1483P- CELL-FREE DNA DOMINANT CLONE ALLELE FREQUENCY ASSOCIATES WITH POOR OUTCOMES IN ADVANCED PANCREATIC CANCER

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ABSTRACT

Background: Circulating cell-free tumor DNA (ctDNA) is an emerging tool under investigation in pancreatic cancer (PC). This study aimed to evaluate the prognostic value of ctDNA variant allele frequency (VAF) in advanced PC collected at diagnosis.

Methods: For analysis we considered the detected gene with highest VAF as the dominant clone allele frequency (DCAF). The DCAF was evaluated in relation to patients' demographics, systemic treatment response, progression-free survival (PFS) and overall survival (OS).

Results: A total of 104 patients were included in the analysis. Somatic alterations were detected in 84.6 % of the patients and were more pronounced in metastatic PC, 91% of metastatic PC patients had at least one genetic alteration detected compared to 74% of patients with locally advanced disease (p=0.03). 66 patients underwent chemotherapy with gemcitabine and nab-paclitaxel (64%) and 29 patients with FOLFIRINOX (28%). The median DCAF was 0.45% (0-55%). DCAF >0.45% was associated with worse median PFS (median PFS: 6 vs. 14 months, p=0.00013) and median OS (median OS: 10 vs. 24 months, p=0.00027).

Conclusions: Patients with advanced PC with DCAF > 0.45% at diagnosis have worse PFS and OS compared to patients with low ctDNA.

OBJECTIVES

- To evaluate the prognostic value of ctDNA variant allele frequency (VAF) in advanced PC collected at diagnosis.

METHODS

- A total of 104 patients with advanced pancreatic cancer and ctDNA collected at time of initial diagnosis were retrospectively evaluated.
- We considered the detected gene with highest VAF as the dominant clone allele frequency (DCAF).
- DCAF was evaluated in relation to patients' demographics, systemic treatments, progression-free survival (PFS) and overall survival (OS).

RESULTS

- Median age was 70 years (43-91), 50% male, 38.5% with LAPC and 61.5% with metastatic disease.
- The most detected genes were KRAS, TP53, CDKN2A and SMAD4.
- 91% of metastatic PC patients had at least one genetic alteration detected compared to 74% of patients with LAPC (p=0.03).
- Median DCAF was 0.45% (0-55%).
- DCAF >0.45% was associated with worse median PFS (median PFS: 6 vs. 14 months, p=0.00013) and median OS (median OS: 10 vs. 24 months, p=0.00027).

FIGURE 1: OVERALL SURVIVAL CURVES STRATIFIED BY CTDNA

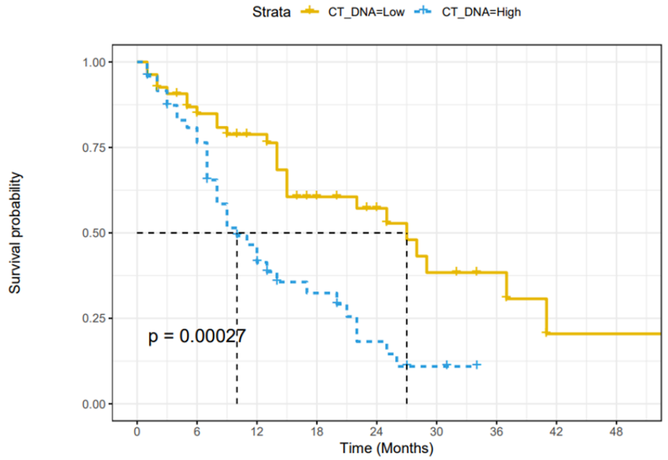
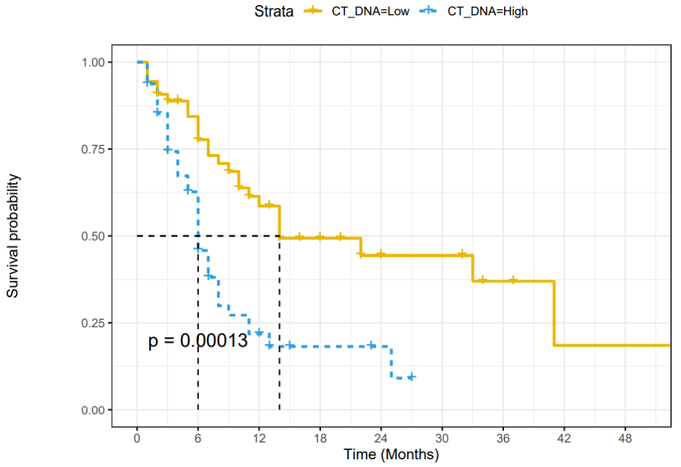


FIGURE 2: PFS CURVES STRATIFIED BY CTDNA



DISCUSSION

- Variant allele frequency of somatic mutations detected by ctDNA is related to outcomes in multiple types of advanced cancer.
- In this study, a higher rate of genetic alterations in ctDNA were detected in metastatic pancreatic cancer when compared to locally advanced disease (p=0.03)
- In our analysis, median of DCAF was 0.45% and is significantly associated with worse PFS and OS.
- These results reinforce that VAF and DCAF can be used as a stratification tool in pancreatic cancer, however the cutoff value to be used should be carefully evaluated in larger cohorts or prospective trials.

CONCLUSIONS

- Patients with advanced PC with DCAF > 0.45% at diagnosis have worse PFS and OS compared to patients with low ctDNA.