Purity Independent Subtyping of Tumor (PurIST[SM]): Real-world data validation of a pancreatic ductal adenocarcinoma (PDAC) gene expression classifier and its prognostic implications

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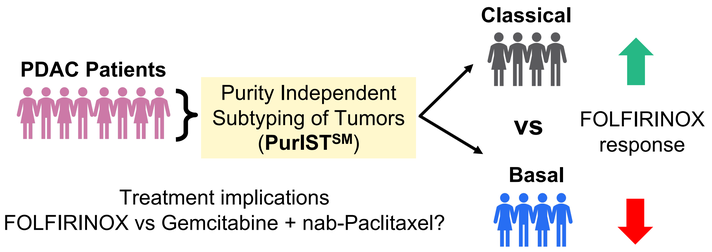
INTRODUCTION

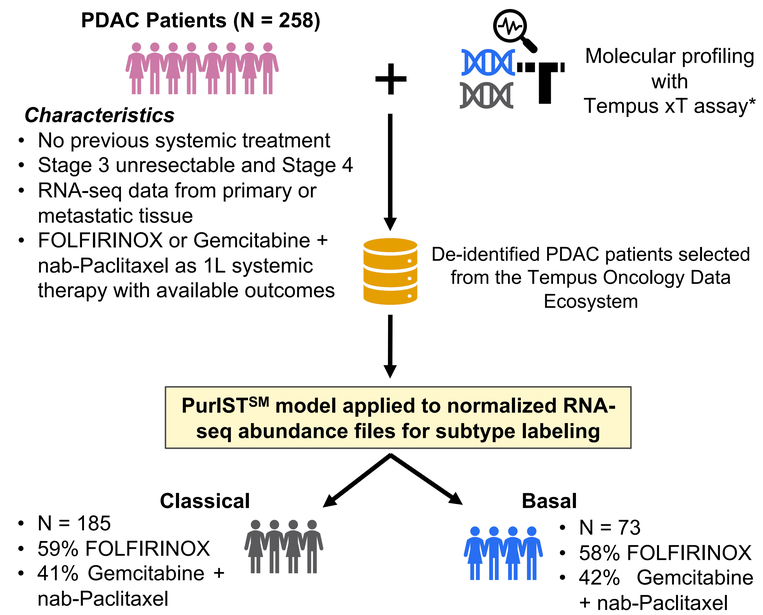
Pancreatic ductal adenocarcinoma (PDAC) is a highly morbid disease with no validated biomarkers for first-line (1L) treatment selection.



The PurIST[SM] molecular subtyping classifier was developed using multiple gene expression data types, including micro-array and poly-A capture RNA-seq, and validated on RNA-seq and NanoString platforms. Prognostic differences between the Basal and Classical subtypes have been demonstrated across early and late stage PDAC, do not associate with biopsy purity, and are highly stable across intra-patient pre- and post-treatment biopsies.

Here, we demonstrate the clinical validity of the PurIST[SM] algorithm implemented as a lab developed test (LDT) on the Tempus Labs sequencing platform, comprising whole-transcriptome RNA sequencing covering 20,061 genes (IDT Exome-capture Panel v2, 34 Mb target region)

METHODS



Predefined statistical analysis parameters included 12-month survival rate & median overall survival (OS) in FOLFIRINOX treated patients. OS was compared using Kaplan-Meier estimates, hazard ratios, and log-rank statistical tests. *Tempus xT solid tumor assay - DNA-seq of 595-648 genes at 500x coverage; Whole-transcriptome RNASeq (IDT Exome-capture Panel v2)

RESULTS

Characteristic	Classical, N = 185	Basal, N = 73	p-val[1]
Sex			0.005*
Female	89 (48%)	21 (29%)	
Male	96 (52%)	52 (71%)	
Age at diagnosis (yrs, IQR)	66 (58, 72)	66 (60, 70)	0.8
Median OS (months, 95% CI)	13.4 (11.6-16.1)	9.3 (7.9-11.9)	
First line therapy regimen			0.8
FOLFIRINOX	109 (59%)	42 (58%)	
Gemcitabine + nab-Paclitaxel	76 (41%)	31 (42%)	
Stage			>0.9
Stage 3	10 (5.4%)	3 (4.1%)	
Stage 4	175 (95%)	70 (96%)	
Presence of liver metastases	128 (69%)	59 (81%)	0.06*

[1]Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test
*In a multivariate survival model including sex and the presence of a liver metastasis as covariates, PurIST[SM] subtype remains a significant predictor of survival for FOLFIRINOX treated patients

Table 1. Demographic & clinical information of patients (N = 258) in the study

12-month survival of FOLFIRINOX-treated PDAC patients

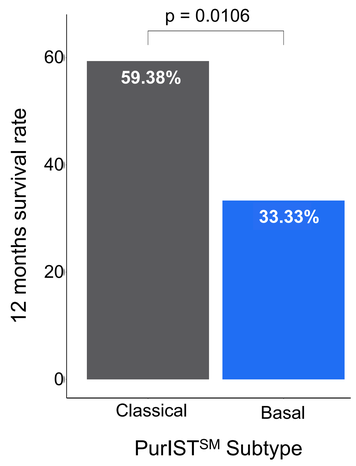


Figure 2. A comparison of the 12-month survival rate between basal and classical subtype PDAC patients treated with FOLFIRINOX. The 12-month survival rate was significantly lower in basal patients receiving FOLFIRINOX vs. classical patients (33.33% vs. 59.38%, p=0.0106).

Overall survival of FOLFIRINOX-treated PDAC patients

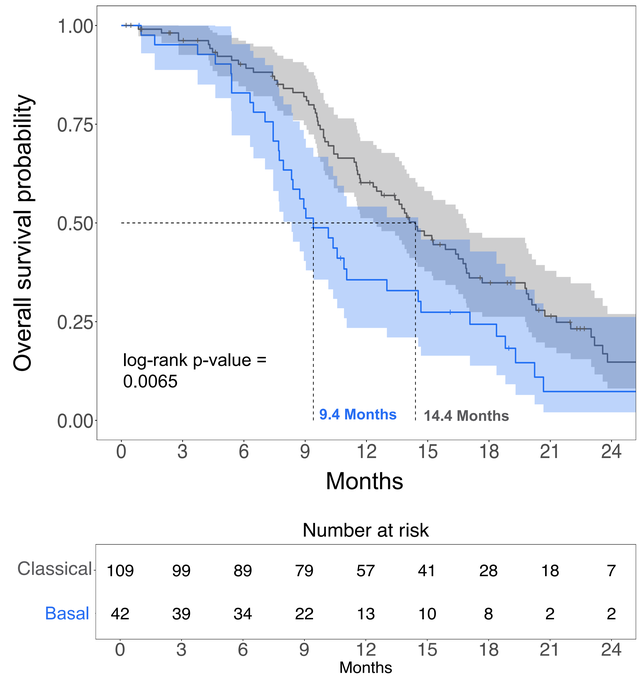


Figure 1. Kaplan-Meier curve comparing survival of classical and basal PDAC patients treated with FOLFIRINOX. The median OS was 14.4 months (95% CI: 12.5-16.87) in classical patients as compared to 9.4 months (95% CI: 8.33-14.53) in basal patients. Hazard Ratio was 1.72 (95% CI = 1.16 -2.56) and and log-rank p-value was 0.0065.

Median overall survival of PDAC patients

	FOLFIRINOX	Gemcitabine + Nab-paclitaxel	Log rank p-value
Classical	14.4 (12.5-16.87)	10.8 (10.23-17.47)	0.046
Basal	9.4 (8.33-14.53)	9.3 (6-17.27)	0.6

Table 2. Comparison of median OS (in months) between 1L regimens (FOLFIRINOX vs Gemcitabine + Nab-paclitaxel) between the classical and basal PDAC patients

SUMMARY

- The association between PurIST[SM] subtypes and PDAC patient survival when administered FOLFIRINOX or Gemcitabine + nab-Paclitaxel in a real-world cohort was validated.
- Among FOLFIRINOX-treated patients, classical patients had significantly better outcomes compared to basal patients.
- Classical patients appear to have improved outcomes with FOLFIRINOX vs. Gemcitabine + nab-Paclitaxel; in contrast, no difference in OS was observed in basal patients between treatment groups.
- **These findings represent underlying biological PDAC differences and demonstrate the clinical validity of PurIST[SM] as a prognostic marker in PDAC patients when performed as an LDT on the Tempus xT platform.**
- PurIST[SM] performance will be continuously monitored through the Tempus Oncology Data ecosystem.

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