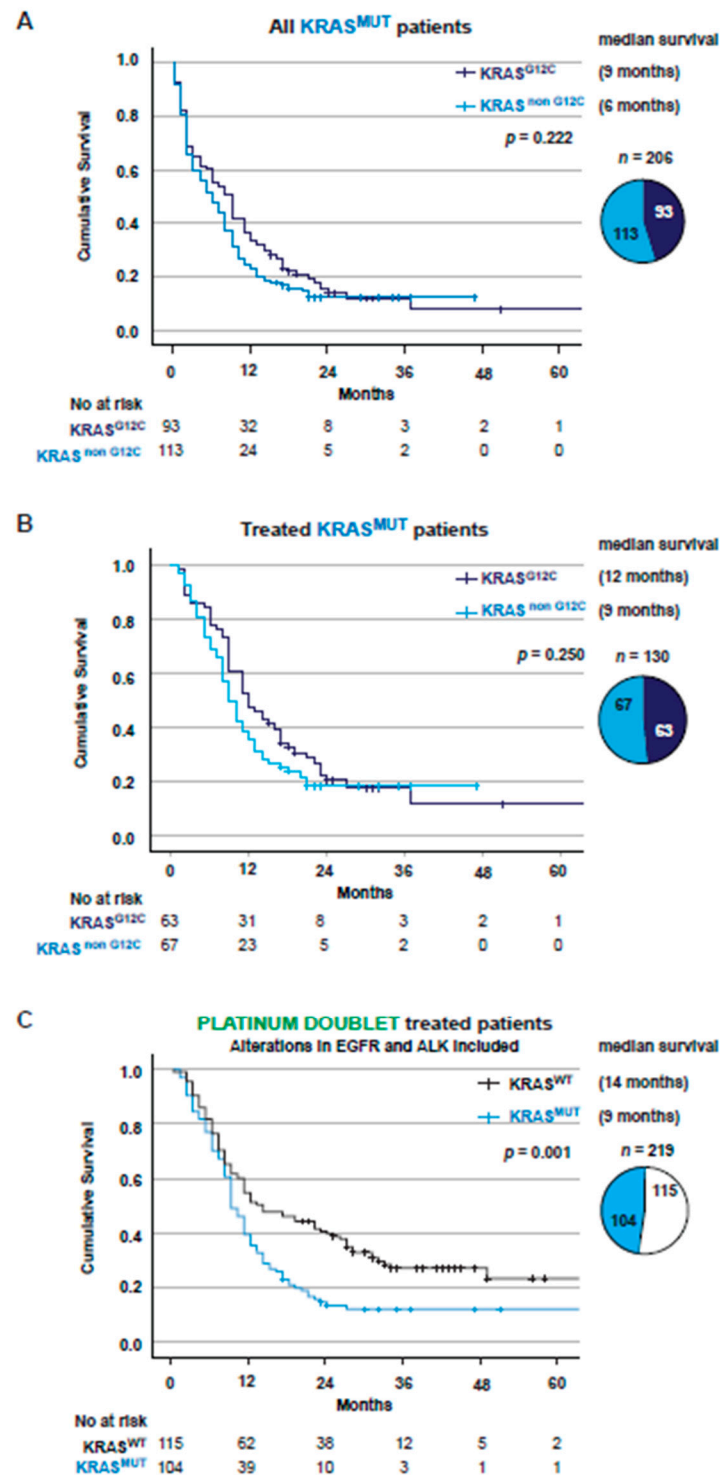


**Figure S1.** (A). Kaplan-Meier estimates comparing overall survival for the full cohort stratified on ECOG PS. Pie chart showing patient distribution between ECOG stages. (B). Kaplan-Meier estimates comparing overall survival for the full cohort stratified on number of metastasis locations. Pie chart showing patient distribution between number of metastasis locations. (C). Kaplan-Meier estimates comparing overall survival for the full cohort stratified on gender. Pie chart showing patient distribution between male and female. ECOG: Eastern Cooperative Oncology Group; PS: Performance Status.



**Figure S2.** (A). Kaplan–Meier estimates comparing overall survival for all KRAS<sup>MUT</sup> stratified on KRAS<sup>G12C</sup> vs. KRAS<sup>non G12C</sup>. Pie chart showing patient distribution between KRAS<sup>G12C</sup> and KRAS<sup>non G12C</sup>. (B). Kaplan–Meier estimates comparing overall survival for all KRAS<sup>MUT</sup> patients receiving treatment with platinum doublet stratified on KRAS<sup>G12C</sup> vs. KRAS<sup>non G12C</sup>. Pie chart showing patient distribution between KRAS<sup>G12C</sup> and KRAS<sup>non G12C</sup>. (C). Kaplan–Meier estimates comparing overall survival for all receiving treatment with platinum doublet stratified on KRAS<sup>WT</sup> vs. KRAS<sup>MUT</sup>. Pie chart showing patient distribution between KRAS<sup>WT</sup> and KRAS<sup>MUT</sup>

**Table S1.** (Related to Figure S2C), Characteristics of all PT treated patients.

<b>Characteristics all Platinum Doublet treated</b>	<b>WT</b>	<b>KRAS MUT</b>
	<i>n</i> (%)	<i>n</i> (%)
Total <i>n</i> = 219	115 (52,5)	104 (47,5)
Age in years, median (range)	69 (24–84)	70 (35–83)
<i>Sex</i>		
Male	49 (42,6)	35 (33,7)
Female	66 (57,4)	69 (66,3)
<i>Smoking history</i>		
Current smoker	38 (33,0)	37 (35,6)
Former smoker	53 (46,1)	60 (57,7)
Never smoker	23 (20,0)	7 (6,7)
Missing	1 (0,9)	0
<i>Performance status</i>		
ECOG 0	22 (19,1)	24 (23,1)
ECOG 1	66 (57,4)	60 (57,7)
ECOG 2	25 (21,7)	20 (19,2)
ECOG 3	2 (1,7)	0
ECOG 4	0	0
Missing	0	0
<i>Histology</i>		
Adenocarcinoma	94 (81,8)	88 (8,6)
NSCLC NOS	9 (7,8)	15 (14,4)
Squamous cell carcinoma	12 (10,4)	1 (1,0)
<i>Mutation status</i>		
None known	77 (67,0)	
ALK	6 (5,2)	
EGFR	18 (15,7)	
BRAF	6 (5,2)	
Other	6 (5,2)	
1RET	2 (1,7)	
<i>KRAS submutation</i>		
G12A		6 (5,8)
G12C		46 (44,2)
G12D		10 (9,6)
G12V		20 (19,2)
Others		22 (19,2)
<i>At last follow up</i>		
Alive	32 (27,8)	14 (13,5)
Deceased	83 (72,2)	90 (86,5)
<i>Survival</i>		
Median survival (months)	14	9
<i>No. of metastatic locations at diagnosis</i>		
1	79 (68,7)	72 (69,2)
2	26 (22,6)	22 (57,7)
3	6 (5,2)	7 (6,7)
>3	1 (0,9)	3 (2,9)
Missing	3 (2,6)	0

**Table S2.** (Related to Figure 5A). Characteristics of all patients treated with first-line ICB.

<b>Characteristics Immune checkpoint blockade monotherapy</b>	<b>WT</b>	<b>KRAS</b>
	<i>n</i> (%)	<i>n</i> (%)
Total <i>n</i> = 37	<i>n</i> = 17(45,9 )	<i>n</i> = 20 (54,1)
Age in years, median (range)	70 (57–83)	69 (46–78)
<i>Sex</i>		
Male	6 (35,3)	12 (60)
Female	11 (64,7)	8 (40)
<i>Smoking history</i>		
Current smoker	7 (41,2)	7 (35)
Former smoker	9 (52,9)	12 (60)
Never smoker	1 (5,9)	1 (5)
Missing	0	0
<i>Performance status</i>		
ECOG 0	3 (17,6)	4 (20)
ECOG 1	8 (47,1)	13 (65)
ECOG 2	6 (35,3)	3 (15)
ECOG 3	0	0
ECOG 4	0	0
Missing	0	0
<i>Histology</i>		
Adenocarcinoma	14 (82,4)	19 (95)
NSCLC NOS	2 (11,8)	1 (5)
Squamous cell carcinoma	1 (5,9)	0
<i>Mutation status</i>		
None known	14 (82,4)	
ALK	0	
EGFR	1 (5,9)	
BRAF	1 (5,9)	
NRAS	1 (5,9)	
ROS1	0	
RET	0	
<i>KRAS submutation</i>		
G12A		2 (10)
G12C		8 (40)
G12D		1 (5)
G12V		2 (10)
G13D		2 (10)
Q61H		2 (10)
Other		3 (15)
<i>PD-L1 status</i>		
High TPS ≥50%	13 (76,5)	20 (100)
Low TPS 1–49%	3 (17,6)	0
Missing	1 (5,9)	0
<i>At last follow up</i>		
Alive	2 (11,8)	10 (50)
Deceased	15 (88,2)	10 (50)
<i>Survival</i>		
Median survival (months)	6	23
<i>No. of metastatic locations at diagnosis</i>		
1	14 (82,4)	10 (50)
2	2 (11,8)	9 (45)
3	1 (5,9)	1 (5)

**Table S3.** Multivariate analyses.

	<b>ALL STAGE IV</b>	<b>95%CI</b>	<b><i>p</i></b>
	<b>HR</b>		
KRAS mutation	1.472	1.207–1.769	<0.001
ECOG >1	3.175	2.622–3.845	<0.001
Gender (female)	0.840	0.700–1.008	0.061
Smoking	1.021	0.803–1.297	0.867
All PT with EGFR and ALK excluded			
	<b>HR</b>	<b>95%CI</b>	<b><i>p</i></b>
KRAS mutation	1.564	1.124–2.177	0.008
ECOG >1	1.906	1.307–7.779	<0.001
Gender (female)	0.957	0.690–1.328	0.794
Smoking	1.089	0.608–1.952	0.774
All ICB treated			
	<b>HR</b>	<b>95%CI</b>	<b><i>p</i></b>
KRAS mutation	0.349	0.148–0.822	0.016
ECOG >1	0.389	0.165–0.963	0.041
Gender (male)	1.459	0.637–3.343	0.372
Smoking	1.263	0.165–9.658	0.882
KRAS MUT PD-L1 status			
	<b>HR</b>	<b>95%CI</b>	<b><i>p</i></b>
PD-L1	0.993	0.986–0.999	0.028
ECOG >1	2.470	1.470–4.273	0.001
Gender (male)	1.026	0.632–1.166	0.918
Smoking	1.212	0.421–3.491	0.721
KRAS WT PD-L1 status			
	<b>HR</b>	<b>95%CI</b>	<b><i>p</i></b>
PD-L1	1.001	0.995–1.007	0.780
ECOG >1	2.865	1.938–4.236	<0.001
Gender (female)	0.926	0.642–1.343	0.918
Smoking	0.743	0.473–1.168	0.198