Molecular characterization of KRAS NSCLC all stages: a single-center cohort

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BACKGROUND

Kirsten rat sarcoma viral oncogene mutation (KRASm) is detected in approximately 25% of non-small cell lung cancer (NSCLC) adenocarcinoma patients. As Next-generation sequencing (NGS) has been increasingly employed, diverse KRASm subtypes with different prognoses, incidences of co-mutations and characteristics have been described.

METHODS

We performed NGS to all stages NSCLC patients from 2019 to 2021. Tissue genotyping was performed through Illumina Focus, a 52 genes targeted NGS panel that simultaneously analyzes DNA and RNA alterations. In addition, a single test for rearrangement assessment was done in necessary cases. Programmed death ligand-1 (PD-L1) expression was tested by SP263 antibody. We analyzed the clinical and pathological characteristics of KRASm patients.

RESULTS

A total of 62 from 123 patients had KRASm. Median age was 67 years [49-92], 79% were male, 87.1% adenocarcinomas, and only 8.1% non-smokers. In 19.4% of patients, NGS was sufficient for molecular characterization, but in 75.8% a single molecular test had to be added. KRASm subtypes in our cohort were: G12C (33.9%), G12V (25.8%), G12D (21%) and Q61H (6.5%).

Table 1: Baseline characteristics of patients

Age (years)	67 [49-92]
Sex	
Men	49 (79%)
Women	13 (21%)
Ethnic origin	
Caucasian	61 (98.4%)
Black	1 (1.6%)
ECOG	
0	15 (24.2%)
1	31 (50%)
2	9 (14.5%)
3	7 (11.3%)
Smoking habit	
Yes	57 (91.9%)
No	5 (8.1%)
Histological subtype	
Adenocarcinoma	54 (87.1%)
Squamous	1 (1.6%)
Others	7 (11.3%)
Clinical stage	
I-II	15 (24.2%)
III	7 (11.3%)
IV	40 (64.5%)
Molecular evaluation	
NGS	12 (19.4%)
NGS + Single test	47 (75.8%)
Single test	3 (4.8%)
Evaluation PD-L1 expression	
Yes	61 (98.5%)
No	1 (1.6%)

Figure 1: Percentage of each KRAS subtype

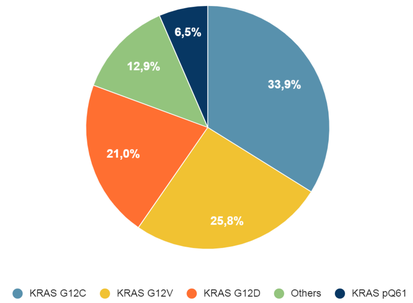

Table 2: characteristics of patients according to the KRAS subtype

	G12C (n=21)	G12V (n=16)	G12D (n=13)	Q61H (n=4)	Others (n=8)
Clinical stage					
I-II	3 (14.3%)	2 (12.6%)	6 (46.2%)	2 (50%)	2 (25%)
III	2 (9.5%)	1 (6.3%)	1 (7.7%)	1 (25%)	2 (25%)
IV	16 (76.2%)	13 (81.3%)	6 (46.2%)	1 (25%)	4 (50%)
PD-L1 expression ≥1					
Yes	5 (23.8%)	7 (43.8%)	5 (38.5%)	2 (50%)	4 (50%)
No	16 (76.2%)	9 (56.3%)	7 (53.8%)	2 (50%)	4 (50%)
Co-mutation					
Yes	5 (23.8%)	6 (37.5%)	1 (7.7%)	2 (50%)	2 (25%)
No	16 (76.2%)	10 (62.5%)	12 (92.3%)	2 (50%)	6 (75%)
	1 BRAF mutation not V600E 2 RET rearrangements 1 FGFR2 mutation 1 PI3KCA mutation	1 EGFR mutation 1 PDGFRA mutation 1 PIK3CA mutation 1 JAK2 mutation 1 C-KIT mutation 1 NRAS mutation	1 KRAS co-mutation	1 ERBB2 + MAP2KI co-mutation 1 mTOR mutation	

Figure 2: Relationship between KRAS subtype and clinical stage (2A), presence of metastasis (2B), PD-L1 expression (2C), presence of co-mutation (2D).

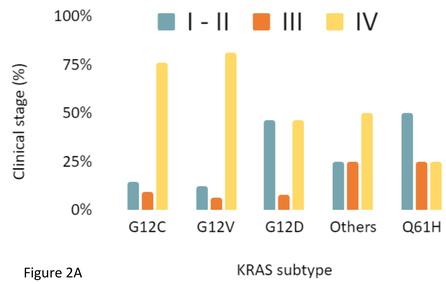

Figure 2A

KRAS subtype	Clinical stage		
	E I - II	E III	E IV
G12C	3	2	16
G12V	2	1	13
G12D	6	1	6
Others	2	2	4
Q61H	2	1	1
Total patients	15	7	40

p = 0,04

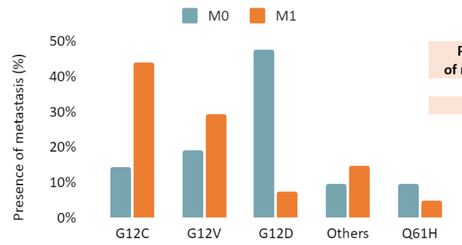

Figure 2B

Presence of metastasis	KRAS subtype					Total patients
	G12C	G12V	G12D	Others	Q61H	62
M0	3	4	10	2	2	21
M1	18	12	3	6	2	41

p = 0,004

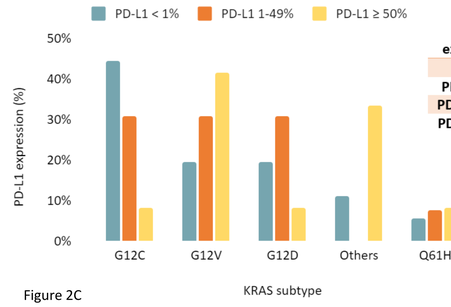

Figure 2C

PD-L1 expression	KRAS subtype					Total patients
	G12C	G12V	G12D	Others	Q61H	61
PD-L1 < 1%	16	7	7	4	2	36
PD-L1 1-49%	4	4	4	0	1	13
PD-L1 ≥ 50%	1	5	1	4	1	12

p = 0,16

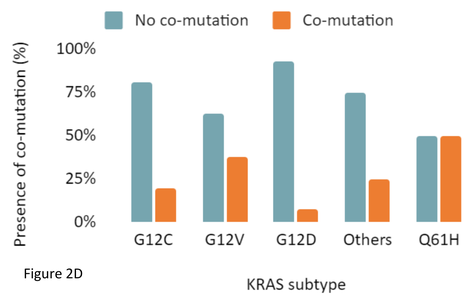

Figure 2D

KRAS subtype	Co-mutation	
	Absence	Presence
G12C	17	4
G12V	10	6
G12D	12	1
Others	6	2
Q61H	2	2
Total patients	47	15

p = 0,26

Figure 3: Overall survival according to the KRAS subtype (3A), PD-L1 expresión (3B) and presence of co-mutation (3C).

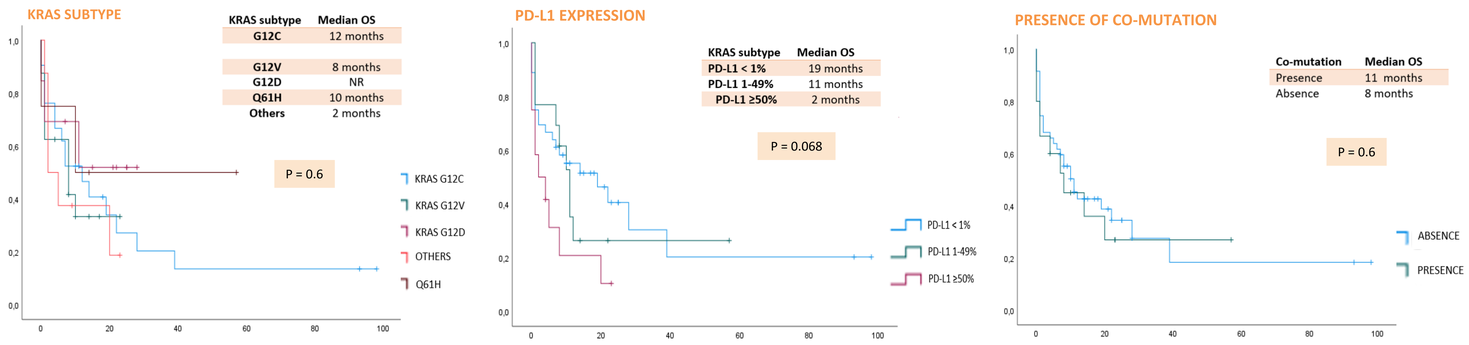

Figure 3A Figure 3B Figure 3C

REFERENCES

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2. M. Drosten, et al. Targeting KRAS mutant lung cancer: light at the end of the tunnel. Molecular Oncology 16 (2022) 1057–1071.

CONCLUSIONS

Our results suggest the importance of knowing the KRAS status and its subtype in NSCLC. This is necessary in metastatic patients but also in the early stages, taking into account the relationship observed between the subtype and the risk of metastasis. PD-L1 status could be a prognostic factor in KRASm patients, but more investigations are required.

E: Clinical stage; KRAS: Kirsten rat sarcoma viral oncogene; M1: presence of metastasis; M0: absence of metastasis; PD-L1: Programmed death-ligand 1;NR: not reached; OS: Overall survival

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Poster 79P

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