12P - Circulating tumor DNA as early marker of response to treatment in stage IV pancreatic cancer

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Background: Circulating tumor DNA (ctDNA) represents a promising tool for diagnosis, prognosis, and treatment monitoring of several malignant diseases. We aimed to investigate ctDNA as early marker of response to treatment, ideally within the first cycle, as current gold standard computed tomography is performed after 3 months of treatment. **Material and Methods:** Liquid biopsy (Digital droplet PCR screening for KRAS G12/13 and Q61) for ctDNA detection was prospectively obtained from patients with stage IV pancreatic ductal adenocarcinoma (PDAC, n=70) prior to a new line of systemic chemotherapy. **Results:** ctDNA was detectable in 64.3% of pretherapeutic samples. Median mutant allele fraction (MAF) was 1.6% (IQR 0.3-5.1). Progressive disease was detectable in 100% of patients at a median of 14 days (IQR 9-21) and non-progressive disease in 95% of patients at a median of 15 days (IQR 12.25-24.5) when using a cut-off for response evaluation of decrease under 50% at first readmission (Fig. 1). Thus, lead time was 10 weeks compared to conventional computed tomography (after 3 months) during clinical routine. Pretherapeutic ctDNA detectability was associated with significantly worse survival independent of treatment line (Fig. 2A-B). Moreover, ctDNA kinetics with a decrease of under 50% after two weeks was identified to be of further prognostic value for OS (5.7 vs. 11.4 months, p=0.009, Fig. 2C-D) and PFS (2.2 vs. 5.6 months, p<0.000). **Conclusion:** Liquid biopsy bears the potential for real time assessment of tumor burden and precision oncology in about 2/3 patients with PDAC, although the actual amount of ctDNA detectable in the patients' blood is low when compared to other tumor entities (f.e. 10-fold higher in colorectal cancer). Apart from prediction of worse clinical outcome in pretherapeutic samples, ctDNA allows early response to treatment and further prognostic evaluation within the first two weeks of systemic chemotherapy by serial liquid biopsy in pancreatic cancer.

Fig. 1 Early ctDNA change after 2 weeks of treatment predicts response to treatment

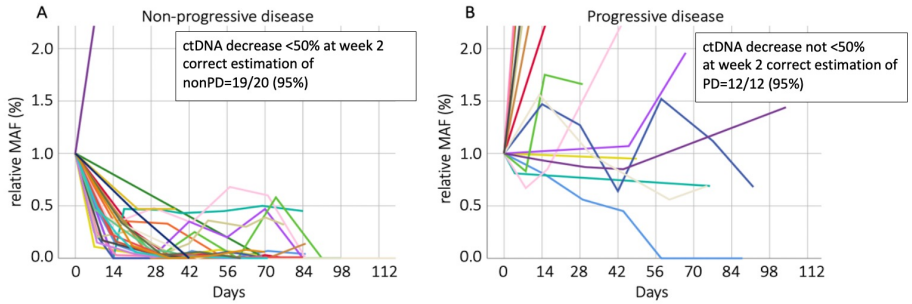
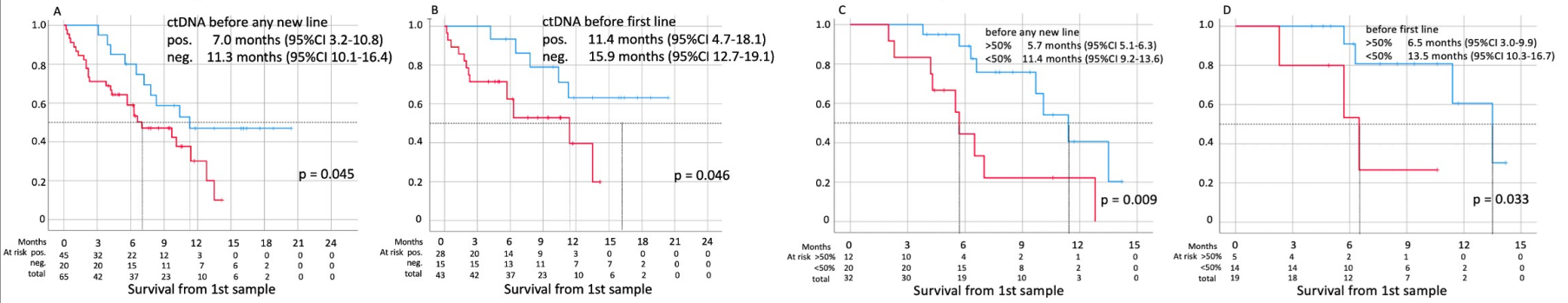


Fig. 2 Pretherapeutic ctDNA detection and ctDNA kinetics after 2 weeks of treatment predict outcome



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