Abstract #366: Renal cell carcinoma (RCC) metastatic to pancreas is associated with a distinct molecular profile and immune cell population

Ryan S Chiang[1], Arya Ashok[2], Elizabeth Mauer[2], Alexander S. Barrett[2], Christian Hoerner[1], Osama Khan[1], Chia-Sui Kao[1], Sumit Shah[1], Sandy Srinivas[1], Alice Fan[1], and Ali Raza Khaki[1]

[1]Stanford University, Stanford, CA // [2]Tempus Labs, Inc., Chicago, IL

INTRODUCTION

- Pancreatic metastases in RCC have been associated with indolent biology, low genomic instability and decreased inflammation, which may lead to worse responses to immunotherapy
- We compared the genomic landscape and immunotherapy biomarkers in patients with metastatic RCC with and without pancreatic metastases

METHODS

- We identified patients in the Tempus database with metastatic RCC who received next generation sequencing via the Tempus xT assay (DNA-seq of 648 genes at 500x coverage; whole-exome capture RNA-seq)
- Patients with RCC and metastases to at least one of: pancreas, liver, brain, or lung (regardless of the presence of other metastases) were included
- If individuals had multiple xT results, results from the most recent sample were included (irrespective of tissue site)
- We compared the prevalence of somatic gene alterations (using false discovery rate corrected q-values) and immunotherapy markers among patients with and without pancreatic metastases
- Statistical significance was determined via the Kruskal-Wallis H test or Chi-squared/Fisher's exact test.

Ryan S Chiang
rschiang@stanford.edu
@RyanChiangMD

Ali Raza Khaki
alikhaki@stanford.edu
@arkhaki

SUMMARY

Patients with **RCC** and **pancreatic metastases** have a distinct molecular profile and lower rates of PD-L1 positivity, which suggests a **unique disease biology** and potential **non-immunogenic phenotype**. Further investigation and prospective validation is needed to determine immunotherapy outcomes in this population.

RESULTS

Patient demographics and clinical characteristics

Characteristic	Overall, N = 540	Pancreas, N = 58	Lung, N = 358	Liver, N = 88	Brain, N = 36
Age at Diagnosis - Median (IR)	61 (53, 68)	58 (50, 66)	62 (54, 69)	61 (51, 67)	60 (51, 64)
Gender					
Male	373 (69%)	33 (57%)	262 (74%)	51 (59%)	27 (75%)
Female	164 (31%)	25 (43%)	94 (26%)	36 (41%)	9 (25%)
Race					
White	277 (83%)	32 (80%)	188 (86%)	39 (71%)	18 (86%)
Black or African American	24 (7.2%)	3 (7.5%)	8 (3.7%)	11 (20%)	2 (9.5%)
Asian	11 (3.3%)	3 (7.5%)	5 (2.3%)	2 (3.6%)	1 (4.8%)
Other Race	22 (6.6%)	2 (5.0%)	17 (7.8%)	3 (5.5%)	0 (0%)
Ethnicity					
Not Hispanic or Latino	135 (76%)	15 (83%)	85 (72%)	24 (86%)	11 (85%)
Hispanic or Latino	42 (24%)	3 (17%)	33 (28%)	4 (14%)	2 (15%)
Primary Cancer Site					
Chromophobe RCC	10 (1.9%)	1 (1.7%)	0 (0%)	7 (8.0%)	2 (5.6%)
Clear Cell RCC	326 (60%)	38 (66%)	218 (61%)	49 (56%)	21 (58%)
Kidney Cancer	201 (37%)	18 (31%)	138 (39%)	32 (36%)	13 (36%)
Non-Clear Cell RCC	3 (0.6%)	1 (1.7%)	2 (0.6%)	0 (0%)	0 (0%)

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Pancreatic metastases display unique immuno-biology

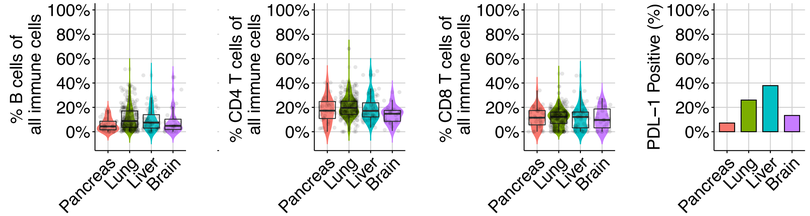

Figure 1. Pancreatic metastases have lower rates of PD-L1 positivity (far right) compared to other metastases. They also have lower proportions of B-cells (far left), similar percentages of CD4 and CD8 T cells (center panels), and higher proportions of NK cells (not shown).

Pancreatic metastases have a unique molecular landscape

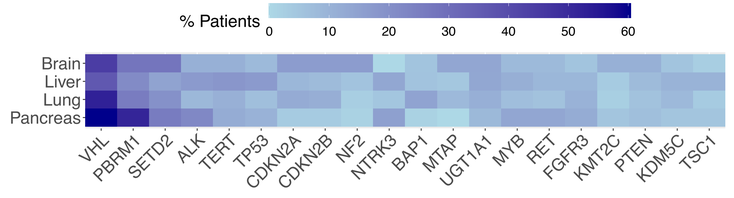

Figure 2. In comparison to brain, liver, and lung metastases, pancreatic metastases had significantly higher frequencies of *PBRM1* mutations (q < 0.001) and trended towards more prevalent copy number loss of *ALK* (22% vs 10%, q = 0.06) and *NTRK3* (16% vs 6%, q = 0.08) as well as less prevalent alterations in *CDKN2A* (3% vs 13%, q = 0.08), *BAP1* (2% vs 13%, q = 0.06) and *MTAP* (0% vs 9%, q = 0.06).