Molecular characterization of resected non-metastatic pancreatic cancer (PC) based on *KRAS* status

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INTRODUCTION

- Surgery is the only potentially curative option for PC. However, only a minority of patients (pts) undergo resection with current perioperative (periop)-chemotherapy (CT).
- In the absence of phase III trials, selection between mFOLFIRINOX and gemcitabine/nab-paclitaxel (gem-nab) is based on limited evidence.
- We assessed whether NGS–based tumor profiling can guide tailoring of CT.

METHODS

Tempus Lens was utilized to identify PC patients sequenced with xT or xF assays. Lens provides access to Workspaces, a computational platform embedded within Lens that enables quick insight extraction from select cohorts of Tempus data using a rich library of tools. Patients were selected as described in **Figure 1**. Clinical and demographic characteristics were compared using Pearson's Chi-squared/Fisher's exact or Wilcoxon rank sum tests, as applicable. Overall survival was evaluated from CT therapy start to death, last follow-up, or study cutoff of 5 years after CT initiation using Kaplan-Meier approach and was restricted to patients with study entry prior to treatment initiation.

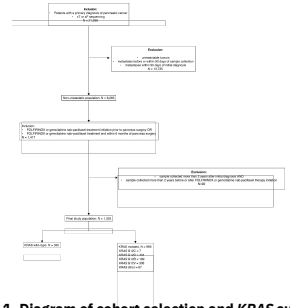


Figure 1. Diagram of cohort selection and *KRAS* subgroups.

SUMMARY

- *KRAS* status does not predict response to mFOLFIRINOX or gem-nab in resected PC.
- *KRAS* status is associated with distinct profiles of potentially targetable co-alterations.,

RESULTS

Table 1. Baseline demographic and clinical characteristics of study cohort by *KRAS* mutation status.

Characteristic	Overall N = 1,325	*KRAS* wt N = 330	*KRAS* mut N = 995	p-value
Age at diagnosis				0.7
Median (Q1, Q3)	66 (59, 72)	66 (59, 72)	66 (59, 72)	
Unknown	3	1	2	
Treatment Setting[1]				**0.002**
Neoadjuvant	664 (50%)	175 (53%)	489 (49%)	
Perioperative	341 (26%)	85 (26%)	256 (26%)	
Treatment start before surgery, treatment end unknown	170 (13%)	51 (15%)	119 (12%)	
Adjuvant	150 (11%)	19 (5.8%)	131 (13%)	
Stage[2]				0.076
Stage 1	136 (27%)	39 (33%)	97 (25%)	
Stage 2	204 (41%)	38 (32%)	166 (44%)	
Stage 3	159 (32%)	41 (35%)	118 (31%)	
Unknown	826	212	614	

[1]Adjuvant = CT start and end after surgery, Perioperative = CT start before surgery and end after surgery, Neoadjuvant = CT start and end before surgery
[2]Documented within 90 days of sample collection

Table 2. Median OS for gemcitabine plus nab-paclitaxel vs FOLFIRINOX across *KRAS* status.

KRAS cohort	Treatment group	Median OS (months)	95% CI	p-value
***KRAS* wt**	Gemcitabine plus nab-paclitaxel (N=69)	26.37	22.39 - 36.43	0.707
	FOLFIRINOX (N=223)	30.05	25.02 - 33.96	
G12C	Overall (N=7)	24.76	8.05 - NA	NA
G12D	Gemcitabine plus nab-paclitaxel (N=99)	14.53	7.89 - 17.42	0.050
	FOLFIRINOX (N=251)	17.79	15.02 - 20.35	
G12V	Gemcitabine plus nab-paclitaxel (N=73)	20.55	15.19 - 24.59	0.392
	FOLFIRINOX (N=197)	22.19	19 - 24.46	
***KRAS* other**	Gemcitabine plus nab-paclitaxel (N=17)	16.93	8.84 - 26.79	0.919
	FOLFIRINOX (N=53)	16.41	13.58 - 19.66	

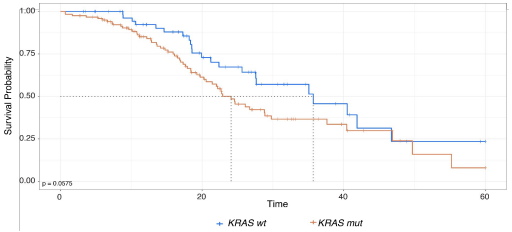
Table 3. Genomic alteration frequency by *KRAS* mutation status

Gene	Overall N = 1,325	*KRAS* wt N = 330	*KRAS* mut N = 995	p-value
***TP53* any**	829 (63%)	73 (22%)	756 (76%)	**<0.001**
***SMAD4* any**	297 (22%)	19 (5.8%)	278 (28%)	**<0.001**
***CDKN2A* any**	355 (27%)	28 (8.5%)	327 (33%)	**<0.001**
***NTRK1* fusion**	2 (0.2%)	2 (0.6%)	0 (0%)	0.062
***NTRK3* fusion**	2 (0.2%)	0 (0%)	2 (0.2%)	>0.9
***BRAF* V600E**	5 (0.4%)	5 (1.5%)	0 (0%)	**<0.001**
***ERBB2* cn amp**	14 (1.1%)	1 (0.3%)	13 (1.3%)	0.2
***NRG1* fusion**	1 (<0.1%)	1 (0.3%)	0 (0%)	0.2
***ARID1A* any**	82 (6.2%)	4 (1.2%)	78 (7.8%)	**<0.001**
***KMT2C* any**	27 (2.0%)	2 (0.6%)	25 (2.5%)	**0.034**
***MYC* cn amp**	20 (1.5%)	3 (0.9%)	17 (1.7%)	0.4
***PIK3CA* any**	20 (1.5%)	4 (1.2%)	16 (1.6%)	0.8
***PTEN* any**	12 (0.9%)	3 (0.9%)	9 (0.9%)	>0.9
***AKT2* any**	16 (1.2%)	2 (0.6%)	14 (1.4%)	0.4
***AKT3* any**	6 (0.5%)	1 (0.3%)	5 (0.5%)	>0.9
***MTAP* cn del**	81 (6.1%)	4 (1.2%)	77 (7.7%)	**<0.001**

Table 4. Immune biomarkers in xT tested population by *KRAS* mutation status

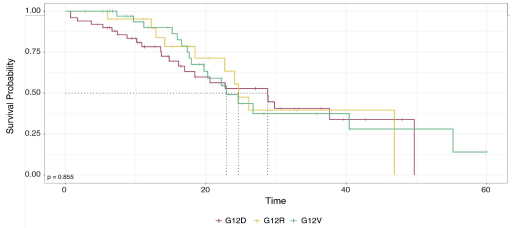
Biomarker	Overall N = 1,176	*KRAS* wt N = 198	*KRAS* mut N = 978	p-value
TMB				**<0.001**
Median (Q1, Q3)	2.29 (1.58, 3.68)	1.58 (0.53, 2.63)	2.63 (1.58, 3.68)	
TMB high (≥10 mut/Mb)	10 (0.9%)	4 (2.0%)	6 (0.6%)	0.071
MSI status				**0.7**
Stable	1,170 (99%)	197 (99%)	973 (99%)	
High	4 (0.3%)	1 (0.5%)	3 (0.3%)	
Equivocal	2 (0.2%)	0 (0%)	2 (0.2%)	
MMR deficient	2 (0.2%)	0 (0%)	2 (0.2%)	>0.9
PD-L1 22C3 TPS				**0.033**
Unknown/not tested	668 (57%)	129 (65%)	539 (55%)	
< 1%	384 (33%)	53 (27%)	331 (34%)	
≥1%	124 (11%)	16 (8.1%)	108 (11%)	

Figure 2. Overall survival by KRAS mutation status in patients with study entry prior to treatment initiation



KRAS Cohort	N	N events	Median OS (95% CI)	p-value
***KRAS* wt**	59	22	35.7 (25.6 - 46.8)	0.0575
***KRAS* mut**	121	57	24.1 (20.3 - 28.9)	

Figure 3. Overall survival by KRAS G12 variant



KRAS Variant	N	N events	Median OS (95% CI)	p-value
G12D	50	23	28.8 (16.1 - NA)	0.855
G12R	22	10	24.7 (18.4 - NA)	
G12V	40	17	22.9 (17.9 - 55.2)	

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