Real-world outcomes of first-line immune checkpoint inhibitors with or without chemotherapy in *KRAS* G12C altered NSCLC according to PD-L1 status

Abstract # 9136

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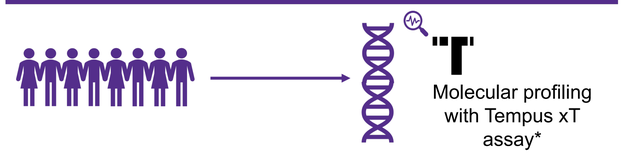
INTRODUCTION

- There is a considerable debate whether treatment approaches should be tailored in advanced *KRAS* G12C-mutated NSCLC.
- Increasing evidence suggests that *KRAS* G12C-mutated NSCLC is associated with genomic heterogeneity that may impact clinical outcomes.
- We report a multimodal, real world outcomes analysis of 1L patients with advanced *KRAS* G12C-mutated NSCLC stratified by PD-L1 status and treatment type.

METHODS



Selection criteria:
- Known PD-L1 status
- Absence of *EGFR*, *ALK* and *ROS1* mutations
- Treatment
  - chemotherapy (CT)
  - pembrolizumab (P)
  - combination therapy (CT + P)

Outcomes analysis:
Median OS (mOS) was estimated using Kaplan-Meier methods. Subgroup analyses were performed using Cox model stratified by *KRAS* G12C status, PD-L1 status, and pathogenic alterations of *STK11* and *KEAP1.*

*Tempus xT assay - a targeted panel that detects single nucleotide variants, insertions and/or deletions, and copy number variants in 598-648 genes, as well as chromosomal rearrangements in 22 genes with high sensitivity and specificity.

SUMMARY

- This study is the **largest, real-world data analysis** to date that demonstrates 1L KRAS G12C NSCLC patients with TPS < 1% and < 50% receiving standard CT + P have inferior outcomes compared to *KRAS* WT patients or those with TPS > 50%.
- TPS < 50 segments, particularly TPS < 1% are enriched for ***KRAS* G12C co-mutations with *STK11* or *KEAP1*** and are associated with poorer outcomes.

RESULTS

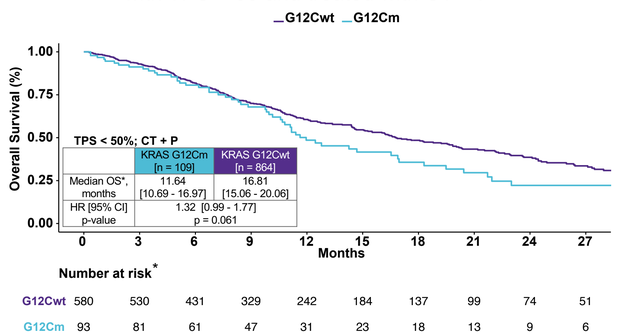
Table 1. Cohort Demographics

	***KRAS* G12Cm No. (%)**	***KRAS* G12Cwt No. (%)**
(n = 1576)	201 (12.75%)	1,375 (87.25%)
Sex		
Male	81 (40.3%)	772 (56.1%)
Female	120 (59.7%)	603 (43.9%)
Race		
White	138 (68.6%)	885 (64.4%)
Asian	4 (2%)	25 (1.8%)
Black	15 (7.5%)	145 (10.4%)
Missing	44 (21.9%)	320 (23.4%)
Histology		
Non-Squamous	186 (92.5%)	1,049 (76.3%)
Squamous	4 (2%)	269 (19.6%)
NOS	11 (5.5%)	57 (4.1%)
PD-L1 TPS		
<1 %	49 (24.4%)	527 (38.3%)
1-49 %	73 (36.3%)	441 (32.1%)
>= 50%	79 (39.3%)	407 (29.6%)
Smoking History		
Never Smoker	4 (2%)	152 (11.1%)
Former or Current Smoker	189 (94%)	1,153 (83.8%)
Unknown	8 (4%)	70 (5.1%)
***STK11* (Pathogenic)**		
Mutant	33 (16.4%)	165 (12%)
Wild-type	168 (83.6%)	1,210 (88%)
***KEAP1* (Pathogenic)**		
Mutant	17 (8.4%)	125 (9.1%)
Wild-type	184 (91.6%)	1,250 (90.9%)
***TP53* (Pathogenic)**		
Mutant	94 (46.7%)	847 (61.6%)
Wild-type	107 (53.3%)	528 (38.4%)

Table 2. Overall Survival by *KRAS* Status and Therapy Type

		CT + P		P	
		***KRAS* G12Cm**	***KRAS* G12Cwt**	***KRAS* G12Cm**	***KRAS* G12Cwt**
TPS <1	mOS (m)	11.18 (n=46)	16.44 (n=489)	16.31 (n=3)	15.71 (n=38)
	HR [95% CI] p-value	1.67 [1.12 - 2.50] p=0.01		1.57 [0.34 - 7.06] p=0.56	
TPS 1-49	mOS (m)	16.91 (n=63)	19.58 (n=375)	NA (n=10)	23.70 (n=66)
	HR [95% CI] p-value	1.12 [0.73 - 1.73] p=0.59		0.35 [0.05 - 2.69] p =0.32	
TPS <50	mOS (m)	11.64 (n=109)	16.81 (n=864)	16.31 (n=13)	15.72 (n=104)
	HR [95% CI] p-value	1.32 [0.99 - 1.77] p=0.06		0.72 [0.22 - 2.35] p=0.58	
TPS ≥50	mOS (m)	NA (n=34)	18.02 (n=171)	30.03 (n=45)	25.03 (n=236)
	HR [95% CI] p-value	0.60 [0.29 - 1.22] p=0.16		0.94 [0.54 - 1.64] p=0.83	

Figure 1. Kaplan-Meier Curve for Overall Survival of Patients with TPS < 50 and treated with CT + P



* Differences in N are due to removal of squamous histology to control for imbalances.

Table 3. Overall Survival in KRAS-altered Group Based on Co-mutational Analyses and PD-L1 Score

	***KRAS* G12Cm, N = 201**		
		STK11m	***KEAP1m***
TPS <1	N	16	10
	Mutation Prevalence	32.65%	20.41%
	mOS, months	8.89	7.23
	*HR [95% CI], p-value	HR= 2.02, p=0.05	HR=2.52, p=0.02
TPS 1-49	N	14	3
	Mutation Prevalence	19.18%	4.11%
	mOS, months	11.97	NA
	*HR [95% CI], p-value	HR=0.12, p=0.04	NA
TPS <50	N	30	13
	Mutation Prevalence	24.59%	10.66%
	mOS, months	10.59	7.63
	*HR [95% CI], p-value	HR=1.01, p=0.81	HR=2.14, p=0.03

*HR comparisons to *KRAS* G12Cwt regardless of therapy

STUDY LIMITATIONS

- This is a retrospective, real-world data analysis with a limited sample size in specific subsets.
- There may be selection biases in treatment decisions that are implemented in real-world practice that have not been adjusted for.
- Descriptive data; lacks multivariate analysis.

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