Supplementary

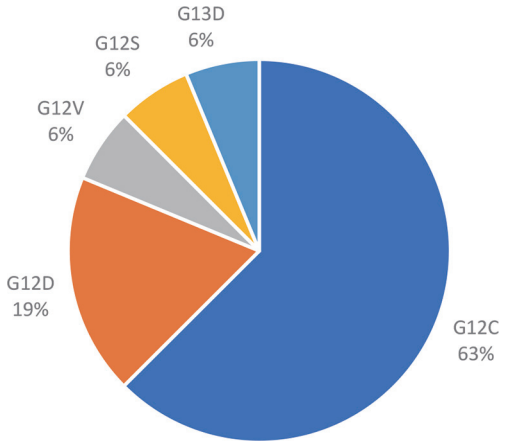

Figure S1 Percent of patients with history of additional malignancies based on *KRAS* mutation profile. Patients with previous or concurrent malignancies were seen in *KRAS* G12C, G12D, G12V, G12S, G13D driver mutations.

Table S1 Summary of treatments for each KRAS driver mutation

KRAS Mutation (Stage at Diagnosis)	Chemotherapy Regimens +/−combined Immunotherapy (cycles)	Immunotherapy Regimens (monotherapy) (cycles)	Mean cycle of systemic therapy	Radiation Therapy	Surgical Resection
G12C (I)	—	—		Yes	Yes
G12C (I)	—	—		Yes	—
G12C (I)	Carboplatin/ Pemetrexed/ Pembrolizumab[a]	—	1	—	Yes
G12C (I)	Carboplatin/ Pemetrexed/ Pembrolizumab[a]	—		—	Yes
G12C (I)	—	—		—	Yes
G12C (I)	—	—		—	Yes
G12C (I)	—	—		—	Yes
G12C (I)	—	—		—	—
G12C (II)	Carboplatin/ Paclitaxel	—	6	Yes	—
G12C (II)	Carboplatin/ Pemetrexed[a]	—	4	—	Yes
G12C (IV)[a]	Bevacizumab/ Carboplatin/ Paclitaxel; Navelbine/ Gemcitabine	—	6/4	—	Yes
G12C (IV)	Avastin	—	Unknown	—	Yes
G12C (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab	—	1	—	Yes
G12C (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab	—	1	—	Yes
G12C (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab; Pemetrexed/ Carboplatin	—	3/3	—	Yes

Table S1 (*continued*)

https://dx.doi.org/10.21037/jtd-21-432

Table S1 (*continued*)

KRAS Mutation (Stage at Diagnosis)	Chemotherapy Regimens +/−combined Immunotherapy (cycles)	Immunotherapy Regimens (monotherapy) (cycles)	Mean cycle of systemic therapy	Radiation Therapy	Surgical Resection
G12C (IV)	—	—	—	—	Yes
G12C (IV)	—	Pembrolizumab	2	—	Yes
G12C (IV)	—	—	—	—	Yes
G12C (IV)	—	—	—	—	—
G12C (IV)	—	—	—	—	—
G12C (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab; Pemetrexed/ Pembrolizumab	—	4/5	—	—
G12C (IV)	—	Ipilimumab/ Nivolumab; Nivolumab	4/7	—	—
G12C (IV)	—	Pembrolizumab	28	—	—
G12C (IV)	—	—	—	—	—
G12C (IV)	—	—	—	—	—
G12C (IV)	—	—	—	—	—
G12V (I)	—	—	—	—	Yes
G12V (I)	Carboplatin/ Pemetrexed/ Pembrolizumab	—	Unknown	—	Yes
G12V (I)	—	—	—	—	Yes
G12V (IV)[β]	Carboplatin/ Paclitaxel	—	5	Yes	—
G12V (IV)	—	—		—	—
G12V (IV)	Carboplatin/ Pemetrexed	—	>2 cycles	—	—
G12V (IV)	—	—	—	—	—
G12S (I)	—	—	—	—	Yes
G12S (III)	Carboplatin/ Durvalumab[b]/ Pembrolizumab	—	7	Yes	Yes
G12S (IV)[€]	Carboplatin/ Pemetrexed/ Pembrolizumab	Pembrolizumab (13)	4	Yes	—
G12S (IV)	—	—	—	Yes	—
G12D (I)	—	—	—	Yes	Yes
G12D (II)[¥]	—	Pembrolizumab; Nivolumab (15;3)	—	Yes	Yes
G12D (III)	Carboplatin/ Paclitaxel/ Pembrolizumab	—		Yes	—
G12D (III)[a]	Cisplatin/ Venorelbine	—	4	Yes	Yes
G12D (III)	Carboplatin/ Pemetrexed	—	4	Yes	Yes
G12D (IV)[a]	Cisplatin/ Gemcitabine	Pembrolizumab (4)	3	—	Yes

Table S1 (*continued*)

https://dx.doi.org/10.21037/jtd-21-432

Table S1 (*continued*)

KRAS Mutation (Stage at Diagnosis)	Chemotherapy Regimens +/−combined Immunotherapy (cycles)	Immunotherapy Regimens (monotherapy) (cycles)	Mean cycle of systemic therapy	Radiation Therapy	Surgical Resection
G12D (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab	—	4	Yes	—
G12D (IV)	Carboplatin/ Pemetrexed	—	2	Yes	—
G12D (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab	—	2	—	—
G12D (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab; Pemetrexed/ Pembrolizumab; Carboplatin/ Paclitaxel	Atezolizumab/ Bevacizumab (3); nivolumab/ olaparib (9)	3; 8; 3	—	—
G12A (I)	—	—	—	Yes	—
G12A (I)	—	—	—	—	Yes
G13C (IV)	Carboplatin/ Pemetrexed/ Pembrolizumab; Docetaxel/ Ramucirumab	—	6; 3	—	—
G13V (IV)	Carboplatin/ Paclitaxel; Carboplatin/ Pemetrexed/ Pembrolizumab; Nab—paclitaxel/ Gemcitabine	—	1; 2; 2	Yes	—
G13D (I)	—	—	—	—	Yes
G13D (II)	—	—	—	Yes	—
G13D (IV)	—	—	—	Yes	—
G13D (IV)	—	Pembrolizumab (2)	—	—	—
Q61L (IV)	Carboplatin/ Gemcitabine	—	1	—	—
Q61H (I)	—	—	—	—	Yes
Q61E (III)	Carboplatin/ Paclitaxel	—	6	Yes	—

[a]: Adjuvant chemotherapy+/—immunotherapy; [b]: could not tolerate Durvalumab after 2 cycles, switched to Pembrolizumab; [α]: Previous Lobectomy and adjuvant chemotherapy in 2004 with cisplatin/etoposide, and carboplatin/pemetrexed in 2014 for recurrence. Recurrence with KRAS positive disease in 2019; [β]: Previously diagnosed in 2013, had lobectomy at that time; [€]: Previous Lobectomy in 2012; [¥]: Had a second KRAS V141 mutation with metastatic recurrence. Also received oncolytic viral injection as part of an ongoing clinical trial.

https://dx.doi.org/10.21037/jtd-21-432

Table S2 Specific second malignancies

Malignancy	G12C	G12D	G12V	G12S	G13D	Total
Breast[β]	3	0	0	0	0	3
CLL	1	0	0	0	0	1
Mantle Cell Lymphoma	0	0	0	1	0	1
RCC	2	0	0	0	0	2
Cervical[€]	1	1	0	0	0	2
Bladder[α]	1	0	0	0	0	1
Prostate[α]	1	1	0	0	0	2
Acoustic Neuroma	1	0	0	0	0	1
Meningiomas[β]	1	0	0	0	0	1
Hurthle Cell Carcinoma	1	0	0	0	0	1
Salivary Gland Carcinoma[€]	0	1	0	0	0	1
Renal Oncocytoma	0	1	0	0	0	1
Colorectal Carcinoma	0	0	1	0	1	2

[α]: Patient previously had urothelial cancer and prostate cancer; [β]: Patient had both breast cancer and meningioma history; [€]: Patient previously had cervical cancer and carcinoma of the salivary gland.

Table S3 Causes of Death in KRAS mutated NSCLC

KRAS Driver Mutation	Disease Progression	Other
Total	24	7
G12C	11	5: PEA Arrest, Pneumonia, hemorrhagic pericardial effusion, Respiratory failure, unreported cause
G12D	3	0
G12V	4	0
G12S	1	1: PEA Arrest
G13D	2	1: Pneumonia
G12A	-	-
Q61H	-	-
Q61L	1	0
Q61E	-	-
G13V	1	0
G13C	1	0

PEA: Pulseless Electrical Activity.

https://dx.doi.org/10.21037/jtd-21-432