Detecting early failure in pancreatic cancer:

Persistent ctDNA identifies chemotherapy resistance after neoadjuvant therapy

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Background

- Pancreatic ductal adenocarcinoma (PDAC) has a 5-year survival of <10%, with a **recurrence rate of 70-80%** within 2 years.[1,2]
- Circulating tumor DNA (ctDNA) is an emerging prognostic biomarker for identifying **minimal residual disease (MRD)**, but its role as a quantitative measure for stratifying recurrence risk is unclear.[3]
- ***KRAS* mutations** are primary drivers in >90% of PDAC, making it a practical target of interest.[4]

Research Objectives

To evaluate *KRAS* ctDNA for identifying MRD and risk of early recurrence in patients with resected PDAC who received neoadjuvant chemotherapy (NAC).

Methods

- Patients with localized PDAC were enrolled in a prospective trial October 2020-December 2024.
- Blood samples were drawn at diagnosis, after NAC, and after resection and analyzed for *KRAS* G12D, G12V, or G12R ctDNA using digital droplet PCR (ddPCR).
- This study included patients receiving both NAC and resection.
- Analyses were conducted in R (v.4.5.1).

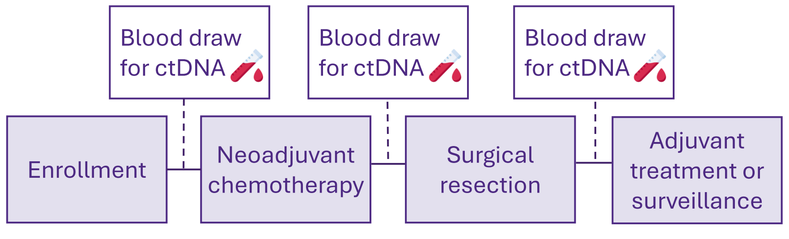
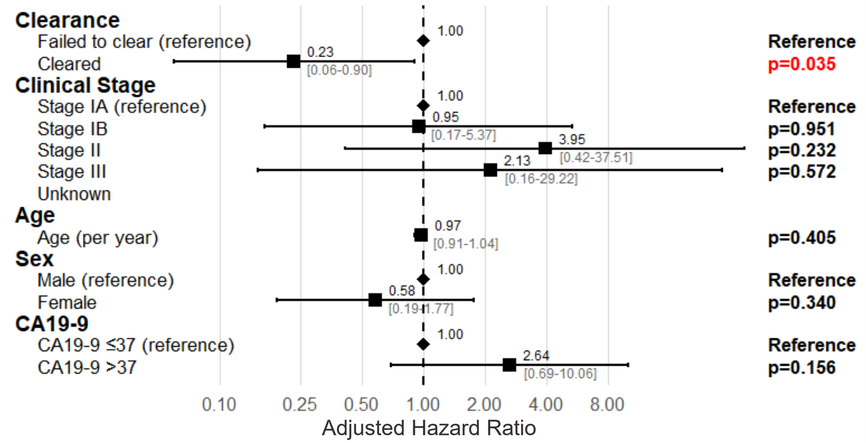
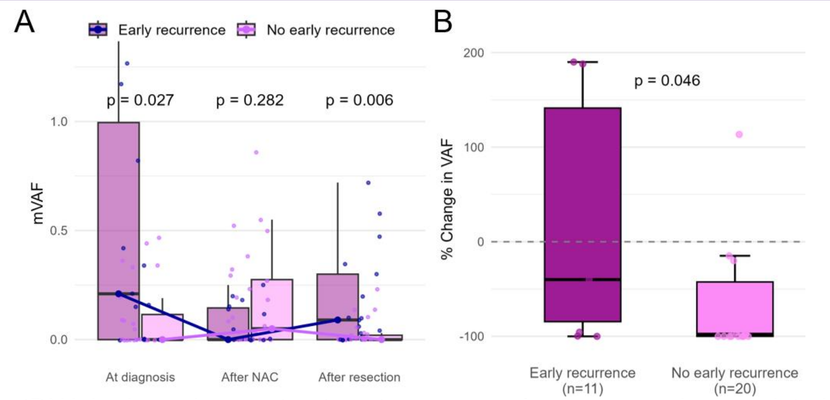


Figure 1. RFS by ctDNA clearance



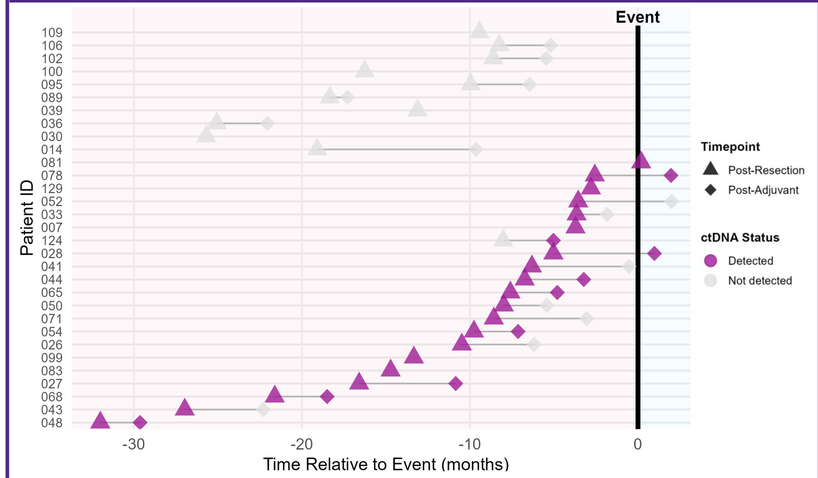
- ctDNA clearance is **independently prognostic**, with **complete clearance** predicting improved recurrence-free survival (RFS)

Figure 2. Quantitative ctDNA burden



- ctDNA is dynamic over treatment course; early recurrence is associated with **higher maximum VAF (mVAF)**
- **Even in the absence of full clearance,** quantity cleared is clinically meaningful; more cleared is associated with better outcomes

Figure 3. Timing of ctDNA detection



- ctDNA is detected **prior** to radiographic confirmation of recurrence by a median of **7.8 months**

Limitations

This study was limited by its modest sample size (n=55), single institution design, and limited post-resection follow up (15 months).

Conclusions

- *KRAS* ctDNA after multimodality treatment may **identify MRD and early recurrence** in PDAC.
- Patients with persistent ctDNA after NAC and surgery may derive greater benefit from *KRAS*-targeted treatments.

References

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