Clinicopathological Characteristics, Treatment Patterns, and Outcomes in Patients with *KRAS* p.G12C Mutant Advanced Non-Small Cell Lung Cancer in the Flatiron Health-Foundation Medicine Clinico-Genomic Database

Shivani Aggarwal, Hil Hsu, Huakang Tu, Gillis Carrigan, Xuena Wang, Gataree Ngarmchamnanrith, Victoria Chia

Amgen Inc., Thousand Oaks, CA, USA

ESMO Virtual Congress 2020, September 19–21, 2020
Poster Number: 1339P

INTRODUCTION

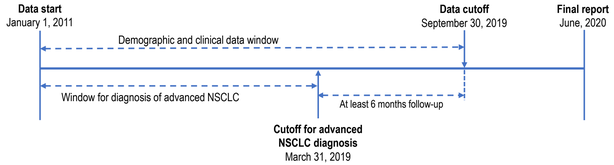
- The Flatiron Health-Foundation Medicine Clinico-Genomic Database (FH-FMI CGDB) integrates comprehensive genomic profiling results with clinical data from electronic health records (EHRs)
  - The FH-FMI CGDB, which includes ~29,000 patients from over 280 oncology practices in the United States (US), allows for a longitudinal view of a patient's clinical, diagnostic, and therapeutic outcomes
  - Findings from a previously published study using data from the non–small cell lung cancer (NSCLC) cohort of the FH-FMI CGDB demonstrated the feasibility of using a CGDB derived from routine clinical care to represent the corresponding real-world patient population and the well-established genomic correlations with clinical outcomes[1]
- *KRAS* is the most frequently mutated oncogene; *KRAS* p.G12C mutation, which accounts for ~40% of all *KRAS* mutations, occurs in ~13% of lung adenocarcinoma[2]
- There is a lack of robust real-world evidence on clinical characteristics and outcomes in patients with *KRAS* p.G12C-mutant NSCLC

OBJECTIVES, ENDPOINTS, AND DATA ANALYSIS

- The primary objectives of this retrospective study were as below
  - To describe the clinicopathological characteristics and treatment patterns in patients with advanced NSCLC overall and with *KRAS* p.G12C mutation
  - To estimate overall survival (OS) and real-world progression-free survival (rw-PFS) in patients with advanced NSCLC overall and with *KRAS* p.G12C mutation
- Endpoints
  - Demographic and clinical characteristics, including age, race, Eastern Cooperative Oncology Group performance status, disease stage at initial diagnosis, treatment patterns, co-mutation profile, etc
  - OS and rw-PFS, stratified by lines of therapy and types of therapy
    - OS was defined as the time from start of therapy to death, censoring at the last activity, or end of study
    - Rw-PFS was defined as the time from start of therapy to disease progression, death, censoring at the last activity, or end of study*
- This study was descriptive in nature
  - Descriptive statistics (mean, median, etc) were presented for continuous variables
  - OS/rw-PFS and corresponding 95% confidence intervals were calculated using Kaplan-Meier estimates

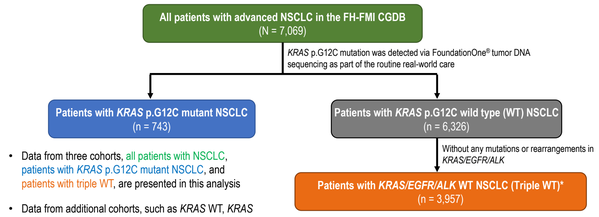
*Real-world progression was defined as a distinct episode, in which the treating clinician concluded that there had been growth or worsening of the tumor

Study Timeline and Data Source



- Study data were collected from **FH-FMI CGDB**; all data were from **United States**
- Patients with advanced NSCLC were included
  - Patients were diagnosed with advanced NSCLC between January 1, 2011 and March 31, 2019, allowing for least 6 months of follow up
  - Over **80%** of the patients included in this analysis were diagnosed and treated after March 2015 when checkpoint inhibitors gained the first approval in NSCLC
  - NSCLC cohort was defined by identifying patients who had chart-confirmed NSCLC within their EHRs
  - Advanced disease was defined as the initial diagnosis of stage IIIB/C or IV, or initial diagnosis of stage I–IIIA with subsequent recurrence or progression

Patient Disposition



- Data from three cohorts, all patients with NSCLC, patients with *KRAS* p.G12C mutant NSCLC, and patients with triple WT, are presented in this analysis
- Data from additional cohorts, such as *KRAS* WT, *KRAS* mutant, and *KRAS* p.G12C WT, have been analyzed, but results are not included in this poster

*Triple WT cohort excluded all *KRAS* mutants.

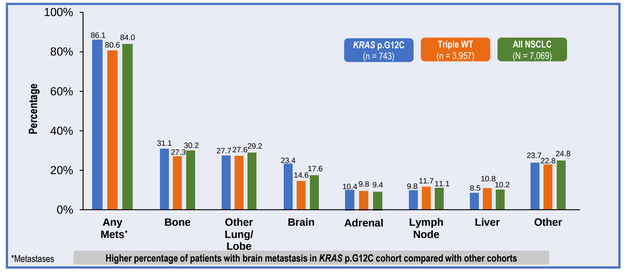
RESULTS

Baseline Characteristics

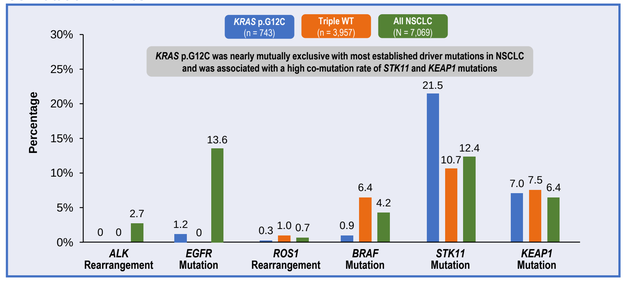
	KRAS p.G12C (n = 743)	Triple WT* (n = 3,957)	All NSCLC (N = 7,069)
Age at advanced diagnosis – years, median (range)	68 (29–85)	69 (26–85)	68 (24–85)
Female sex – n (%)	454 (61.1)	1,665 (42.1)	3,532 (50.0)
Race – n (%)			
Asian	7 (0.9)	71 (1.8)	223 (3.2)
Black	38 (5.1)	258 (6.5)	401 (5.7)
Hispanic or Latino	2 (0.3)	2 (0.1)	4 (0.1)
White	550 (74.0)	2,800 (70.8)	4,951 (70.0)
Other	80 (10.8)	489 (12.4)	882 (12.5)
Not available	66 (8.9)	337 (8.5)	608 (8.6)
Current or former smoker – n (%)	719 (96.8)	3,430 (86.7)	5,786 (81.9)
Histology of NSCLC – n (%)			
Nonsquamous	675 (90.8)	2,506 (63.3)	5,382 (76.1)
Squamous	31 (4.2)	1,252 (31.6)	1,387 (19.6)
Not otherwise specified	37 (5.0)	199 (5.0)	300 (4.2)
Stage at initial diagnosis – n (%)			
Stage ≤ IIIA	213 (28.7)	1,078 (27.2)	1,825 (25.8)
Stage IIIB–IVB	513 (69.0)	2,776 (70.2)	5,079 (71.8)
Not reported	17 (2.3)	103 (2.6)	165 (2.3)
Diagnosed in 2015 or later – n (%)#	611 (82.2)	3,307 (83.6)	5,810 (82.2)
Practice type – n (%)			
Academic	46 (6.2)	245 (6.2)	537 (7.6)
Community	697 (93.8)	3,712 (93.8)	6,532 (92.4)
Number of total lines of therapy in advanced setting – n (%)			
0	149 (20.1)	681 (17.2)	1,206 (17.1)
1	293 (39.4)	1,381 (34.9)	2,479 (35.1)
2	150 (20.2)	1,015 (25.7)	1,755 (24.8)
3	83 (11.2)	491 (12.4)	871 (12.3)
≥ 4	68 (9.2)	389 (9.8)	758 (10.7)

KRAS/EGFR/ALK wild type
#Checkpoint inhibitor therapy gained its first approval in NSCLC in March 2015

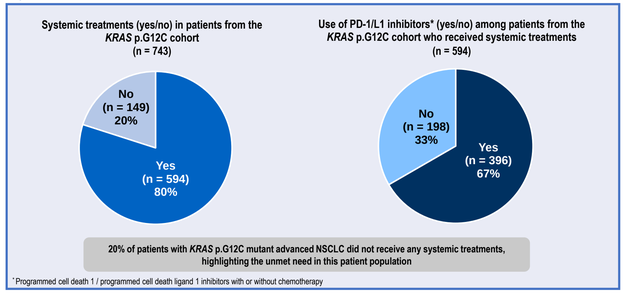
Distant Metastases at Diagnosis



Co-mutation Profiles



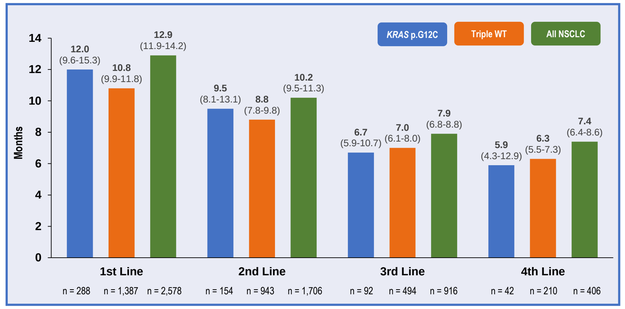
Systemic Treatment in the KRAS p.G12C Mutant Cohort



20% of patients with *KRAS* p.G12C mutant advanced NSCLC did not receive any systemic treatments, highlighting the unmet need in this patient population

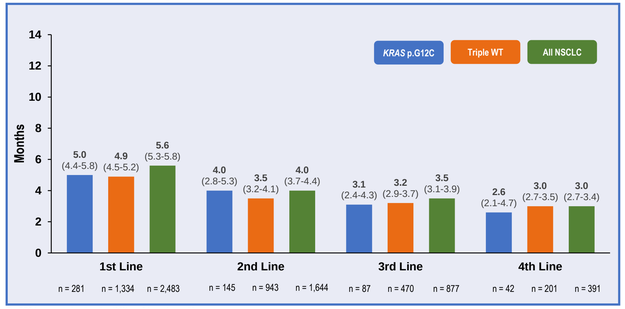
*Programmed cell death 1 / programmed cell death ligand 1 inhibitors with or without chemotherapy

Median Overall Survival by Line of Therapy



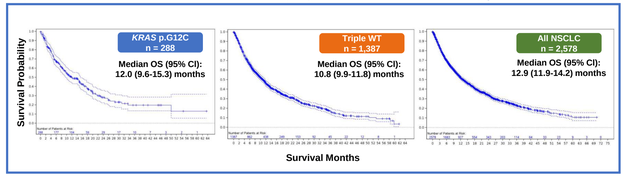
OS is presented as "median (95% confidence interval)"

Median Real-World Progression-Free Survival by Line of Therapy

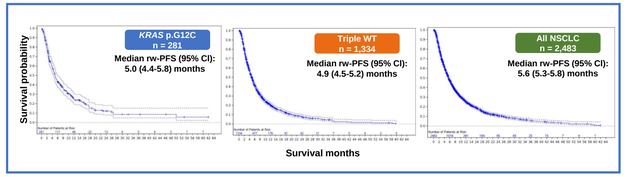


Rw-PFS is presented as "median (95% confidence interval)"

Kaplan-Meier Curves for Overall Survival (OS) After First-Line of Therapy



Kaplan-Meier Curves for Real-World Progression-Free Survival (rw-PFS) After First-Line of Therapy



CONCLUSIONS

- Compared with the overall advanced NSCLC cohort and the *KRAS/EGFR/ALK* wild type (triple WT) cohort, the *KRAS* p.G12C cohort had a higher percentage of patients who were female, current/former smokers, or had a nonsquamous histology
- *KRAS* p.G12C mutation was nearly mutually exclusive with known driver mutations established in NSCLC and was associated with a co-mutation rate of 21.5% for *STK11* and 7.0% for *KEAP1*, both of which are associated with poor prognosis[3,4]
- One in five patients with advanced NSCLC harboring the *KRAS* p.G12C mutation did not receive systemic therapy. Among those who received systemic therapy, 67% were treated with PD-1/PD-L1 inhibitors-based regimen
- Despite high usage of checkpoint inhibitors (67%), the outcomes for the *KRAS* p.G12C mutant cohort were as poor as the overall advanced NSCLC cohort and the triple WT cohort
- These results, supported by others, highlight that patients with *KRAS* p.G12C mutant NSCLC remain in need for new, safer, and more efficacious treatment options[5,6]

REFERENCES

1. Singal G, et al. *JAMA*. 2019;321:1391-1399.
2. Biernacka A, et al. *Cancer Genet*. 2016;209:195-198.
3. Bange E, et al. *JCO Precis Oncol*. 2019;3:1200.
4. Arbour CK, et al. *Clin Cancer Res*. 2018;24:334-340.
5. Nadal E, et al. *J Thorac Oncol*. 2014;9:1513-1522.
6. Park S, et al. *Korean J Intern Med*. 2017; 32: 514-522.

DISCLOSURES

- Presenter Dr. Shivani Aggarwal reports the following financial disclosures:
  - employment and stock ownership with Amgen Inc.

ADDITIONAL INFORMATION

- This study was funded by Amgen Inc.
- Medical writing assistance was provided by Yang Li, PhD (Amgen Inc.)
- For more information, please contact Amgen Medical Information: medinfo@amgen.com

Presenter contact information: shivania@amgen.com