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J Immunother Cancer

A

Variable	Hazard Ratio	HR 95% CI	P Value
Biomarker			
— BRAF_V600E vs. KRAS	0.584	(0.348, 0.978)	0.041
— BRAF_nonV600E vs. KRAS	0.817	(0.526, 1.268)	0.367
— HER2 vs. KRAS	1.114	(0.638, 1.945)	0.705
— EGFR_Classic vs. KRAS	0.911	(0.585, 1.421)	0.682
— EGFR_Exon20 vs. KRAS	0.805	(0.507, 1.277)	0.357
— MET vs. KRAS	0.960	(0.583, 1.581)	0.872
— Fusions vs. KRAS	0.851	(0.506, 1.434)	0.546
Age Group			
— <65 vs. >=65	1.320	(1.088, 1.601)	0.005
Gender			
— M vs. F	1.370	(1.134, 1.654)	0.001
Smoking History			
— History of smoking vs. No history of smoking	0.794	(0.602, 1.048)	0.103
PD-L1 Status			
— Positive vs. Negative	0.570	(0.352, 0.922)	0.022
— Unknown/Untested vs. Negative	0.932	(0.636, 1.367)	0.720
Prior Tx Lines			
— >=2 vs. 0-1	1.258	(0.978, 1.617)	0.074
Prior TKI			
— Yes vs. No	1.570	(1.075, 2.291)	0.019
TMB Category (cutoff=10)			
— >=10 vs. <10	0.659	(0.530, 0.818)	<0.001
— Missing vs. <10	1.324	(0.944, 1.856)	0.103

Supplementary Table S1. Multivariable analysis for progression-free survival in the CGDB Immunotherapy cohort. A) TMB cutoff of 10 mutations/Mb; B) TMB cutoff of 16 mutations/Mb.

CGDB: Clinico-Genomic Database; M: male; F: female; Tx: treatment; TKI: tyrosine kinase inhibitor; TMB: tumor mutational burden.

B

Variable	Hazard Ratio	HR 95% CI	P Value
Biomarker			
— BRAF_V600E vs. KRAS	0.626	(0.375, 1.046)	0.074
— BRAF_nonV600E vs. KRAS	0.835	(0.538, 1.296)	0.422
— HER2 vs. KRAS	1.193	(0.684, 2.081)	0.535
— EGFR_Classic vs. KRAS	0.969	(0.622, 1.510)	0.889
— EGFR_Exon20 vs. KRAS	0.868	(0.547, 1.376)	0.546
— MET vs. KRAS	0.993	(0.604, 1.632)	0.978
— Fusions vs. KRAS	0.906	(0.539, 1.523)	0.710
Age Group			
— <65 vs. >=65	1.334	(1.099, 1.618)	0.004
Gender			
— M vs. F	1.363	(1.129, 1.646)	0.001
Smoking History			
— History of smoking vs. No history of smoking	0.803	(0.609, 1.060)	0.122
PD-L1 Status			
— Positive vs. Negative	0.620	(0.383, 1.006)	0.053
— Unknown/Untested vs. Negative	0.962	(0.656, 1.409)	0.842
Prior Tx Lines			
— >=2 vs. 0-1	1.291	(1.002, 1.662)	0.048
Prior TKI			
— Yes vs. No	1.588	(1.084, 2.325)	0.017
TMB Category (cutoff=16)			
— >=16 vs. <16	0.565	(0.422, 0.755)	<0.001
— Missing vs. <16	1.395	(0.999, 1.947)	0.051

A

Variable	Hazard Ratio	HR 95% CI	P Value
Biomarker			
— BRAF_V600E vs. KRAS	0.703	(0.443, 1.116)	0.136
— BRAF_nonV600E vs. KRAS	0.746	(0.486, 1.145)	0.180
— HER2 vs. KRAS	0.862	(0.481, 1.543)	0.617
— EGFR_Classic vs. KRAS	0.838	(0.554, 1.266)	0.401
— EGFR_Exon20 vs. KRAS	0.878	(0.580, 1.328)	0.537
— MET vs. KRAS	0.696	(0.417, 1.160)	0.164
— Fusions vs. KRAS	0.641	(0.380, 1.082)	0.096
Smoking History			
— History of smoking vs. No history of smoking	0.847	(0.654, 1.096)	0.206
ECOG at 1st ICB			
— >=2 vs. 0-1	1.652	(1.321, 2.066)	<0.001
— Missing vs. 0-1	1.242	(0.946, 1.630)	0.119
Prior Tx Lines			
— >=2 vs. 0-1	1.220	(0.960, 1.551)	0.104
Prior TKI			
— Yes vs. No	1.325	(0.915, 1.918)	0.136
TMB Category (cutoff=10)			
— >=10 vs. <10	0.762	(0.608, 0.956)	0.019
— Missing vs. <10	1.359	(1.070, 1.726)	0.012

Supplementary Table S2. Multivariable analysis for overall survival in the CGDB Immunotherapy cohort.

A) TMB cutoff of 10 mutations/Mb; B) TMB cutoff of 16 mutations/Mb.

CGDB: Clinico-Genomic Database; ICB: immune checkpoint blockade; ECOG: Eastern Cooperative Oncology Group; Tx: treatment; TKI: tyrosine kinase inhibitor; TMB: tumor mutational burden.

B

Variable	Hazard Ratio	HR 95% CI	P Value
Biomarker			
— BRAF_V600E vs. KRAS	0.726	(0.459, 1.149)	0.172
— BRAF_nonV600E vs. KRAS	0.749	(0.488, 1.150)	0.186
— HER2 vs. KRAS	0.887	(0.495, 1.589)	0.687
— EGFR_Classic vs. KRAS	0.860	(0.571, 1.297)	0.473
— EGFR_Exon20 vs. KRAS	0.904	(0.599, 1.365)	0.632
— MET vs. KRAS	0.703	(0.422, 1.171)	0.176
— Fusions vs. KRAS	0.654	(0.388, 1.102)	0.110
Smoking History			
— History of smoking vs. No history of smoking	0.845	(0.653, 1.094)	0.202
ECOG at 1st ICB			
— >=2 vs. 0-1	1.659	(1.327, 2.074)	<0.001
— Missing vs. 0-1	1.239	(0.944, 1.627)	0.123
Prior Tx Lines			
— >=2 vs. 0-1	1.232	(0.969, 1.566)	0.089
Prior TKI			
— Yes vs. No	1.325	(0.915, 1.919)	0.137
TMB Category			
— >=16 vs. <16	0.659	(0.489, 0.889)	0.006
— Missing vs. <16	1.394	(1.106, 1.756)	0.005

	MDACC cohort						CGDB Immunotherapy cohort								
	BRAF	Classic EGFR	EGFR exon 20	HER2	KRAS	P-value	BRAF V600E	BRAF non-V600E	Classic EGFR	EGFR exon 20	HER2	KRAS	MET	Fusions	P-value
Number	10*	28	25	15	87		37	45	66	47	28	601	34	36	
Age - years															
Median	69	60	60	61	66	0.047	71	71	70	69	66	69	76	62	<0.001
Range	57-83	32-82	28-81	34-75	36-87		38-85	48-85	36-85	39-83	37-85	27-85	49-85	34-85	
Sex – N (%)															
Female	6 (60)	17 (61)	15 (60)	10 (67)	52 (60)	0.995	24 (65)	24 (53)	42 (64)	28 (60)	22 (79)	368 (61)	18 (53)	19 (53)	0.411
Male	4 (40)	11 (39)	10 (40)	5 (33)	35 (40)		13 (35)	21 (47)	24 (36)	19 (40)	6 (21)	233 (39)	16 (47)	17 (47)	
Smoking – N (%)															
Never	1 (10)	20 (71)	16 (64)	11 (73)	9 (10)	<0.001	9 (24)	2 (4)	30 (46)	21 (45)	19 (68)	42 (7)	11 (32)	25 (69)	<0.001
Ever	9 (90)	8 (29)	9 (36)	4 (27)	78 (90)		28 (76)	43 (96)	36 (54)	26 (55)	9 (32)	559 (93)	23 (68)	11 (31)	
Histology – N (%)															
Non-squamous	9 (90)	28 (100)	25 (100)	13 (87)	86 (99)	0.035	36 (97)	40 (89)	61 (92)	46 (98)	28 (100)	537 (89)	30 (88)	33 (92)	0.432
Squamous	1 (10)	0 (0)	0 (0)	2 (13)	1 (1)		1 (3)	4 (9)	5 (8)	0 (0)	0 (0)	43 (7)	3 (9)	1 (3)	
Carcinoma NOS	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)	1 (2)	0 (0)	1 (2)	0 (0)	21 (4)	1 (3)	2 (6)	
PS – N (%)															
0-1	8 (80)	23 (82)	23 (92)	11 (73)	64 (74)	0.528	23 (62)	29 (64)	42 (64)	34 (72)	18 (64)	411 (68)	24 (71)	30 (83)	0.082
≥2	2 (20)	5 (18)	2 (8)	4 (27)	18 (21)		7 (19)	11 (24)	9 (14)	6 (13)	2 (7)	113 (19)	8 (24)	5 (14)	
Not available	0 (0)	0 (0)	0 (0)	0 (0)	5 (6)		7 (19)	5 (11)	15 (23)	7 (15)	8 (29)	77 (13)	2 (6)	1 (3)	
Prior treatment lines – N (%)															
0-1	3 (30)	7 (25)	14 (56)	11 (73)	61 (70)	<0.001	32 (86)	39 (87)	35 (53)	32 (68)	23 (82)	514 (86)	28 (82)	25 (69)	<0.001
≥2	7 (70)	21 (75)	11 (44)	4 (27)	26 (30)		5 (14)	6 (13)	31 (47)	15 (32)	5 (18)	87 (14)	6 (18)	11 (31)	
Prior TKI therapy – N (%)															
Yes	3 (30)	22 (79)	8 (32)	3 (20)	3 (3)	<0.001	5 (14)	3 (7)	39 (59)	12 (26)	3 (11)	15 (2)	33 (97)	10 (27)	<0.001
No	7 (70)	6 (21)	17 (68)	12 (80)	84 (97)		32 (86)	43 (93)	27 (41)	35 (74)	25 (89)	586 (98)	1 (3)	26 (72)	
Subsequent lines of therapy – N (%)															
Yes	4 (40)	19 (68)	21 (84)	9 (60)	48 (55)	0.042	14 (38)	16 (36)	34 (52)	26 (55)	14 (50)	217 (36)	15 (44)	19 (53)	0.022
No	5 (50)	9 (32)	4 (16)	5 (33)	38 (44)		23 (62)	29 (64)	32 (48)	21 (45)	14 (50)	384 (64)	19 (56)	17 (47)	
Not available	1 (10)	0 (0)	0 (0)	1 (7)	1 (1)		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
PD-L1 status – N (%)															
Positive	3 (30)	7 (25)	10 (40)	2 (13)	15 (17)	0.369	8 (22)	5 (11)	4 (6)	4 (8)	1 (4)	88 (15)	3 (9)	1 (3)	0.089
Negative	2 (20)	5 (18)	4 (16)	4 (27)	28 (32)		1 (3)	3 (7)	4 (6)	1 (2)	4 (14)	31 (5)	4 (12)	2 (6)	
Not available	5 (50)	16 (57)	11 (44)	9 (60)	44 (51)		28 (76)	37 (82)	58 (88)	42 (89)	23 (82)	482 (80)	27 (79)	33 (92)	
TMB – Mutations/Mb															
Available	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	30 (81)	31 (69)	49 (74)	36 (77)	22 (79)	501 (83)	26 (76)	29 (81)	0.214
Median	NA	NA	NA	NA	NA	NA	5.6	11.3	2.6	2.6	3.5	8.7	4.4	2.4	<0.001
Range	NA	NA	NA	NA	NA		1-19	0-34	0-10	0-28	0-28	0-448	0-16	0-24	

Supplementary Table S3. Patient characteristics for the MDACC and CGDB Immunotherapy cohorts.

PS: performance status; TKI: tyrosine kinase inhibitor; TMB: tumor mutational burden.

*: V600E: n = 3 / non-V600E: n = 7

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Variable	Level	P-value	HR	95% CI		Overall p-value
PD-L1	Positive vs. Negative	0.0086	0.50	0.30	0.84	0.0318
	NA vs. Negative	0.1740	0.76	0.52	1.13	
Oncogene group	Classic EGFR vs. KRAS	0.0225	2.01	1.10	3.65	0.0109
	EGFR Ex20 vs. KRAS	0.4375	1.25	0.71	2.18	
	HER-2 vs. KRAS	0.1155	1.68	0.88	3.21	
	BRAF vs. KRAS	0.0324	0.36	0.14	0.92	
Age	>=65 vs. <65	0.1485	0.77	0.54	1.10	0.1485
Smoking	Former/Current vs. Never	0.4072	0.83	0.53	1.29	0.4072
Prior TKI	Yes vs. No	0.6243	1.13	0.69	1.85	0.6243

Supplementary Table S4. Multivariable analysis for progression-free survival in the MDACC cohort.
TKI: tyrosine kinase inhibitor.

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Variable	Level	P-value	HR	95% CI for HR		Overall p-value
PD_L1	Positive vs. Negative	0.0110	0.45	0.24	0.83	0.0381
	NA vs. Negative	0.1396	0.71	0.45	1.12	
Biomarker group	Classic EGFR vs. KRAS	0.2627	1.49	0.74	2.98	0.2901
	EGFR Ex20 vs. KRAS	0.3692	0.74	0.39	1.42	
	HER2 vs. KRAS	0.4815	1.28	0.65	2.53	
	BRAF vs. KRAS	0.4545	0.69	0.27	1.81	
Age group	>=65 vs. <65	0.0159	0.59	0.39	0.91	0.0159
Gender	Male vs. Female	0.0129	1.69	1.12	2.55	0.0129
TKI	Yes vs. No	0.2355	1.41	0.80	2.49	0.2355
Subsequent line	Yes vs. No	0.4714	1.18	0.75	1.85	0.4714

Supplementary Table S5. Multivariable analysis for overall survival in the MDACC cohort.

TKI: tyrosine kinase inhibitor.

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Variable	Level	KRAS	BRAF (V600E)	BRAF (non-V600E)	HER2	EGFR (Classic)	EGFR (Exon 20)	MET	Fusions	p-value
n		575	34	51	35	91	34	48	65	
Age at 1st Chemo (year) (median [range])		67.00 [30.00, 85.00]	68.50 [54.00, 83.00]	66.00 [47.00, 84.00]	67.00 [42.00, 84.00]	67.00 [50.00, 84.00]	68.00 [38.00, 81.00]	76.00 [56.00, 85.00]	62.00 [29.00, 83.00]	<0.001
Age at 1st Chemo (year) (mean (SD))		66.55 (9.73)	69.06 (7.43)	66.47 (9.90)	66.40 (10.06)	66.71 (9.39)	65.94 (9.83)	74.77 (7.05)	59.34 (12.57)	<0.001
Age Group at 1st Chemo (%)	>=65	332 (57.7)	25 (73.5)	30 (58.8)	19 (54.3)	53 (58.2)	21 (61.8)	43 (89.6)	27 (41.5)	<0.001
	<65	243 (42.3)	9 (26.5)	21 (41.2)	16 (45.7)	38 (41.8)	13 (38.2)	5 (10.4)	38 (58.5)	
Gender (%)	F	349 (60.7)	23 (67.6)	30 (58.8)	23 (65.7)	60 (65.9)	20 (58.8)	26 (54.2)	40 (61.5)	0.883
	M	226 (39.3)	11 (32.4)	21 (41.2)	12 (34.3)	31 (34.1)	14 (41.2)	22 (45.8)	25 (38.5)	
Race (%)	White	434 (75.5)	22 (64.7)	40 (78.4)	16 (45.7)	56 (61.5)	21 (61.8)	36 (75.0)	41 (63.1)	<0.001
	Asian	10 (1.7)	1 (2.9)	1 (2.0)	4 (11.4)	13 (14.3)	4 (11.8)	0 (0.0)	4 (6.2)	
	Black or African American	26 (4.5)	1 (2.9)	5 (9.8)	3 (8.6)	2 (2.2)	1 (2.9)	4 (8.3)	7 (10.8)	
	Other Race	45 (7.8)	4 (11.8)	4 (7.8)	7 (20.0)	10 (11.0)	5 (14.7)	4 (8.3)	9 (13.8)	
	Missing	60 (10.4)	6 (17.6)	1 (2.0)	5 (14.3)	10 (11.0)	3 (8.8)	4 (8.3)	4 (6.2)	
Smoking History (%)	No history of smoking	40 (7.0)	12 (35.3)	1 (2.0)	26 (74.3)	49 (53.8)	21 (61.8)	19 (39.6)	36 (55.4)	<0.001
	History of smoking	533 (93.0)	22 (64.7)	49 (98.0)	9 (25.7)	42 (46.2)	13 (38.2)	29 (60.4)	29 (44.6)	
Histology (%)	Non-squamous cell carcinoma	507 (88.2)	32 (94.1)	46 (90.2)	33 (94.3)	81 (89.0)	31 (91.2)	39 (81.2)	61 (93.8)	0.888
	Squamous cell carcinoma	47 (8.2)	1 (2.9)	4 (7.8)	2 (5.7)	7 (7.7)	2 (5.9)	6 (12.5)	3 (4.6)	
	NSCLC histology NOS	21 (3.7)	1 (2.9)	1 (2.0)	0 (0.0)	3 (3.3)	1 (2.9)	3 (6.2)	1 (1.5)	
ECOG at 1st Chemo (%)	0-1	346 (60.2)	21 (61.8)	26 (51.0)	17 (48.6)	48 (52.7)	20 (58.8)	27 (56.2)	33 (50.8)	0.168
	>=2	65 (11.3)	3 (8.8)	12 (23.5)	3 (8.6)	12 (13.2)	0 (0.0)	6 (12.5)	8 (12.3)	
	Missing	164 (28.5)	10 (29.4)	13 (25.5)	15 (42.9)	31 (34.1)	14 (41.2)	15 (31.2)	24 (36.9)	
Prior TKI Used (%)	No	567 (98.6)	32 (94.1)	48 (94.1)	34 (97.1)	57 (62.6)	28 (82.4)	46 (95.8)	62 (95.4)	<0.001
	Yes	8 (1.4)	2 (5.9)	3 (5.9)	1 (2.9)	34 (37.4)	6 (17.6)	2 (4.2)	3 (4.6)	
PD-L1 Status (%)	Positive	49 (8.5)	1 (2.9)	2 (3.9)	0 (0.0)	3 (3.3)	3 (8.8)	6 (12.5)	5 (7.7)	0.003
	Negative	31 (5.4)	0 (0.0)	8 (15.7)	6 (17.1)	5 (5.5)	0 (0.0)	5 (10.4)	2 (3.1)	
	Unknown/Untested	495 (86.1)	33 (97.1)	41 (80.4)	29 (82.9)	83 (91.2)	31 (91.2)	37 (77.1)	58 (89.2)	
Prior Tx Lines (%)	0-1	562 (97.7)	33 (97.1)	50 (98.0)	33 (94.3)	73 (80.2)	30 (88.2)	47 (97.9)	62 (95.4)	<0.001
	>=2	13 (2.3)	1 (2.9)	1 (2.0)	2 (5.7)	18 (19.8)	4 (11.8)	1 (2.1)	3 (4.6)	
TMB before Chemo? (%)	No	158 (27.5)	8 (23.5)	10 (19.6)	10 (28.6)	22 (24.2)	13 (38.2)	10 (20.8)	21 (32.3)	0.524
	Yes	417 (72.5)	26 (76.5)	41 (80.4)	25 (71.4)	69 (75.8)	21 (61.8)	38 (79.2)	44 (67.7)	
TMB Category before Chemo (%)	<16	334 (58.1)	25 (73.5)	27 (52.9)	23 (65.7)	69 (75.8)	19 (55.9)	36 (75.0)	43 (66.2)	<0.001
	>=16	83 (14.4)	1 (2.9)	14 (27.5)	2 (5.7)	0 (0.0)	2 (5.9)	2 (4.2)	1 (1.5)	
	Missing	158 (27.5)	8 (23.5)	10 (19.6)	10 (28.6)	22 (24.2)	13 (38.2)	10 (20.8)	21 (32.3)	
TMB before 1st Chemo (median [range])		8.70 [0.00, 80.91]	2.61 [0.87, 19.14]	9.57 [0.00, 53.94]	3.48 [0.00, 27.84]	3.48 [0.00, 13.05]	2.61 [0.00, 19.14]	4.35 [0.00, 29.58]	2.07 [0.00, 24.36]	<0.001
TMB before 1st Chemo (mean (SD))		10.86 (9.84)	3.91 (3.69)	14.35 (12.85)	5.10 (6.43)	3.55 (2.92)	4.19 (5.02)	5.58 (6.34)	3.10 (3.92)	<0.001
Subsequent Tx? (%)	No	202 (35.1)	8 (23.5)	18 (35.3)	11 (31.4)	27 (29.7)	7 (20.6)	17 (35.4)	18 (27.7)	0.483
	Yes	373 (64.9)	26 (76.5)	33 (64.7)	24 (68.6)	64 (70.3)	27 (79.4)	31 (64.6)	47 (72.3)	
No. of Subsequent Tx (median [range])		1.00 [0.00, 9.00]	1.00 [0.00, 8.00]	1.00 [0.00, 7.00]	1.00 [0.00, 4.00]	1.00 [0.00, 10.00]	1.50 [0.00, 6.00]	1.00 [0.00, 4.00]	1.00 [0.00, 7.00]	0.048
No. of Subsequent Tx (mean (SD))		1.20 (1.33)	1.62 (1.84)	1.08 (1.31)	1.09 (1.01)	1.31 (1.51)	1.91 (1.62)	1.40 (1.36)	1.71 (1.74)	0.009

Supplementary Table S6. Patient characteristics for the CGDB Chemotherapy cohort.
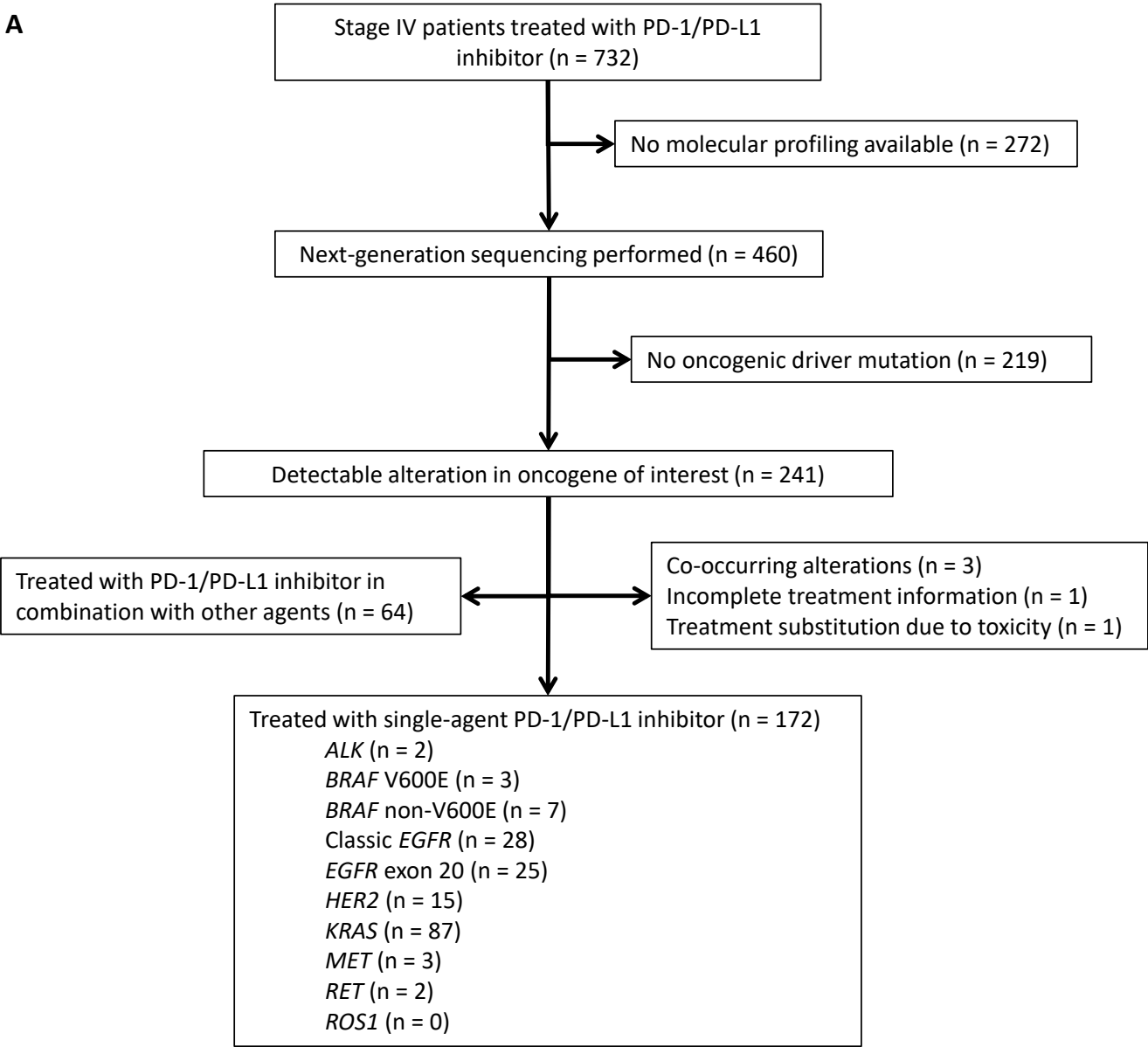PS: performance status; TKI: tyrosine kinase inhibitor

	ALK N=194	*BRAF* V600E N=118	*BRAF* non-V600E N=208	Classic *EGFR* N=732	*EGFR* Exon 20 N=166	*HER2* N=105	*KRAS* N=2240	*MET* N=145	*RET* N=54	*ROS1* N=55
TMB – median (range)	1.7 (0.0-16.2)*	3.5 (0.0-28.8)*	9.6 (0.0-72.2)*	2.6 (0.0-38.8)*	3.5 (0.0-27.8)*	2.6 (0.0-42.5)*	7.8 (0.0-67.9)	4.4 (0.0-27.0)*	2.5 (0.0-10.4)*	2.6 (0.0-44.4)*
PD-L1 ≥ 1% – N (%)	136 (70)	89 (75)	116 (56)	368 (50)**	75 (45)**	50 (48)	1384 (62)	115 (79)**	42 (78)	40 (73)
PD-L1 < 1% – N (%)	58 (30)	29 (25)	92 (44)	364 (50)**	91 (55)**	55 (52)	856 (38)	30 (21)**	12 (22)	15 (27)
PD-L1 ≥ 50% – N (%)	67 (34)	57 (48)	60 (29)	140 (19)**	33 (20)**	21 (20)**	822 (37)	80 (55)**	20 (37)	23 (42)
PD-L1 < 50% – N (%)	127 (66)	61 (52)	148 (71)	592 (81)**	133 (80)**	84 (80)**	1418 (63)	65 (45)**	34 (63)	32 (58)

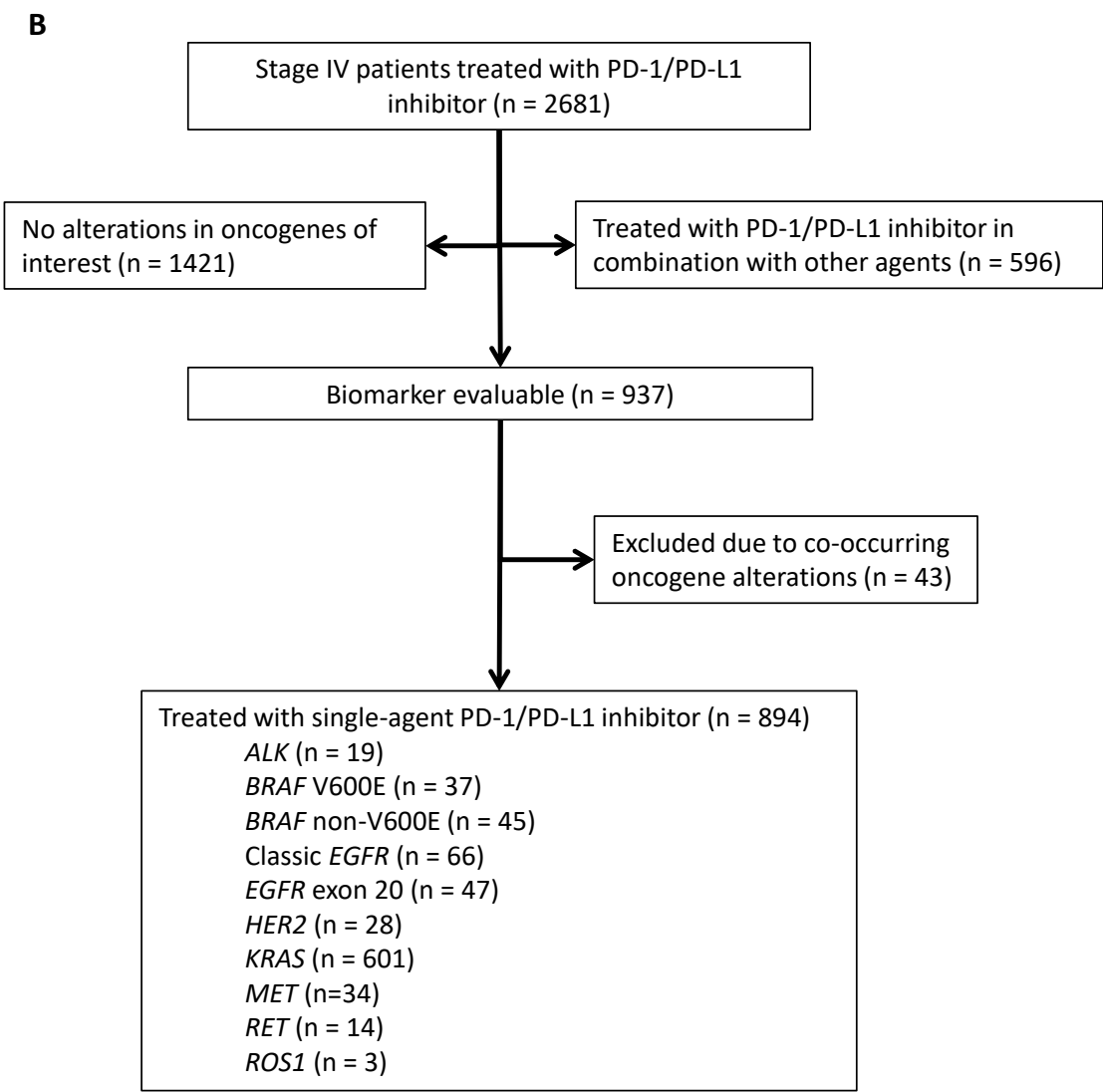**Supplementary Table S7.** Tumor mutational burden and PD-L1 status according to molecular group in the Foundation Medicine database.

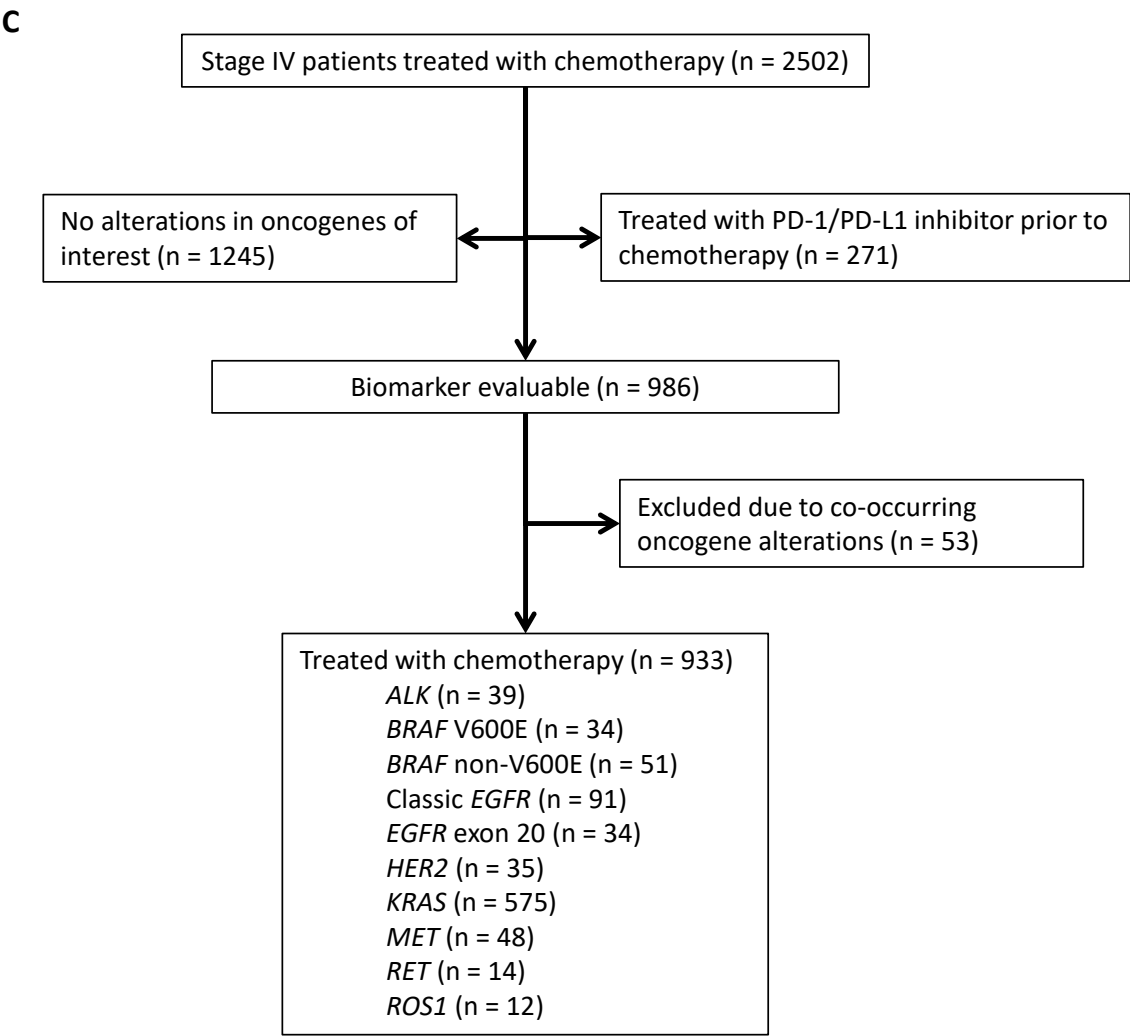TMB: tumor mutational burden; mutations/megabase.

*: adjusted p<0.01 vs *KRAS;* **: adjusted p<0.05 vs *KRAS*

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Stage IV patients treated with PD-1/PD-L1 inhibitor (n = 732)

No molecular profiling available (n = 272)

Next-generation sequencing performed (n = 460)

No oncogenic driver mutation (n = 219)

Detectable alteration in oncogene of interest (n = 241)

Treated with PD-1/PD-L1 inhibitor in combination with other agents (n = 64)

Co-occurring alterations (n = 3)
Incomplete treatment information (n = 1)
Treatment substitution due to toxicity (n = 1)

Treated with single-agent PD-1/PD-L1 inhibitor (n = 172)
       ALK (n = 2)
       BRAF V600E (n = 3)
       BRAF non-V600E (n = 7)
       Classic *EGFR* (n = 28)
       EGFR exon 20 (n = 25)
       HER2 (n = 15)
       KRAS (n = 87)
       MET (n = 3)
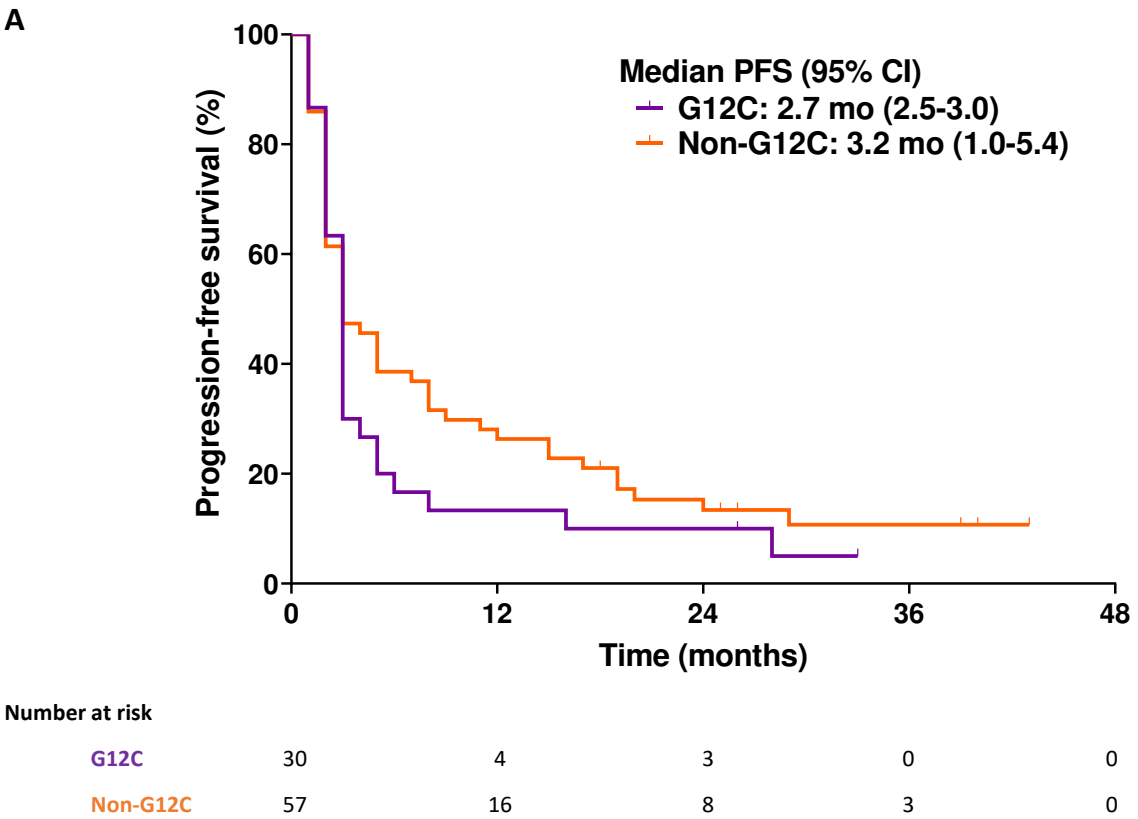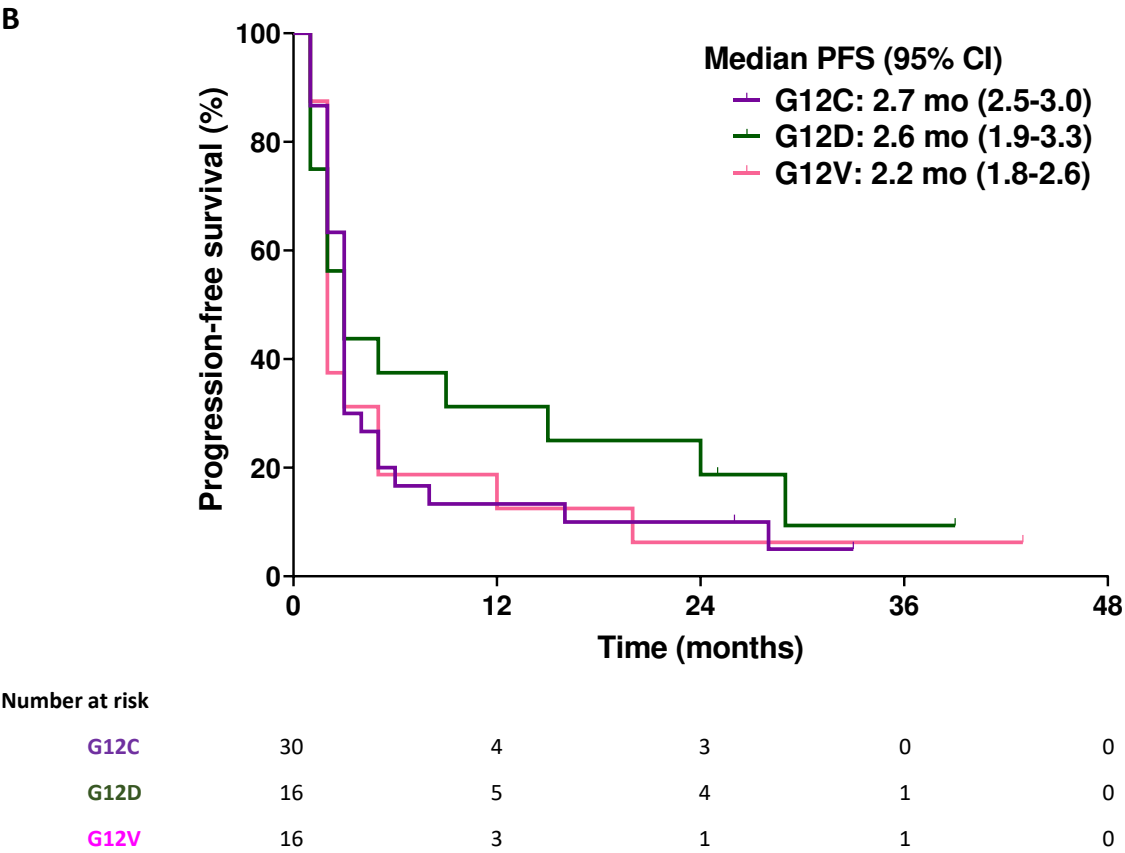   *RET* (n = 2)
       ROS1 (n = 0)

Supplementary Figure S1. Study flow diagram. **A)** MD Anderson cohort; **B)** CGDB Immunotherapy cohort; **C)** CGDB Chemotherapy cohort.

B

C

Stage IV patients treated with chemotherapy (n = 2502)

No alterations in oncogenes of interest (n = 1245)

Treated with PD-1/PD-L1 inhibitor prior to chemotherapy (n = 271)

Biomarker evaluable (n = 986)

Excluded due to co-occurring oncogene alterations (n = 53)

Treated with chemotherapy (n = 933)
  ALK (n = 39)
  BRAF V600E (n = 34)
  BRAF non-V600E (n = 51)
  Classic *EGFR* (n = 91)
  EGFR exon 20 (n = 34)
  HER2 (n = 35)
  KRAS (n = 575)
  MET (n = 48)
  RET (n = 14)
  ROS1 (n = 12)

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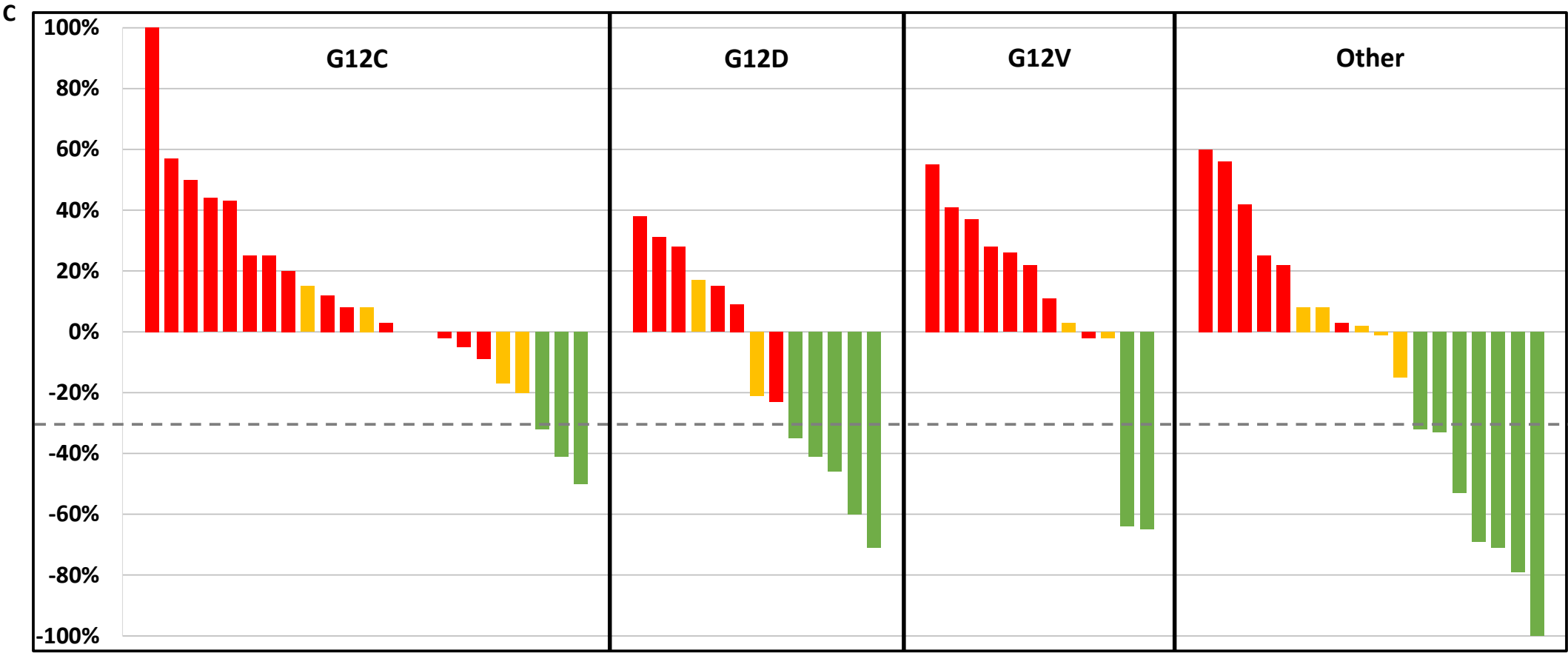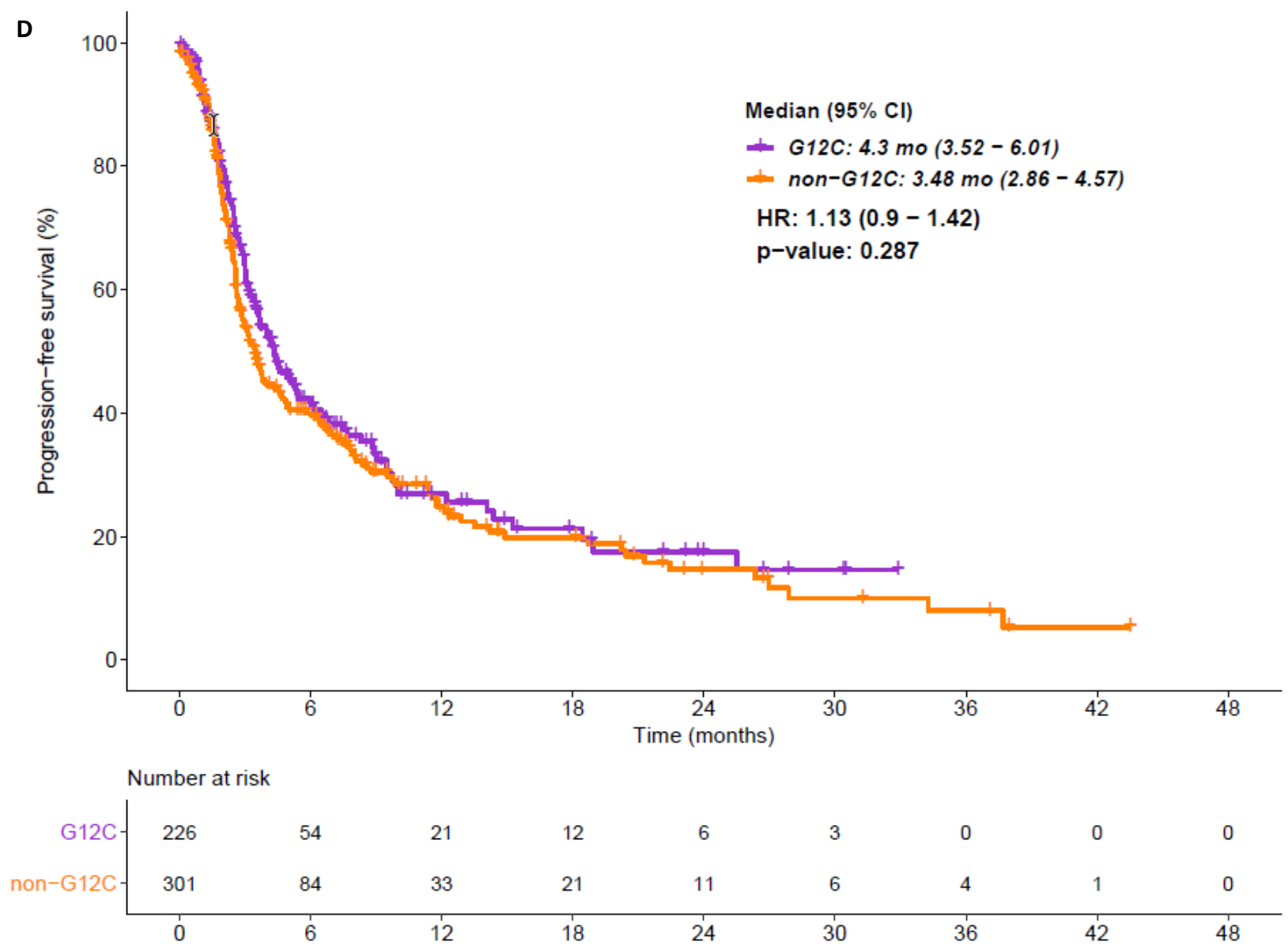
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Supplementary Figure S2. Clinical outcomes across subgroups of *KRAS*-mutant non-small cell lung cancers upon treatment with single-agent PD-1/PD-L1 immune checkpoint inhibitor. **A)** Progression-free survival in MDACC cohort for G12C vs non-G12C; **B)** Progression-free survival in MDACC cohort for G12C vs G12D vs G12V; **C)** Objective responses in the MDACC cohort; **D)** Progression-free survival in CGDB Immunotherapy cohort for G12C vs non-G12C; **E)** Progression-free survival in CGDB Immunotherapy cohort for G12C vs G12D vs G12V.

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Number at risk

G12C	30	4	3	0	0
G12D	16	5	4	1	0
G12V	16	3	1	1	0

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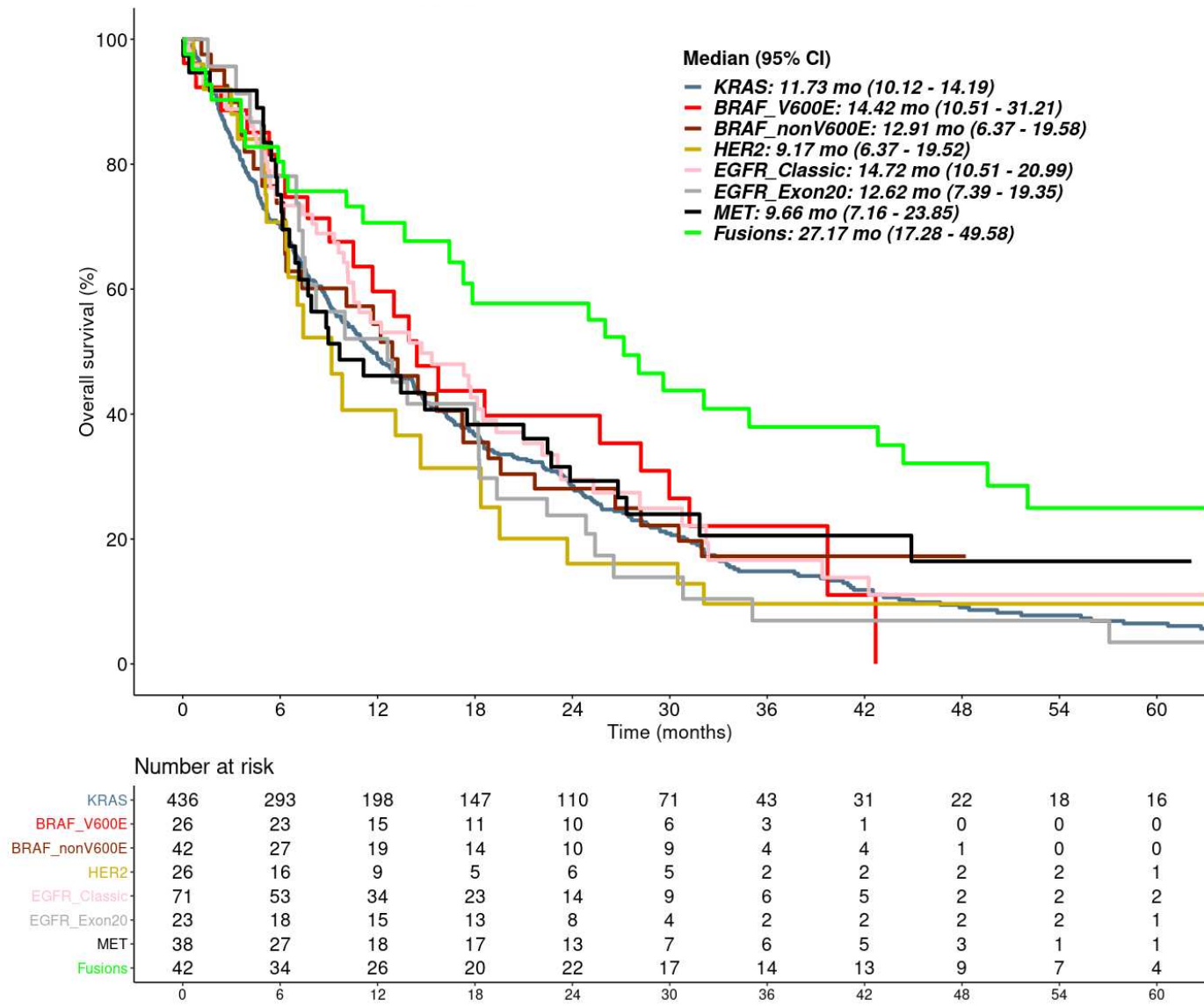
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A

Supplementary Figure S3. Clinical outcomes across different molecular groups of oncogene-driven non-small cell lung cancers in the CGDB Chemotherapy cohort. **A)** Overall survival and **B)** Progression-free survival.

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