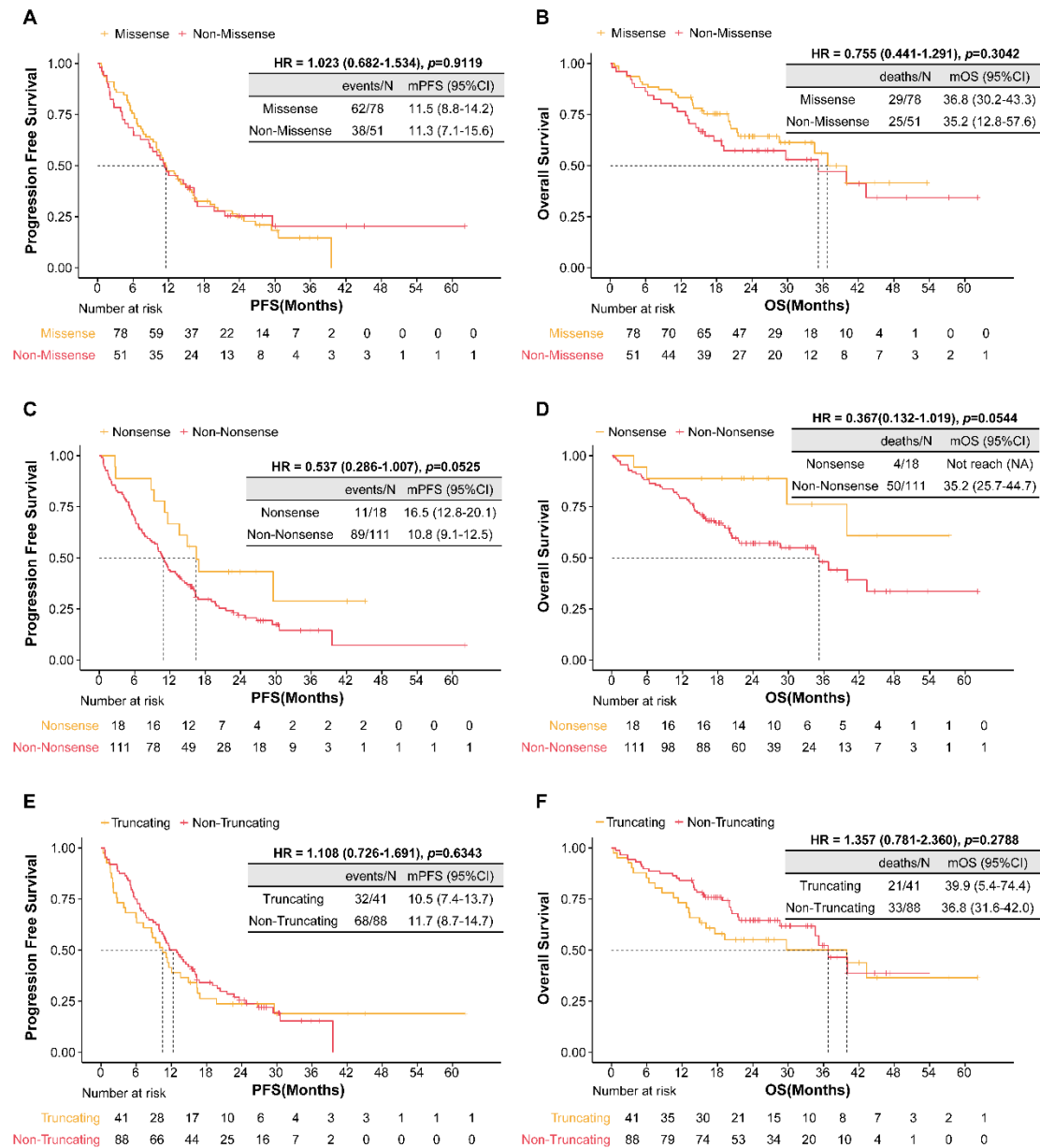


Figure S5 Kaplan-Meier curves for PFS and OS between different *TP53* mutation subtypes. (A,B) PFS (A) and OS (B) of *TP53* missense mutation group versus non-missense mutation group. (C,D) PFS (C) and OS (D) of *TP53* nonsense mutation group versus non-nonsense mutation group. (E,F) PFS (E) and OS (F) of *TP53* truncating (including nonsense and frameshift mutations) mutation group versus non-truncating mutation group. CI, confidence interval; HR, hazard ratio; NA, not available; OS, overall survival; PFS, progression-free survival.

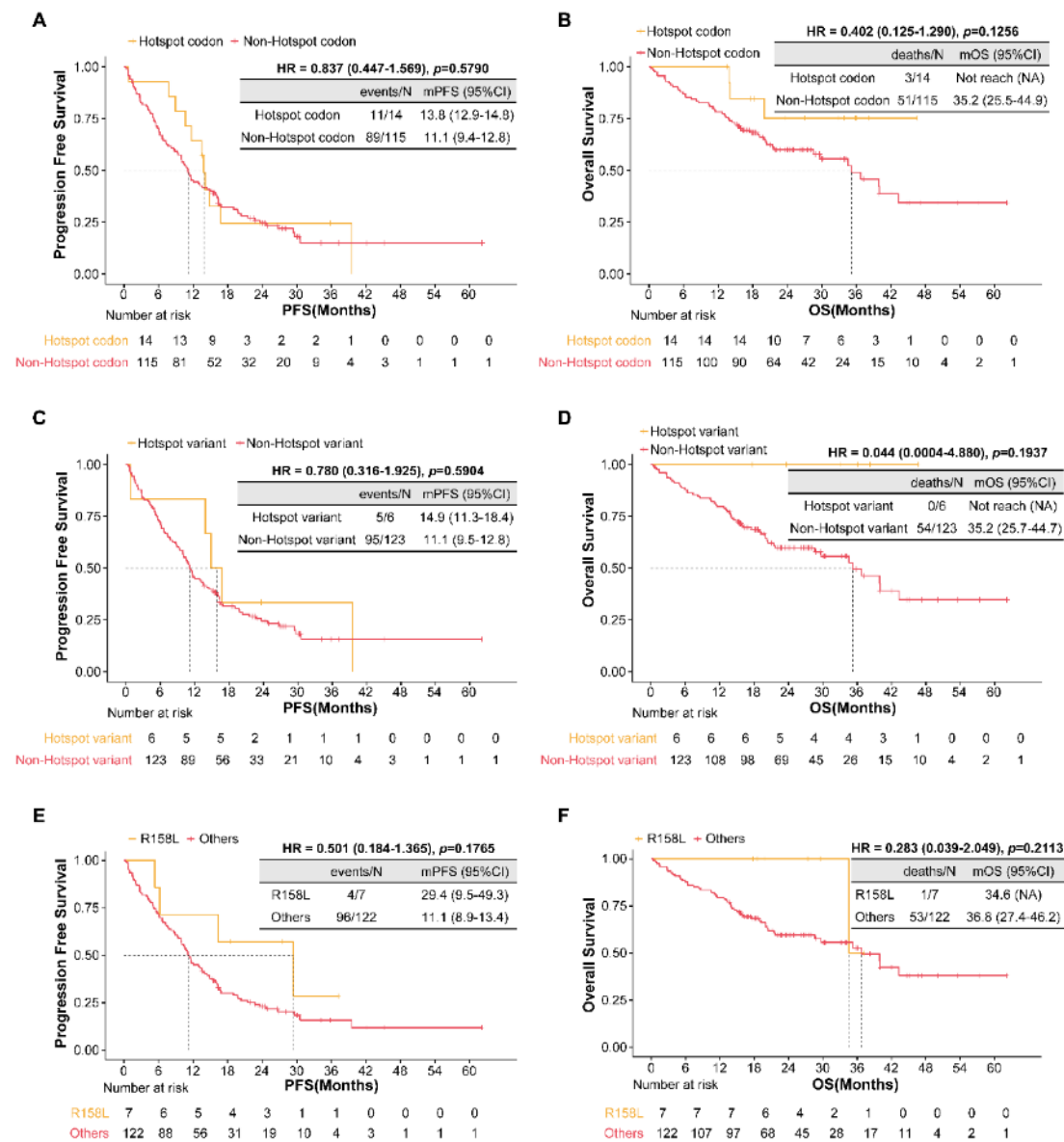


Figure S6 Kaplan-Meier curves for PFS and OS between *TP53* hotspot mutations and non-hotspot mutations. (A,B) PFS (A) and OS (B) of *TP53* hotspot codon group versus non-hotspot codon group. (C,D) PFS (C) and OS (D) of *TP53* hotspot variant group versus non-hotspot variant group. (E,F) PFS (E) and OS (F) of *TP53* R158L mutation versus all other mutations. CI, confidence interval; HR, hazard ratio; NA, not available; OS, overall survival; PFS, progression-free survival.

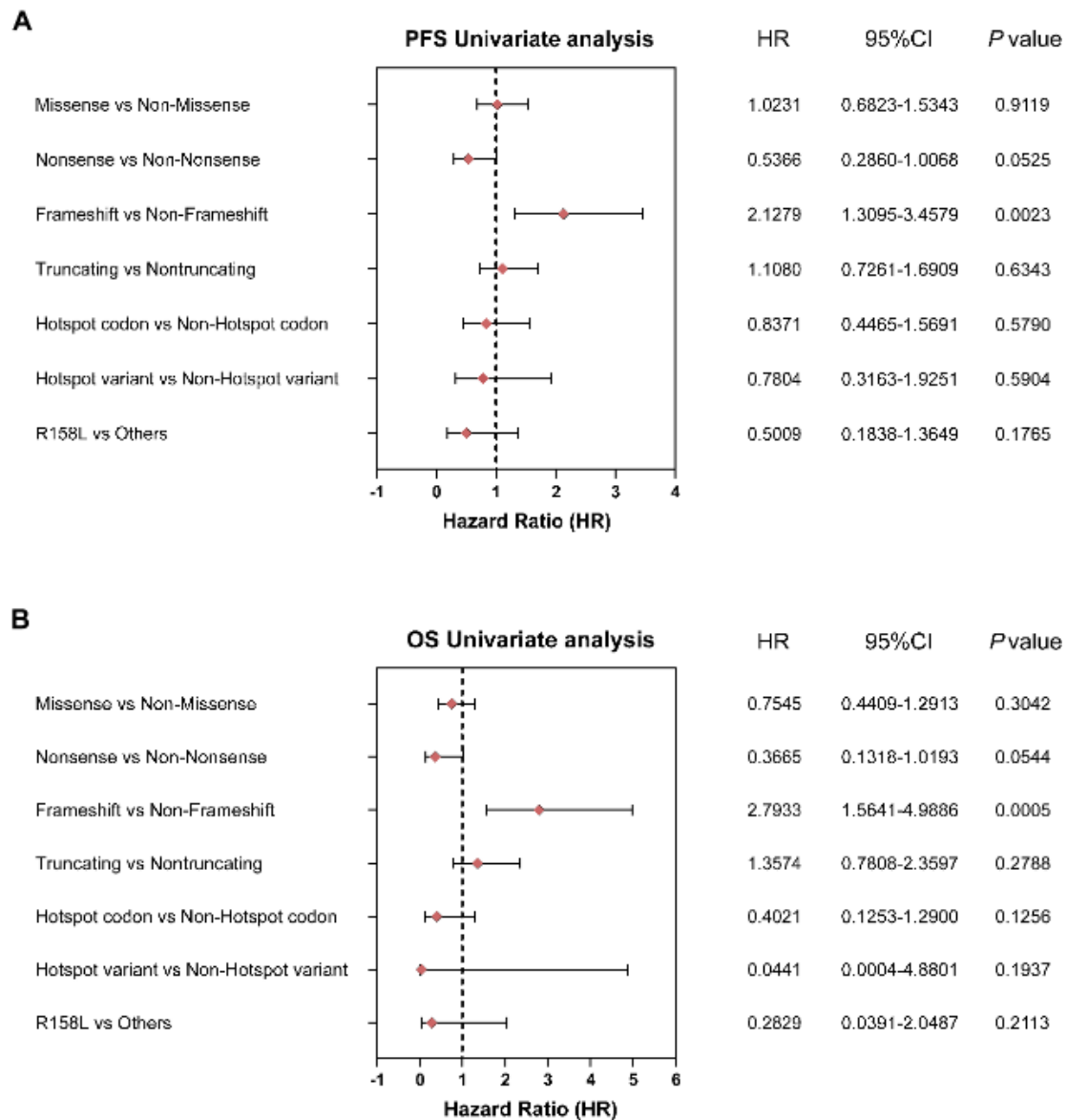


Figure S7 Forest plot illustrating outcomes across various *TP53* mutation subtypes. (A) Forest plot between *TP53* mutation subtypes and PFS. (B) Forest plot between *TP53* mutation subtypes and OS. CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

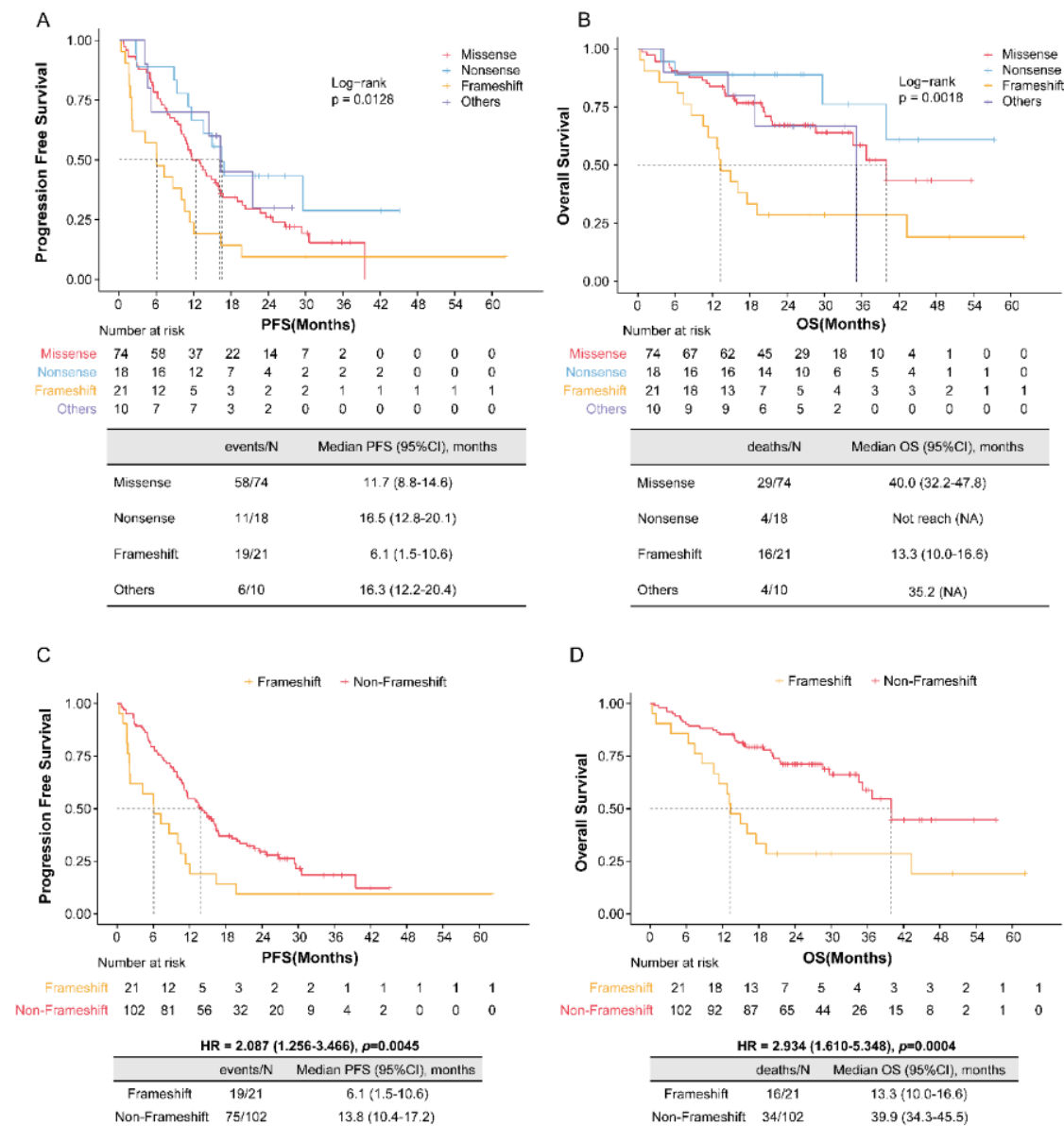


Figure S8 Kaplan-Meier curves for PFS and OS among 123 patients receiving first-line immunochemotherapy in our cohort. (A) Kaplan-Meier estimates of PFS among four *TP53* mutation subtypes. (B) Kaplan-Meier estimates of OS among four *TP53* mutation subtypes. (C) PFS of *TP53* frameshift mutation group versus non-frameshift mutation group. (D) OS of *TP53* frameshift mutation group versus non-frameshift mutation group. CI, confidence interval; HR, hazard ratio; NA, not available; OS, overall survival; PFS, progression-free survival.

Table S1 OncoScreen 68 genes list

<i>ALK</i>	<i>BRAF</i>	<i>EGFR</i>	<i>ERBB2</i>	<i>KRAS</i>
<i>MET</i>	<i>RET</i>	<i>ROS1</i>	<i>AKT1</i>	<i>APC</i>
<i>AR</i>	<i>ARAF</i>	<i>ATM</i>	<i>AXL</i>	<i>BCL2L1</i>
<i>BRCA1</i>	<i>BRCA2</i>	<i>CCND1</i>	<i>CD74</i>	<i>CDK4</i>
<i>CDK6</i>	<i>CDKN2A</i>	<i>CTNNB1</i>	<i>DDR2</i>	<i>ERBB3</i>
<i>ERBB4</i>	<i>ESR1</i>	<i>FGF19</i>	<i>FGF3</i>	<i>FGF4</i>
<i>FGFR1</i>	<i>FGFR2</i>	<i>FGFR3</i>	<i>FLT3</i>	<i>HRAS</i>
<i>IDH1</i>	<i>IDH2</i>	<i>IGF1R</i>	<i>JAK1</i>	<i>JAK2</i>
<i>KDR</i>	<i>KIT</i>	<i>MAP2K1</i>	<i>MTOR</i>	<i>MYC</i>
<i>NF1</i>	<i>NOTCH1</i>	<i>NRAS</i>	<i>NRG1</i>	<i>NTRK1</i>
<i>NTRK2</i>	<i>NTRK3</i>	<i>PDGFRA</i>	<i>PIK3CA</i>	<i>PTCH1</i>
<i>PTEN</i>	<i>RAF1</i>	<i>RB1</i>	<i>SMAD4</i>	<i>SMO</i>
<i>STK11</i>	<i>TOP2A</i>	<i>TP53</i>	<i>TSC1</i>	<i>TSC2</i>
<i>CYP2D6</i>	<i>DPYD</i>	<i>UGT1A1</i>		

Table S2 Baseline clinicopathological characteristics of patients between *TP53* frameshift mutation group and non-frameshift mutation group

Characteristics	Overall (n=129)	<i>TP53</i> mutation subgroup		P value
		Frameshift (n=23)	Non-Frameshift (n=106)	
Age				0.30
<65	66 (51.2)	14 (60.9)	52 (49.1)	
≥65	63 (48.8)	9 (39.1)	54 (50.9)	
Gender				0.54
Male	104 (80.6)	17 (79.3)	87 (82.1)	
Female	25 (19.4)	6 (26.1)	4 (17.9)	
Smoking				0.43
Yes	69 (53.5)	14 (60.9)	55 (51.9)	
No	60 (46.5)	9 (39.1)	51 (48.1)	
ECOG PS score				0.54
0	58 (45.0)	9 (39.1)	49 (46.2)	
≥1	71 (55.0)	14 (60.9)	57 (53.8)	
PD-L1 TPS				0.82
<1%	36 (27.9)	7 (30.4)	29 (27.4)	
1-49%	43 (33.3)	9 (39.1)	34 (32.1)	
≥1%	41 (31.8)	6 (26.1)	35 (33.0)	

NA	9 (7.0)	1 (4.3)	8 (7.5)	
Clinical Stage				0.50
III	20 (15.5)	2 (8.7)	18 (17.0)	
IV	109 (84.5)	21 (91.3)	88 (83.0)	
Brain Metastasis				0.22
No	97 (75.2)	15 (65.2)	82 (77.4)	
Yes	32 (24.8)	8 (34.8)	24 (22.6)	
First-line treatment				0.64
ICI monotherapy	6 (4.7)	2 (8.7)	4 (3.8)	
ICI combined with chemotherapy	123 (95.3)	21 (91.3)	102 (96.2)	

Data are presented as n (%). ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; NA, not available; PD-L1, programmed cell death ligand-1; TPS, tumor proportion score.

Table S3 Distribution of mutation frequencies for all genes included in the sequencing panel across *TP53* frameshift and non-frameshift groups

Gene	TP53_Framshift_mutation_group	TP53_Non-Framshift_mutation_group	P_value	Significance	TP53_Framshift_Mutant	TP53_Framshift_WT	TP53_Framshift_Frequency	TP53_Non-Framshift_Mutant	TP53_Non-Framshift_WT	TP53_Non-Framshift_Frequency
<i>KRAS</i>	3 (13.04%)	37 (34.91%)	0.047297	*	3	20	13.04%	37	69	34.91%
<i>IGF1R</i>	3 (13.04%)	3 (2.83%)	0.069373		3	20	13.04%	3	103	2.83%
<i>RAF1</i>	2 (8.7%)	1 (0.94%)	0.081799		2	21	8.70%	1	105	0.94%
<i>ARAF</i>	2 (8.7%)	1 (0.94%)	0.081799		2	21	8.70%	1	105	0.94%
<i>FGF4</i>	2 (8.7%)	1 (0.94%)	0.081799		2	21	8.70%	1	105	0.94%
<i>BRAF</i>	4 (17.39%)	7 (6.6%)	0.107036		4	19	17.39%	7	99	6.60%
<i>PDGFR A</i>	0 (0%)	13 (12.26%)	0.123149		0	23	0%	13	93	12.26%
<i>CTNNB1</i>	2 (8.7%)	2 (1.89%)	0.145742		2	21	8.70%	2	104	1.89%
<i>CCND1</i>	2 (8.7%)	2 (1.89%)	0.145742		2	21	8.70%	2	104	1.89%
<i>FGF19</i>	2 (8.7%)	2 (1.89%)	0.145742		2	21	8.70%	2	104	1.89%
<i>CDK6</i>	1 (4.35%)	0 (0%)	0.178295		1	22	4.35%	0	106	0%
<i>KDR</i>	0 (0%)	11 (10.38%)	0.211534		0	23	0%	11	95	10.38%
<i>NTRK3</i>	0 (0%)	11 (10.38%)	0.211534		0	23	0%	11	95	10.38%

<i>ERBB3</i>	2 (8.7%)	3 (2.83%)	0.21667 6		2	21	8.70%	3	103	2.83%
<i>FLT3</i>	2 (8.7%)	3 (2.83%)	0.21667 6		2	21	8.70%	3	103	2.83%
<i>CDK4</i>	4 (17.39%)	9 (8.49%)	0.24665 9		4	19	17.39%	9	97	8.49%
<i>FGF3</i>	2 (8.7%)	4 (3.77%)	0.29032 7		2	21	8.70%	4	102	3.77%
<i>KIT</i>	2 (8.7%)	4 (3.77%)	0.29032 7		2	21	8.70%	4	102	3.77%
<i>ERBB2</i>	5 (21.74%)	13 (12.26%)	0.31539		5	18	21.74%	13	93	12.26%
<i>AR</i>	1 (4.35%)	1 (0.94%)	0.32594 5		1	22	4.35%	1	105	0.94%
<i>PIK3CA</i>	0 (0%)	8 (7.55%)	0.34911		0	23	0%	8	98	7.55%
<i>JAK2</i>	0 (0%)	8 (7.55%)	0.34911		0	23	0%	8	98	7.55%
<i>BRCA2</i>	0 (0%)	7 (6.6%)	0.35092 1		0	23	0%	7	99	6.60%
<i>MTOR</i>	0 (0%)	7 (6.6%)	0.35092 1		0	23	0%	7	99	6.60%
<i>NTRK1</i>	0 (0%)	9 (8.49%)	0.36064 3		0	23	0%	9	97	8.49%
<i>ATM</i>	3 (13.04%)	7 (6.6%)	0.38258 2		3	20	13.04%	7	99	6.60%
<i>FGFR1</i>	3 (13.04%)	7 (6.6%)	0.38258 2		3	20	13.04%	7	99	6.60%
<i>CDKN2A</i>	4 (17.39%)	12 (11.32%)	0.48454		4	19	17.39%	12	94	11.32%
<i>FGFR3</i>	1 (4.35%)	3 (2.83%)	0.54877 6		1	22	4.35%	3	103	2.83%
<i>SMO</i>	1 (4.35%)	3 (2.83%)	0.54877 6		1	22	4.35%	3	103	2.83%

<i>NF1</i>	5 (21.74%)	18 (16.98%)	0.558997		5	18	21.74%	18	88	16.98%
<i>SMAD4</i>	0 (0%)	5 (4.72%)	0.584874		0	23	0%	5	101	4.72%
<i>AXL</i>	0 (0%)	5 (4.72%)	0.584874		0	23	0%	5	101	4.72%
<i>IDH1</i>	0 (0%)	5 (4.72%)	0.584874		0	23	0%	5	101	4.72%
<i>RET</i>	0 (0%)	6 (5.66%)	0.590231		0	23	0%	6	100	5.66%
<i>BRCA1</i>	2 (8.7%)	5 (4.72%)	0.607443		2	21	8.70%	5	101	4.72%
<i>NTRK2</i>	2 (8.7%)	5 (4.72%)	0.607443		2	21	8.70%	5	101	4.72%
<i>PTEN</i>	2 (8.7%)	6 (5.66%)	0.632265		2	21	8.70%	6	100	5.66%
<i>PTCH1</i>	2 (8.7%)	7 (6.6%)	0.661517		2	21	8.70%	7	99	6.60%
<i>MET</i>	1 (4.35%)	10 (9.43%)	0.687696		1	22	4.35%	10	96	9.43%
<i>NOTCH1</i>	1 (4.35%)	11 (10.38%)	0.691931		1	22	4.35%	11	95	10.38%
<i>ERBB4</i>	3 (13.04%)	11 (10.38%)	0.714572		3	20	13.04%	11	95	10.38%
<i>HRAS</i>	0 (0%)	3 (2.83%)	1		0	23	0%	3	103	2.83%
<i>IDH2</i>	0 (0%)	1 (0.94%)	1		0	23	0%	1	105	0.94%
<i>AKT1</i>	0 (0%)	1 (0.94%)	1		0	23	0%	1	105	0.94%
<i>NRAS</i>	0 (0%)	1 (0.94%)	1		0	23	0%	1	105	0.94%
<i>TP53</i>	23 (100%)	106 (100%)	1		23	0	100%	106	0	100%
<i>EGFR</i>	3 (13.04%)	16 (15.09%)	1		3	20	13.04%	16	90	15.09%

<i>APC</i>	2 (8.7%)	10 (9.43%)	1		2	21	8.70%	10	96	9.43%
<i>TSC2</i>	1 (4.35%)	7 (6.6%)	1		1	22	4.35%	7	99	6.60%
<i>MYC</i>	1 (4.35%)	4 (3.77%)	1		1	22	4.35%	4	102	3.77%
<i>STK11</i>	2 (8.7%)	9 (8.49%)	1		2	21	8.70%	9	97	8.49%
<i>RBI</i>	2 (8.7%)	12 (11.32%)	1		2	21	8.70%	12	94	11.32%
<i>JAK1</i>	1 (4.35%)	5 (4.72%)	1		1	22	4.35%	5	101	4.72%
<i>TOP2A</i>	1 (4.35%)	5 (4.72%)	1		1	22	4.35%	5	101	4.72%
<i>TSC1</i>	0 (0%)	4 (3.77%)	1		0	23	0%	4	102	3.77%
<i>DDR2</i>	1 (4.35%)	6 (5.66%)	1		1	22	4.35%	6	100	5.66%
<i>ALK</i>	2 (8.7%)	10 (9.43%)	1		2	21	8.70%	10	96	9.43%
<i>MAP2K1</i>	0 (0%)	4 (3.77%)	1		0	23	0%	4	102	3.77%
<i>ROS1</i>	2 (8.7%)	9 (8.49%)	1		2	21	8.70%	9	97	8.49%
<i>FGFR2</i>	0 (0%)	4 (3.77%)	1		0	23	0%	4	102	3.77%

*, P<0.05.