Real-World Patient Characteristics and Treatment Patterns in previously treated Non-Small Cell Lung Cancer (NSCLC) Patients with KRAS p.G12C Mutant Tumors in Italy

Malapelle U[1], Giannopoulou A[2], Moscetti A[3], Laino V[3], Passiglia F[4]

[1]University of Naples Federico II, Naples, Italy, [2]Amgen (Europe) GmbH, Rotkreuz, ZG, Switzerland, [3]Amgen SRL, Milan, Italy, [4]San Luigi Gonzaga University Hospital, Orbassano, Italy

BACKGROUND

Inhibition of KRAS, and particularly mutant KRAS p.G12C, has been the focus of extensive research in NSCLC but information on what is these patients' clinical profile and how they are managed in the real-world setting in Italy is limited.

OBJECTIVES

This study aimed to describe the clinical characteristics and treatment patterns in patients with locally advanced and unresectable or metastatic KRAS p.G12C mutant NSCLC in the real-world setting in Italy.

METHODS

- Annually updated Italian Cancerology NSCLC database
- 40 oncologists in general/non-university (65%),university hospitals (25%) and other sites (7.5% oncology reference centers; 2.5% private hospital/clinic)
- Retrospective medical chart data extracted for patients selected consecutively in reverse chronological order of visits
- Data fully anonymized
- **Patient inclusion criteria:**
  - adult NSCLC patients with KRAS p.G12C mutant tumors
  - without other onco-driver mutations (i.e. EGFR, ALK,ROS-1, BRAF, MET, RET, NTRK)
  - receiving or having discontinued their second (2L) or later lines of anti-tumor systemic treatment ('index line') during July 1st to December 31st, 2019 ('index period')
- **Patient exclusion criteria:**
  - receipt of index treatment as part of an interventional trial or an early access program
  - KRAS status unknown.

RESULTS

- A total of 136 patients with a KRAS p.G12C mutation were included in the analysis, among which the majority in 2L (n=130/136). Their demographic and clinical characteristics are presented in Table 1.
- The mean time from diagnosis of locally advanced and unresectable or metastatic disease (stage IIIB/C or IV) to inclusion in the study was 20.5 months (SD: 6.6 months).
- During the study index period, most patients had completed their index treatment line (53%) and were alive (73%) (Table 2).
- The most commonly used 2L regimen was an anti-PD-L1 monotherapy(59%; 66% nivolumab, 22% pembrolizumab, 12% atezolizumab), followed by chemotherapy (32%; 12% docetaxel monotherapy) (Figure 1). Prior (1L) treatment included chemotherapy (88%) and much less commonly anti-PD-L1 as monotherapy (6%) or combined with chemotherapy (3%) (Figure 2).

Figure 1. Distribution of therapies received in index 2L

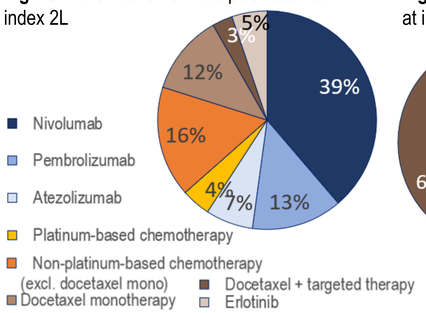

Figure 2. Exposure to prior therapy (1L), for patients at index 2L

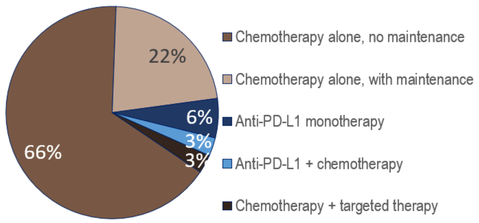

Table 2. Patients' status during index period

	Overall N= 136	Index 2L N= 130	Index 3L N= 6
Treatment status at index (%)			
Ongoing	47%	47%	52%
Completed	53%	53%	48%
Patient status upon study inclusion (%)			
Still alive	73%	74%	52%
Deceased	23%	21%	48%
Lost to follow-up	4%	5%	0%

Table 1. Demographic and clinical characteristics of patients with *KRAS* p.G12C mutant tumors included

	Overall N= 136	Index 2L N= 130	Index 3L N= 6
Age, years (mean, SD)	67.4 (6.7)	67.3 (6.8)	68.7 (3.5)
Age groups (%)			
<65	30%	31%	15%
65-74	57%	55%	85%
75-84	13%	14%	0%
Gender, male (%)	70%	70%	85%
BMI, kg/m² (mean, SD)	24.8 (2.6)	24.8 (2.6)	24.3 (1.5)
Smoking history, ever-smoker (%)	81%	80%	100%
Treated at out-patient setting (%)	95%	95%	100%
Number of comorbidities at index period (%)			
0	16%	16%	15%
1	57%	58%	33%
2	20%	20%	31%
3	6%	6%	22%
4+	1%	2%	0%
CCI score (%)			
0	24%	23%	36%
1	42%	41%	49%
2+	35%	36%	15%
Type of comorbidity (%)			
COPD/Pulmonary	29%	29%	48%
CV-related	24%	25%	
Other	21%	20%	38%
Diabetes	20%	20%	31%
Hepatic disease	10%	10%	10%
Renal disease	6%	7%	0%
Immune systemic	3%	3%	0%
GI-related	1%	1%	0%
None	16%	16%	15%
Disease stage at primary diagnosis of NSCLC (%)			
I or II	6%	6%	
IIIA	6%	5%	16%
IIIB or IIIC	2%	3%	
IV	85%	85%	84%
Missing	1%	1%	

Table 1. (continued)

	Overall N= 136	Index 2L N= 130	Index 3L N= 6
Disease stage at index line (%)			
Locally advanced and unresectable (IIIB/IIIC)	8%	8%	0%
Metastatic (IV)	92%	92%	100%
Histology (%)			
Squamous	16%	16%	
Non-squamous			
Adenocarcinoma	77%	76%	100.00%
Bronchioalveolar	3%	3%	0%
Large-cell	3%	4%	0%
Other non-squamous	1%	1%	0%
ECOG PS (%)			
0	29%	29%	15%
1	57%	57%	52%
2+	14%	14%	33%
PD-L1 expression level (%)			
<1%	13%	13%	23%
1% - <50%	69%	70%	45%
50%-100%	13%	13%	15%
Not tested	5%	4%	19%
Metastasis location at index line (%)			
Lymph node or bone only	4%	4%	0%
Visceral +/- bone (no brain)*	76%	77%	67%
Brain +/- visceral +/- bone	13%	11%	33%
No distant metastasis (*locally advanced unresectable patients*)	8%	8%	0%

BMI= Body mass index; **CCI=** Charlson comorbidity index; **COPD=** Chronic obstructive pulmonary disease; **CV=** cardiovascular; **ECOG PS=** Eastern Cooperative Oncology Group Performance Status; **GI=** Gastrointestinal; **PD-L1=** Programmed death-ligand 1; **SD=** Standard deviation

CONCLUSIONS

- This study provides a descriptive summary of the clinical-pathological characteristics and the treatment patterns of NSCLC patients with KRAS p.G12C mutant tumors in the Italian real-world setting.
- In 2019, the studied real-world 2L patients with advanced KRAS p.G12C NSCLC received primarily anti-PD-L1 monotherapy, after exposure to chemotherapy in 1L, reflecting the treatment choices common for that period and that given patient profile of high PD-L1 expressors in the real-world setting in Italy.
- Follow-up observational research reflecting the fast-evolving treatment and reimbursement landscape in NSCLC in Italy would be of interest.

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