102P

Clinical Analysis of Patients With Different KRAS Mutations in NSCLC: Different Entities Analyzed by NGS

J. Rubio[1], M. Fernández-Ochoa[1], M.Avedillo[1], P. Villalba[1],C. Santolaya[1], S.Zazo[2], F. Rojo[2], M. Domine[1]

1. Department of Medical Oncology, University Hospital Fundación Jiménez Díaz (FJD), Madrid 28020, Spain; 2. Department of Pathology, University Hospital Fundación Jiménez Díaz (FJD), Madrid 28020, Spain.

BACKGROUND

KRAS mutation is the most common molecular alteration in non-small cell lung cancer (NSCLC), in particular in adenocarcinoma can be found in 25% of the patients. But KRAS mutations represent different heterogeneous diseases not well characterized. This can be explained because of the genomic commutations or because the type of point mutation may affect downstream signaling differently, which may translate into different clinical features and outcomes.

Due to the recent discovery of several effective KRAS G12C inhibitors, interest in this type of mutation is on the rise. According to the literature KRAS G12C represents almost 35% of patients with KRAS mutation, but there are few specific data presented in our population.

METHODS

We selected patients diagnosed with KRAS mutation non-small cell lung carcinoma (NSCLC) from February 2021 to March 2022 from 4 hospitals in Madrid (most of them from Fundación Jimenez Diaz University Hospital). KRAS status was determinated by using the AVENIO Tumor Tissue Targeted Kit ® (a Next Generation Sequencing test). PD-L1 status was determinated by immunohistochemistry assay (22C3 pharmDx). Molecular and clinicopathological characteristics were collected and we performed a descriptive analysis of our population.

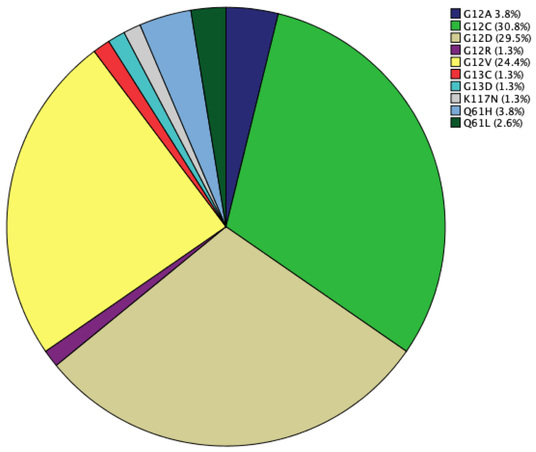
CONCLUSION

RESULTS

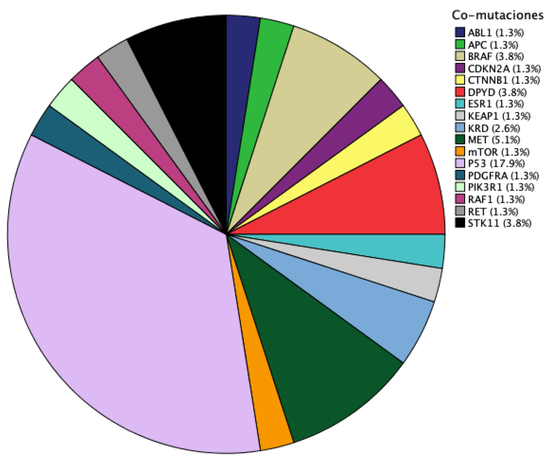
A total of 78 patients were included in this study with a KRAS mutation. Almost 45% were stage IV, with 20% stage III and 35% stages I and II.
Most tumors were adenocarcinomas (88%), followed by squamous carcinomas (8%) and the rest other histologies or mixed tumors.
One third of the patients were KRAS G12C, one third G12D and 25% G12V, followed by others much less frequent such as G12A or Q61H (3.8%).
KRAS G12D is more frequent in the metastatic patient, being the most frequent mutation (40%) followed by G12C (25%) and G12V (22.8%).
PD-L1 status was very similar independent of mutation subtype, being ≥ 50% in 45.8% of KRAS G12C and 42.6% in KRAS non-G12C and <1% in 29.2% of KRAS G12C and 31.5% in KRAS G12C.
34.6% of the patients had one or more co-mutations.
The most frequent mutation was TP53 in 37% of patients, followed by others around 10% such as MET, STK11, DPYD, PI3K or BRAF mutations.

PATIENTS CHARACTERISTICS	
Gender	
Male	50 (64.1%)
Female	28 (35.9%)
ECOG	
0-1	77 (93.6%)
≥ 2	5 (6.4%)
Smoking status	
Never	5 (6.4%)
Smoker	31 (39%)
Former smoker	42 (53.8)
Stage	
I-II	27 (34.6%)
III-IV	51 (65.4%)
PD-L1 status (%)	
<1	24 (30.8%)
1-49	20 (25.6%)
≥ 50	34 (43.6%)
Histology	
Adenocarcinoma	69 (88.5%)
Squamous	6 (7.7%)
Other	3 (3.8%)

KRAS subtype mutation



KRAS Co-mutations



As described in the Caucasian population, KRAS G12C accounts for one third of the KRAS mutations in our patients, being susceptible to new treatments. This mutation is more frequent in early stages, being the most frequent KRAS G12D in metastatic patients. The proportion of high PD-L1 is similar in all high prevalence mutations.

No conflicts of interest to declare - *Correspondance to Jaime Rubio, MD, PhD:* **jrubioperez05@gmail.com**