Molecular features of KRAS mutant NSCLC: weaving a future score for immune-check point inhibitors (ICI)

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Background

Retrospective trials show a tendency of higher efficacy of ICI in NSCLC KRAS mutant subgroup. If KRAS could take part as a biomarker score for ICI efficacy is still unknown.

Methods

Our group performed a retrospective analysis from all NSCLC patients with NGS analyses (Oncomine V3.0, Guardant 360, and Foundation One and Liquid).

Demographics (n= 51)	*n* (%)	Demographics (n= 51)	*n* (%)
Age	62 (43-82)	Chemotherapy	27 (53)
Gender		Unknown	7 (15)
Women	25 (49)	**Level of expression PDL1**	
Men	26 (51)	Negative <1%	16 (34)
ECOG PS		Positive ≥1%	25 (53)
0	28 (55)	PDL1 1-49%	15 (32)
1	18 (35)	PDL1 ≥50%	10 (21)
2	5 (10)	Unknown	6 (13)
Smoking status		**Lymph CD8⁺ (TILs)**	
Current	31 (61)	>25%	9 (18)
Former	17 (33)	≤ 25%	16 (31)
Never	2 (4)	Unkown	26 (51)
Unknown	1 (2)	Stage	
Histology		I-II	4 (8)
Adenocarcinome	45 (88)	III	5 (10)
Carcinoma NOS	6 (12)	IV	42 (82)
Therapy		IVA	18 (43)
Chemo-ImmunoT	13 (26)	IVB	21 (57)
Immunotherapy	3 (6)		***Table 1***

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Results

We identified 51 patients from 201 NSCLC, with KRAS mutation through NGS (25.4%), 53% had PDL1 >1%. High CD8 T Cell infiltration was detected in 18%. *(Table 1)*

KRAS most frequent mutations detected were G12C (43,9%) and G12D (17,1%).

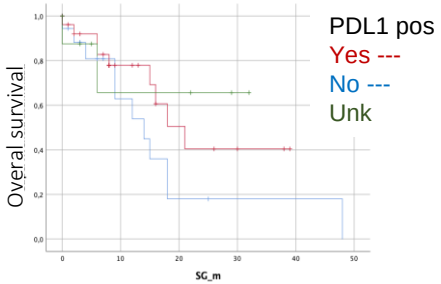
Most KRAS G12C, had PDL1 positive (69%) , 25% had PDL1 >=50% and 25% had high TILs.

KP group showed an immune phenotype respect KL group (*Table* 2)

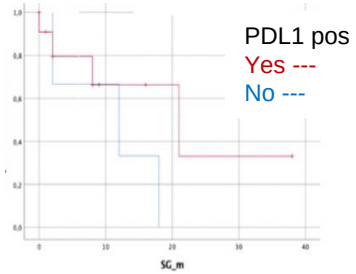
Table 2	Total KRAS *n* (%)	CD8>25 *n* (%)	PDL1	
			≥1%	≥50%
KP group (co-TP53)	19(29)	2 **(25)**	12**(80)**	6**(40)**
KL group (co-STKL11)	6 (9.7)	0 **(0)**	1 **(20)**	0 **(0)**

KRAS*mut* and PDL1 positive, showed better mOS respect PDL1 negative (21 vs 14 months, p= 0,25). Those with PDL1 >=50%, reached median survival of 39 month:

KRAS



KRAS + TP53

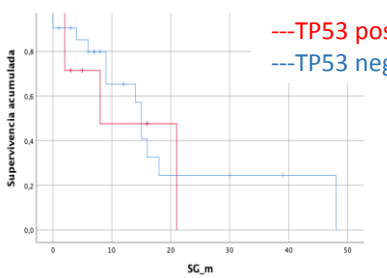


Patients KRAS*mut* and PDL1 negative, obtained similar low survival rates regardless of treatment (OS 15%).

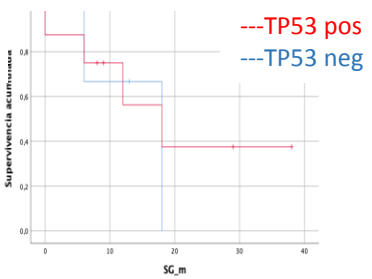
KP group and PDL1 positive showed mOS 21 *vs* 12 months when PDL1 is negative.

Treatment with ICI resulted in better survival respect chemotherapy, irrespective PDL1, in TP53 positive (KP group).

KP group: Chemotherapy

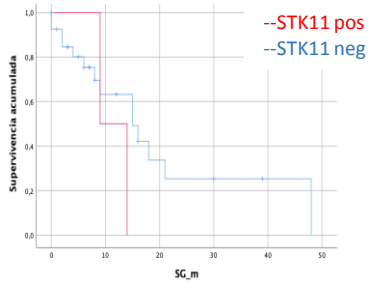


KP group: Chemo-ICI

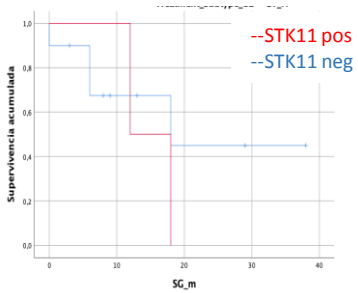


KL group had lower survival respect to STK11wt (17 vs 24,8months). Treatment did not affect survival (mOS 10m for any treatment)

KL group: Chemotherapy



KL group: Chemo-ICI



CONCLUSIONS:

KP group shows an immune phenotype. Therapies with ICI shows better survival in KP group and PDL1 positive.

KL group is a challenging group without real ICI efficacy and results from KRAS inhibitors early trials have shown major benefit in this group.

Our study shows a potential molecular score to select treatment. A wider sample is expected to support this observation.

AUTHOR HAVE NOT DISCLOSURES