Abstract 466: **Clinical Genomic Implications of Transcriptional Subtypes in Pancreatic Cancer**

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Background/Methods:

- Transcriptional profiling of pancreatic cancers (PC) has defined classical and basal subtypes
- Basal subtypes have worse prognosis
- Post therapy Mesenchymal (MES) and neural–like progenitor (NRP) states have been defined
- Initial clinical data suggests differential response of transcriptional subtypes with FOLFIRINOX vs. Gemcitabine-nab-Paclitaxel (Gem/nab-P) in PC.
- Basal tumors may preferentially response to Gem/nab-P

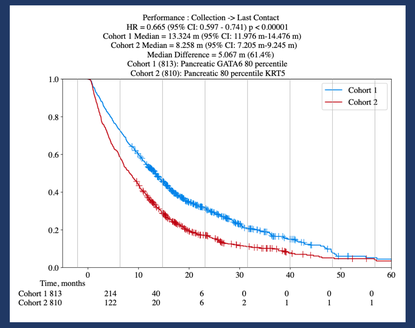
Methods:

- Genomic cohort: 7,250 PCs profiled by Caris Life Sciences
- Clinical cohort: 1,623 PCs with additional clinical data available. Survival data was obtained from insurance claims data. Kaplan-Meier estimates were used for survival analysis.
- Transcriptional cell states were identified using RNA-seq

Results:

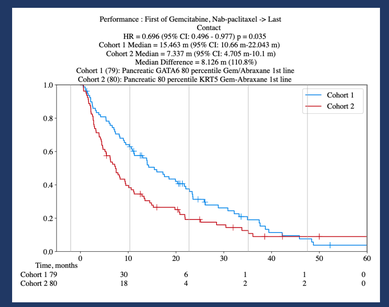
- 3,063 tumors (42.2%) were strongly classical (SC), 2,015 tumors (27.8%) were strongly basal (SB)
- MES and NRP marker genes were significantly co-expressed with each other, with basal genes, and anti-correlated with classical genes.

Basal tumors have worse overall outcomes

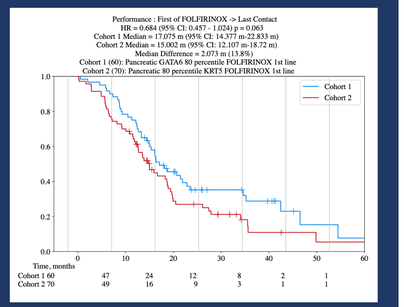


Upfront FOLFIRINOX seems to mitigate worse prognosis of Basal tumors

1st line Gem/Nab-P



1st line FOLFIRINOX



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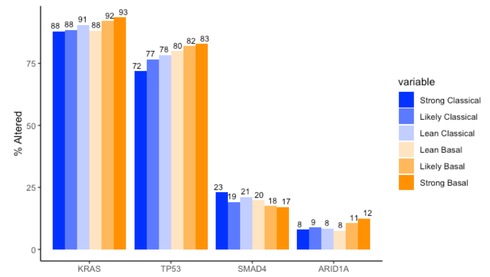
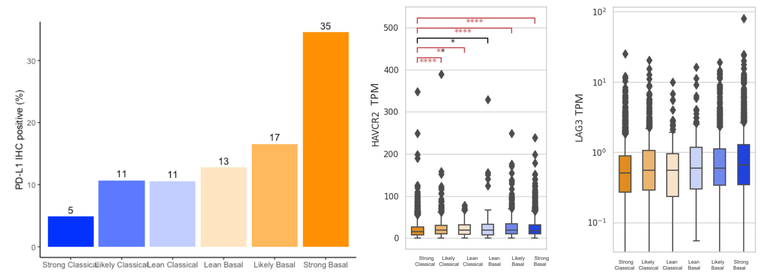
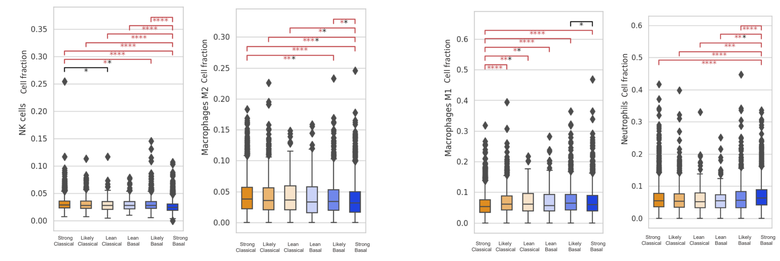
Classical tumors have significantly lower rates of *KRAS*, *TP53* & *ARID1A* mutations & significantly higher rates of SMAD4 mutations:



Basal Tumors display higher levels of PD-L1 and markers of immune exhaustion:



Quantiseq RNA deconvolution identifies potential TME differences:



Higher in classical tumors

Higher in basal tumors

	SC n = 3,063	SB n = 2,015
KRAS	88.0%	93.5%
TP53	71.8%	82.8%
SMAD4	22.9%	17.1%
ARID1A	7.9%	12.4%