SITC 2022

NOVEMBER 8-12 BOSTON MASSACHUSETTS

The Society for Immunotherapy of Cancer 37th Annual Meeting and Pre-Conference Programs

THE LEADING CANCER IMMUNOTHERAPY AND TUMOR IMMUNOLOGY CONFERENCE

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Outcomes following first-line immune check point inhibitors with or without chemotherapy stratified by *KRAS* mutational status – A real world analysis in patients with advanced NSCLC

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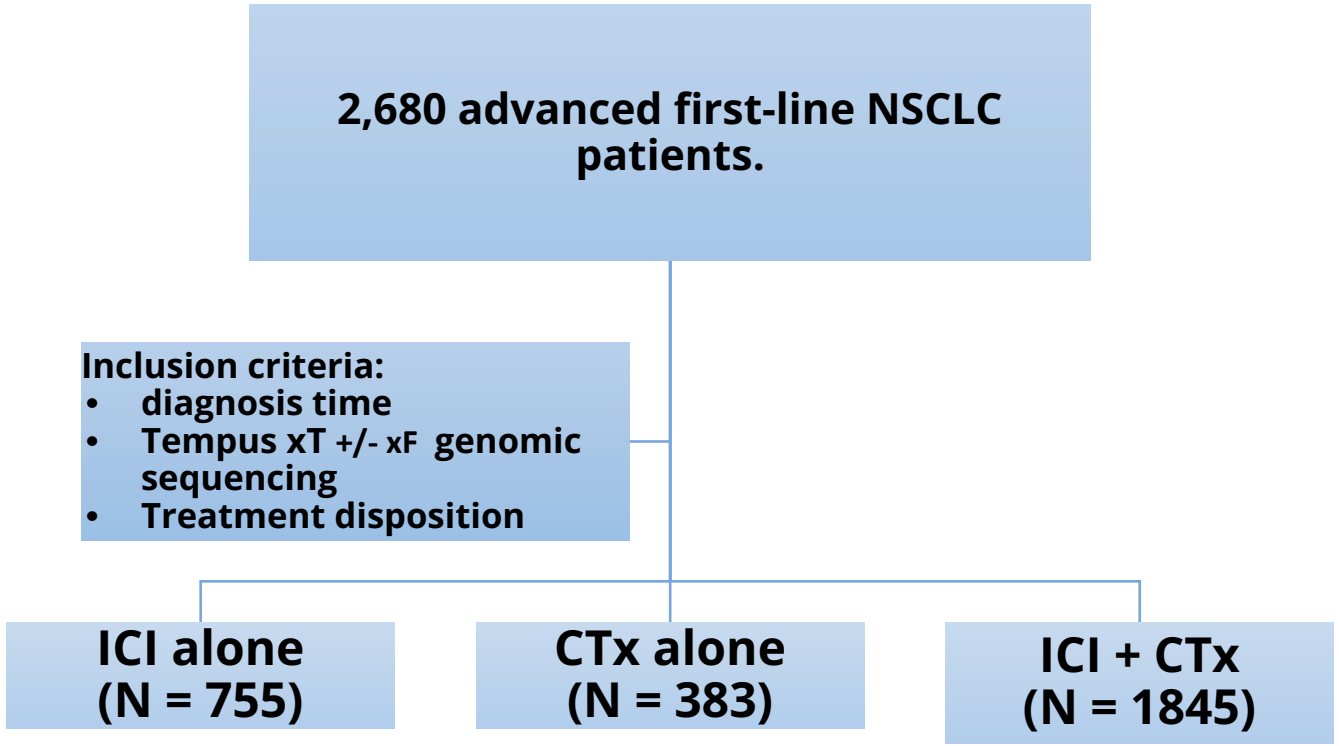
COI statement:

Current treatment of first line *KRAS* Mutated Non-Small Cell Lung Cancer (NSCLC)

- *KRAS* is the most common driver mutation, detected in approximately 30% of nonSq NSCLC
- Standard first line (1L) treatment for advanced disease is immunotherapy (ICI) +/- platinum doublet chemotherapy (CTx)
- In patients with *KRAS* mutation (mt), including G12C, a recent meta-analysis of 12 registrational trials, 1L treatment with ICI + CT demonstrated superior efficacy compared to ICI or CTx alone[1]
- We sought to determine if these findings could be duplicated in patients using Real World Evidence.

1. Nakajima, J Clin Oncol 40, 2022 (suppl 16; abstr 9001)

RWE Treatment Outcomes:
> 2000 patients with NGS from TEMPUS database



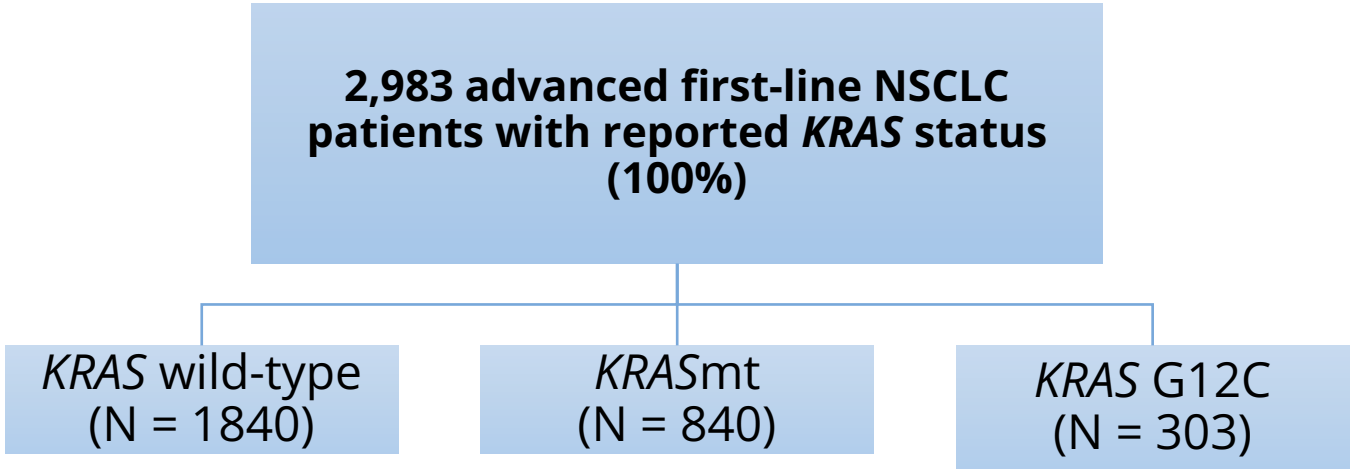
Statistical Analysis

- OS medians and 95%CI estimated with Kaplan-Meier methods

Subgroups

- *KRAS* status (wt/mt/G12C)
- PD-L1 status [High (TPS ≥ 50), Low (TPS ≥ 1-49), Negative (TPS <1)]
- Pathogenic alterations in *STK11, KEAP1,* and *TP53*

RW 1L Advanced NSCLC Cohort Prevalence: *KRAS*,PD L1



	Any *KRAS* Mutation	*KRAS* G12C	*KRAS* wild type
N, (%)	840 (31.4%)	303 (11.3%)	1840 (68.6%)
PD-L1 TPS			
<1 %	237 (28%)	69 (23%)	609 (33%)
1-49 %	230 (27%)	91 (30%)	496 (27%)
≥50%	247 (30%)	94 (31%)	369 (20%)
Unknown	126 (15%)	49 (16%)	366 (20%)

Demographic and Baseline Characteristics

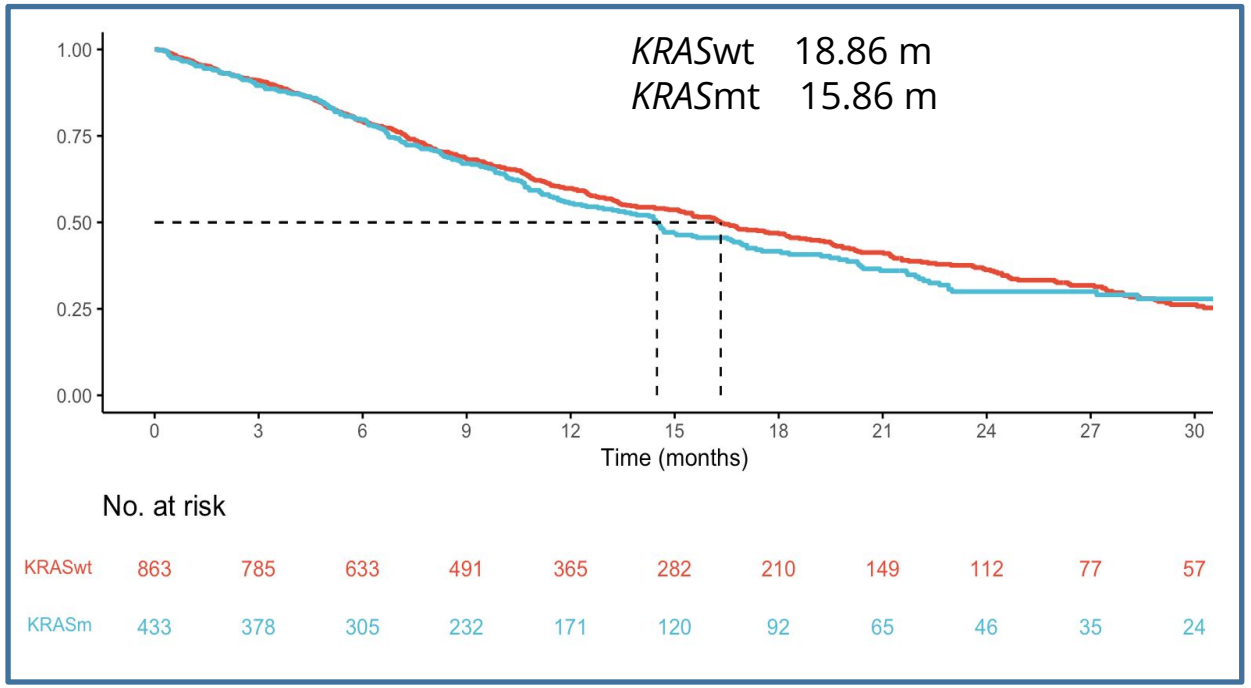
	Any *KRAS* Mutation	*KRAS* G12C	*KRAS* wild type
(n)	840 (31.4%)	303 (11.3%)	1840 (68.6%)
Sex, No. (%)			
Male	390 (46%)	127 (42%)	1,053 (57%)
Female	450 (54%)	176 (58%)	787 (43%)
Race			
White	532 (63%)	192 (63%)	1,145 (62%)
Asian	17 (2%)	5 (2%)	37 (2%)
Black	78 (9%)	28 (9%)	198 (11%)
Missing	213 (26%)	78 (26%)	460 (25%)
Histology			
Squamous	34 (4%)	4 (1%)	458 (25%)
Non-Squamous	778 (93%)	285 (94%)	1,294 (70%)
NOS	28 (3%)	14 (5%)	88 (5%)
PD-L1 TPS			
<1 %	237 (28%)	69 (23%)	609 (33%)
1-49 %	230 (27%)	91 (30%)	496 (27%)
≥50%	247 (30%)	94 (31%)	369 (20%)
Unknown	126 (15%)	49 (16%)	366 (20%)
Smoking History, No. (%)			
Never Smoker	46 (5%)	6 (2%)	241 (14%)
Former or Current Smoker	744 (89%)	279 (92%)	1,476 (80%)
Unknown	50 (6%)	18 (6%)	123 (6%)

mOS of 1L advanced NSCLC patients stratified by PDL1 and *KRAS* status

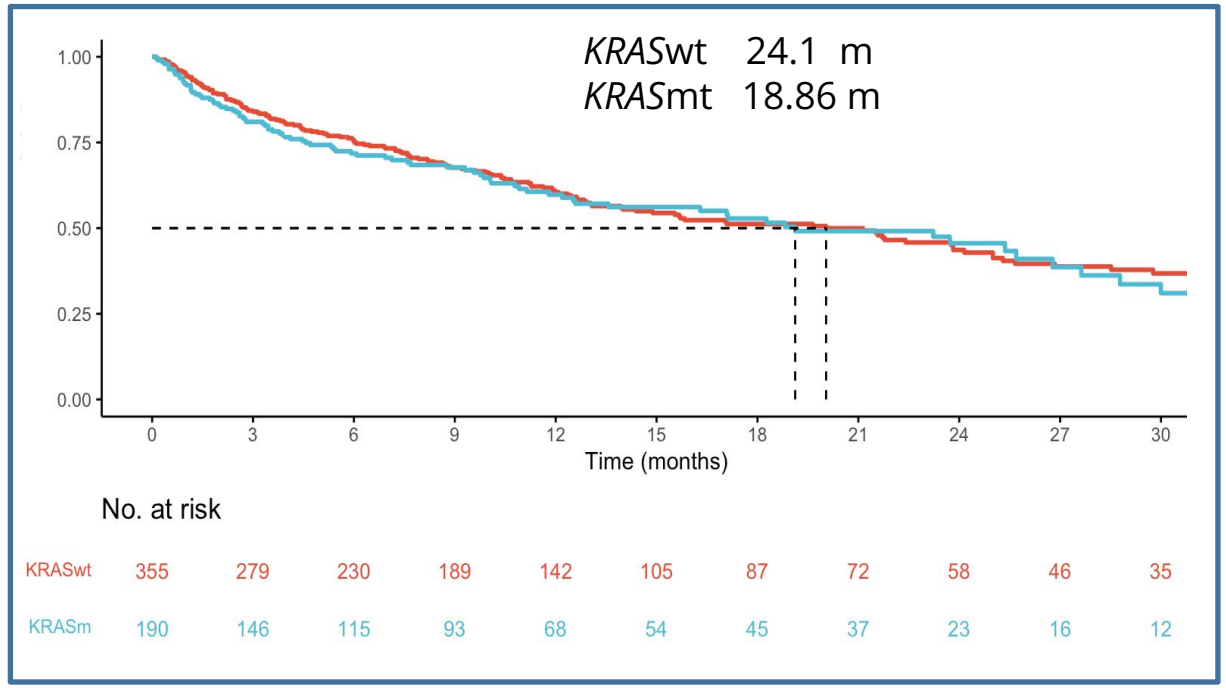
	*KRAS*wt N = 1285 Median OS (months)	*KRAS*mt N = 645 Median OS (months), Hazard Ratio (95% CI)	*KRAS* G12C N =226 Median OS (months), Hazard Ratio (95% CI)
PD-L1 >50%	24.16	27.56 0.97 (0.74 - 1.28) p = 0.87	34.8 0.81 (0.54 - 1.20) p = 0.29
PD-L1 1-49%	19.93	17.13 1.15 (0.90 - 1.46) p = 0.26	19.93 0.98 (0.69 - 1.41) p = 0.04
PD-L1 <1%	17.03	12.96 1.21 (0.98 - 1.51) p = 0.07	11.3 1.69 (1.28 - 2.35) p = 0.0017

Overall Survival: KRAS Status and Treatment Arm

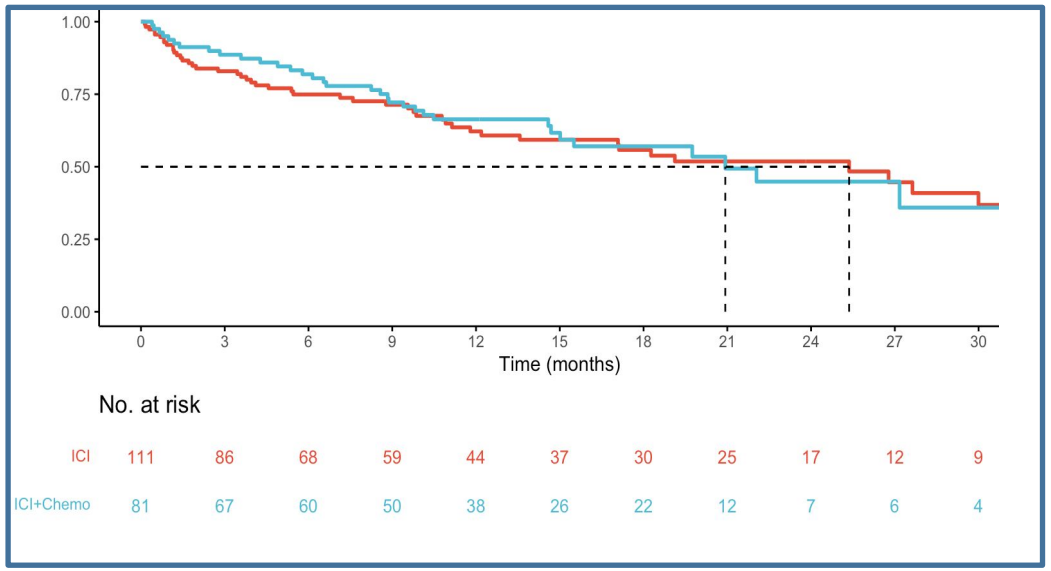
ICI + CTx



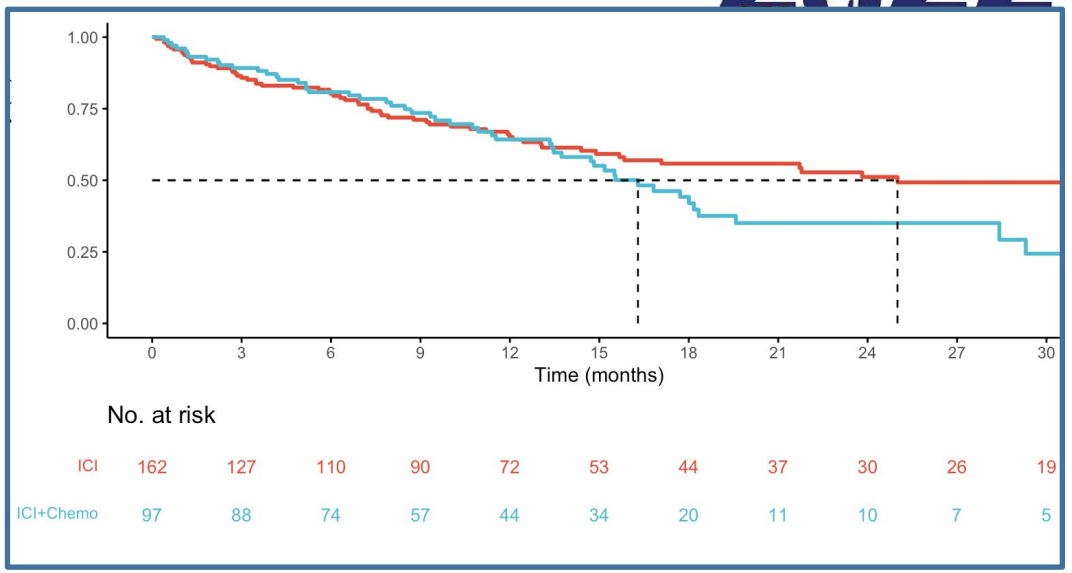
ICI Alone



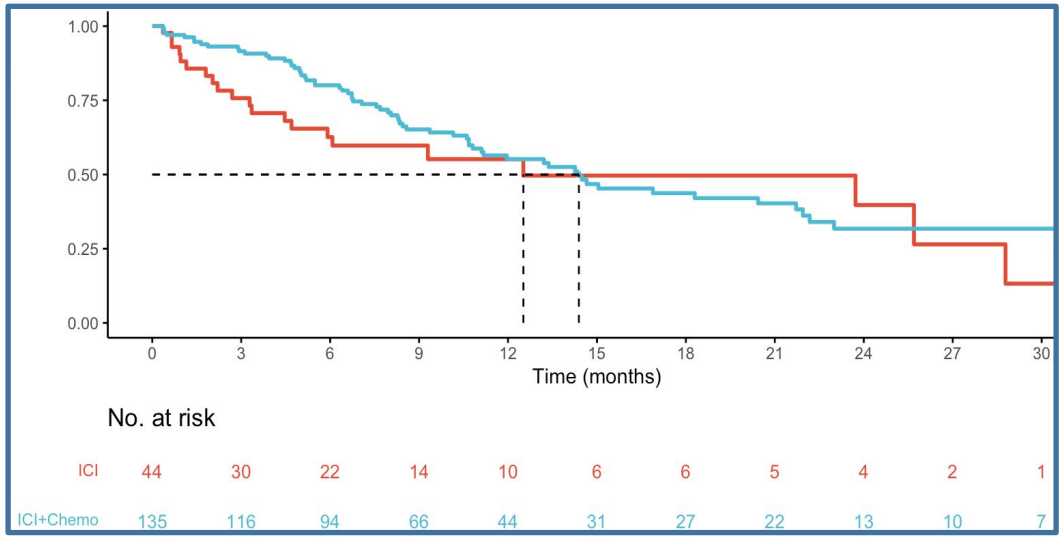
Overall Survival by PD-L1 Status



PD-L1 > 50%

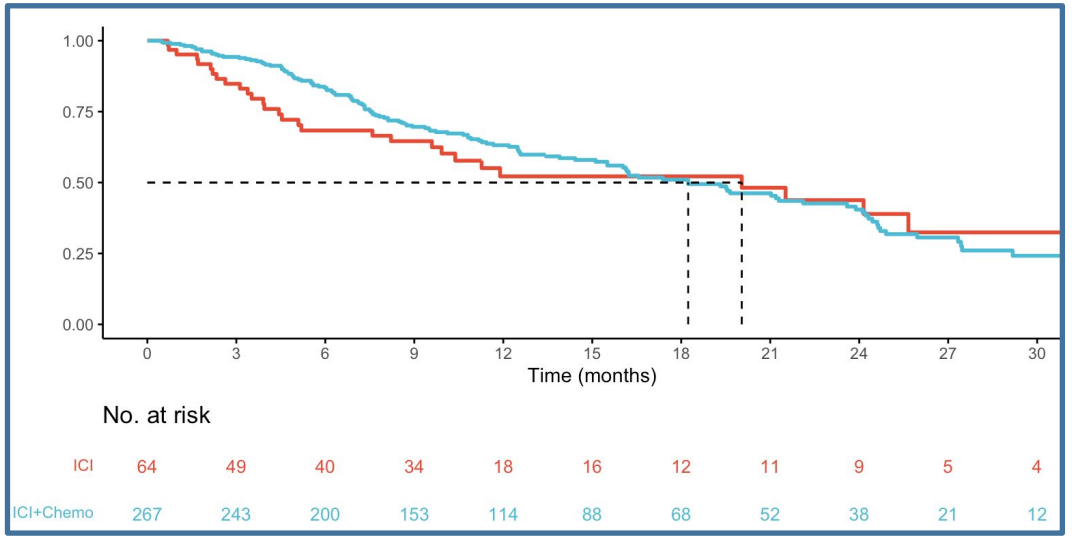


***KRAS*mt**



PD-L1 1-49%

***KRAS*wt**

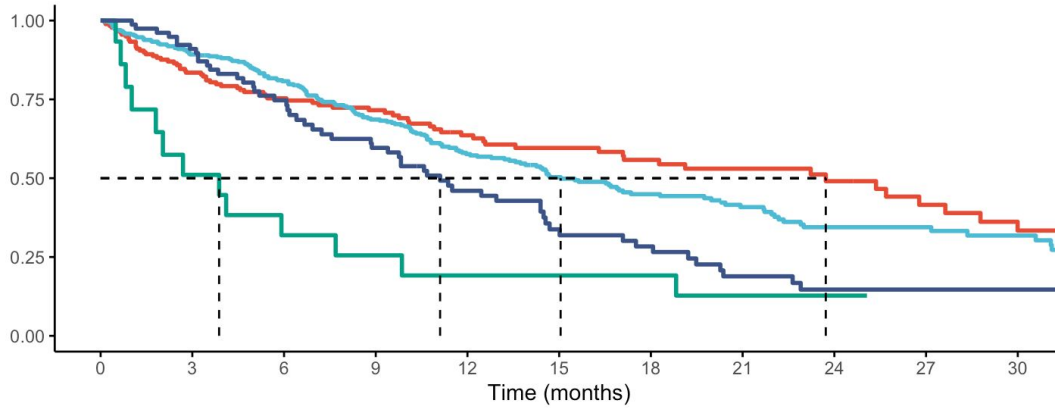


Outcomes by Co-mutational Status

Co-mutation	*KRAS*wt, N = 1285 Median OS (months)	*KRAS*mt, N = 645 Median OS (months), Hazard Ratio (95% CI)	*KRAS*G12C, N =226 Median OS (months), Hazard Ratio (95% CI)
TP53			
*TP53*mt	16.8	17.6, 0.95 (0.80 - 1.13) p = 0.575	17.76, 0.92 (0.69 - 1.22) p = 0.56
*TP53*wt	20.47	16.76, 1.18 (0.98 - 1.41) p = 0.06	18.56, 1.09 (0.84 - 1.40) p = 0.51
STK11			
*STK11*mt	15.93	11.53, 1.35 (0.99 - 1.84) p = 0.052	11.66, 1.20 (0.78 - 1.87) p = 0.4
*STK11*wt	19.2	20.26, 0.96 (0.84 - 1.10) p = 0.61	21.23, 0.92 (0.75 - 1.13) p = 0.45
KEAP1			
*KEAP1*mt	17.53	11.33, 1.26 (0.83 - 1.89) p = 0.26	9.53, 1.99 (1.08 - 3.66) p = 0.026
*KEAP1*wt	18.26	17.6, 1.02 (0.89 - 1.16) p = 0.73	20.73, 0.93 (0.77 - 1.14) p = 0.51

OS by *STK11*, *KEAP1*mt

*KRAS*mt

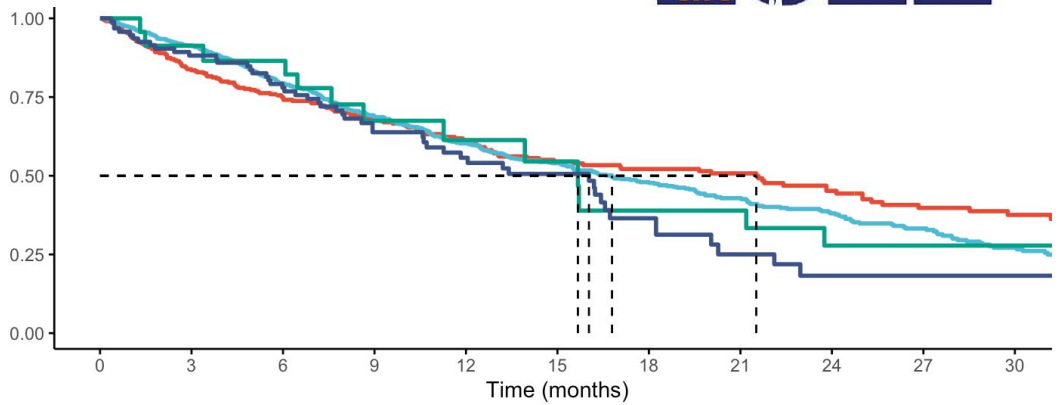


STK11

No. at risk

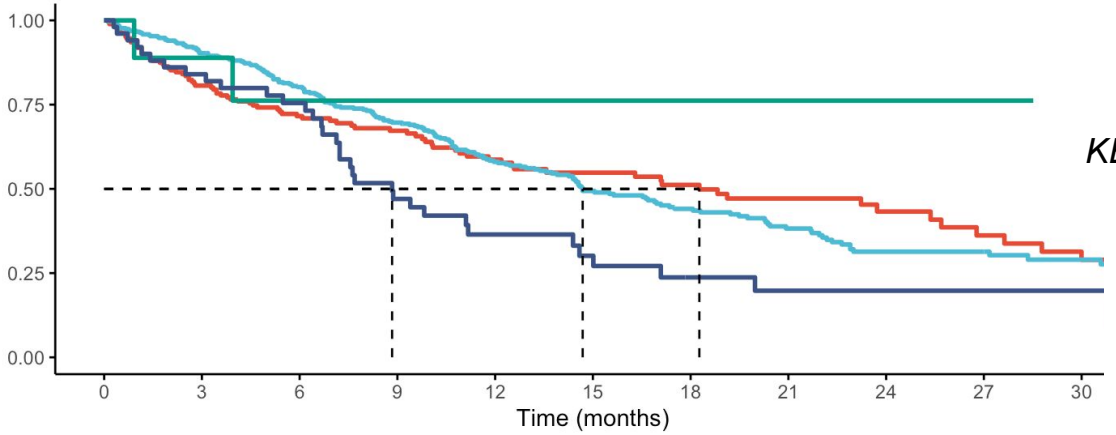
ICI STK11wt	177	138	110	89	65	51	42	36	22	16	12
ICI+Chemo STK11wt	358	308	256	190	142	102	76	56	39	31	22
ICI STK11m	15	8	5	4	3	3	3	1	1	0	0
ICI+Chemo STK11m	77	70	49	44	29	18	16	9	7	4	2

*KRAS*wt



No. at risk

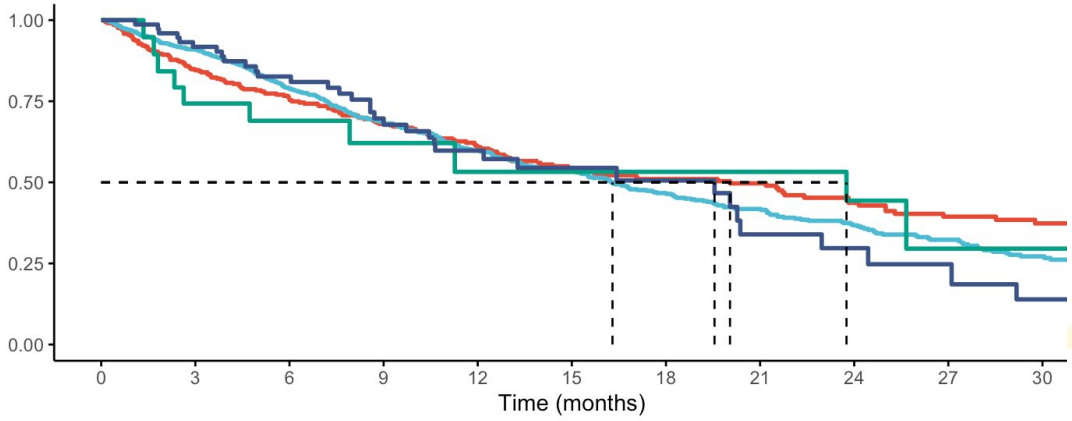
ICI STK11wt	333	260	211	176	132	98	81	66	53	42	32
ICI+Chemo STK11wt	774	706	566	448	331	259	196	141	109	75	53
ICI STK11m	23	19	20	13	10	7	8	7	5	4	3
ICI+Chemo STK11m	94	79	67	43	34	23	14	8	3	4	4



KEAP1

No. at risk

ICI KEAP1wt	182	139	109	86	62	49	40	33	20	15	12
ICI+Chemo KEAP1wt	382	337	272	212	158	110	86	60	42	32	22
ICI KEAP1m	9	7	7	7	6	5	5	4	3	1	0
ICI+Chemo KEAP1m	51	41	33	21	13	10	6	5	4	3	2



No. at risk

ICI KEAP1wt	335	264	220	179	135	99	82	67	54	45	34
ICI+Chemo KEAP1wt	790	720	584	455	342	267	196	141	106	73	54
ICI KEAP1m	21	15	11	10	7	6	6	6	4	1	1
ICI+Chemo KEAP1m	75	65	49	36	23	15	14	8	6	4	3

Conclusions

- Our analysis suggests that advanced NSCLC patients with *KRAS*mt, including *KRAS* G12C with high PD-L1, had the best outcomes when treated with 1L ICI either alone or in combination with chemotherapy.

- Outcomes were significantly worse when *STK11/KEAP1* co-mutations were present.

- This RW analysis implies that patients with *KRAS*mt NSCLC may represent a heterogeneous group requiring a tailored 1L treatment approach to account for variabilities in outcome

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Leora Horn:AZ
Nataliya Trunova:AZ
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