Does Molecular Landscape differ based on the site of metastasis in Pancreatic ductal adenocarcinoma (PDAC)?

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Background

- Liver is the most common site of metastatic spread in PDAC.
- Liver metastasis (LM) is associated with poor prognosis.
- Here, we examine the difference in the molecular landscape of PDACs with LM versus other metastatic sites (OM).

Methods

- A total of 7,979 PDAC tumors underwent next-generation sequencing of DNA (592-gene or whole exome) and RNA (whole transcriptome) at Caris Life Sciences (Phoenix, AZ).
- Tumors were then evaluated and divided into LM (N=4988) site vs OM (N=3073) sites based on tissue specimen sites.
- RNA expression data was used to analyze transcriptional signatures and the tumor immune microenvironment (TME) using Quantiseq.
- Real-world overall survival (rwOS) information was obtained from insurance claims data and calculated from the time of collection or first treatment time to last contact.
- The hazard ratio (HR) was calculated using the Cox proportional hazards model, and P values were calculated using the log-rank test.
- Significance for molecular comparisons was calculated using either chi-square, Fisher's exact, or Mann-Whitney U test, with p-values adjusted for multiple comparisons (q <0.05).

Table 1: Metastatic categories based on tissue specimen sites.

Category	N
Liver Mets	4936
Lung Mets	514
Lymph node Mets	344
Peritoneal Mets	658
Other Mets	1527
Total	**7979**

Results

Figure 4: Volcano plot of significantly different mutations in LM vs OM.

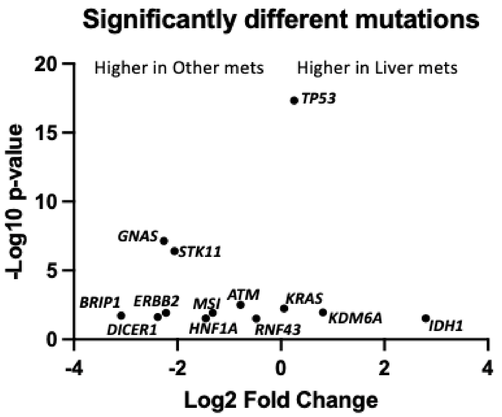


Figure 3: TME (Quantiseq) and RNA signatures significantly different in LM vs OM.

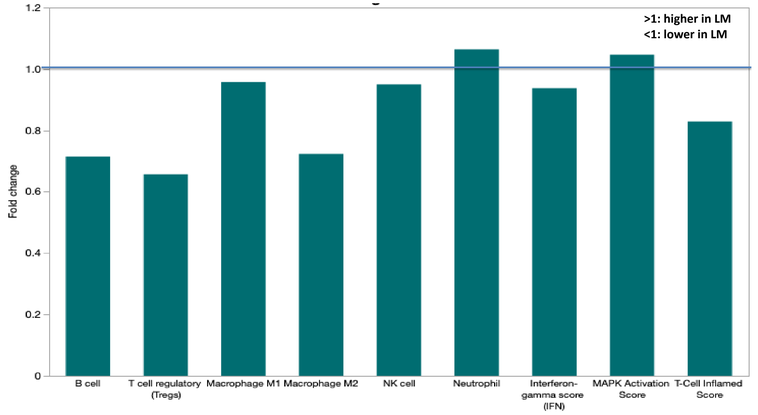


Figure 1B: OS from start of ICI to last contact

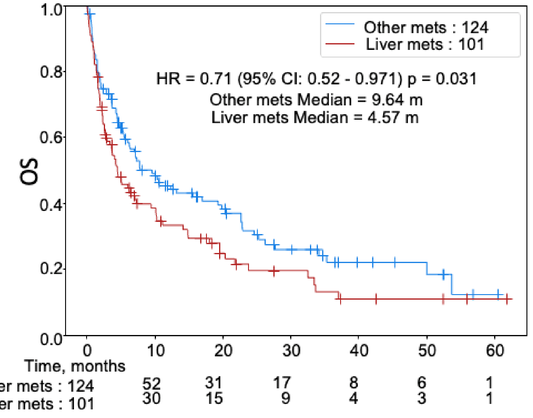
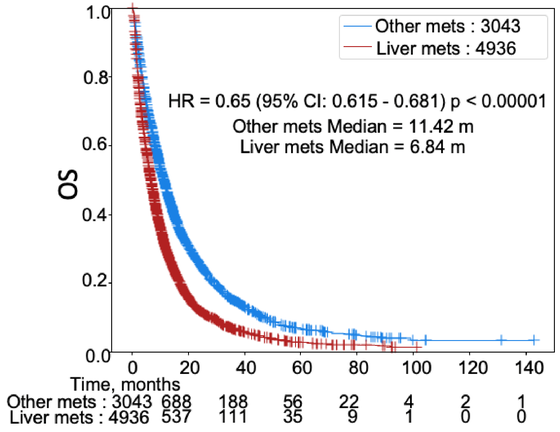


Figure 1A: OS from collection to last contact



Conclusions

- When comparing pancreatic LM to OM sites, our data reinforces the observation that OS is better in OM when compared to LM and response to ICI was better in OM vs. LM.
- Significant differences were observed in the molecular landscape, tumor immune microenvironment as well and signatures that are predictive of immunotherapy response (TIS and IFG scores).

Figure 1C: OS from start of Gemcitabine/Nab-paclitaxel to last contact