Abstract #518574: Ultrasensitive Structural Variant-based ctDNA detection of MRD in Colorectal Cancer – the CITCCA study

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Background

- Colorectal cancer (CRC) is the second-leading cause of cancer death globally, and incidence of CRC is rising
- Treatment is increasingly individualized
- Sensitive methods to detect molecular residual disease (MRD) and guide neoadjuvant and adjuvant treatment are needed
- Circulating tumor DNA (ctDNA) can identify patients with a high risk of relapse and may be a useful biomarker to aid clinical decision making
- We evaluate an ultrasensitive structural variant (SV)-based ctDNA assay (Pathlight™) for detection of MRD in CRC

Methods

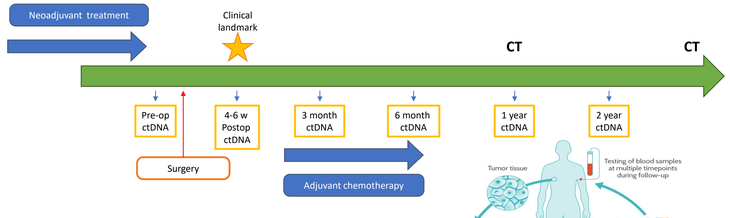


Figure 1. CITCCA trial, ctDNA sampling

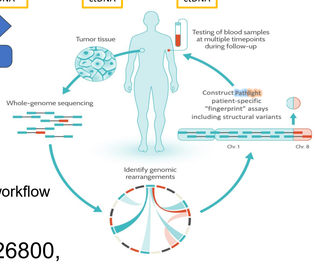


Figure 2. Pathlight workflow

- Prospective cohort study (NCT04726800, **C**irculating **T**umour DNA (ctDNA) as a Prognostic and Predictive Marker in **C**olorectal **Ca**ncer, CITCCA)
- 377 patients, colon cancer (n=232) and rectal cancer (n=145), stage I-III, SOC treatment and follow-up
- Seven centres in Sweden (Oct 2020 - Jan 2024)
- Tumor-informed SV-based ctDNA assay
- Primary endpoint: Association between ctDNA and RFI
- Secondary endpoint: Pathlight's clinical performance

Results

ctDNA tracking in stage I-III colorectal cancer is highly prognostic

Ultrasensitive SV-based ctDNA detection can inform adjuvant treatment decisions

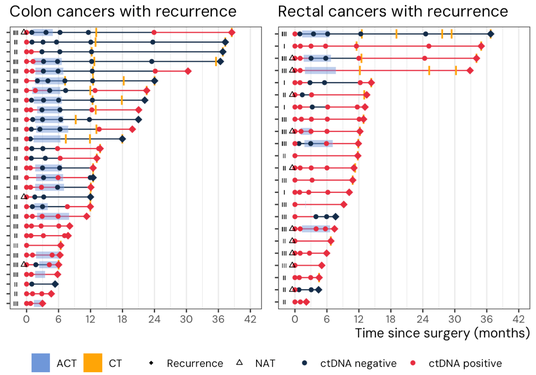
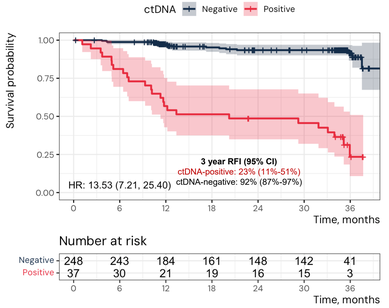


Figure 3. Swimmer plots for patients with recurrence, from time of surgery.
Note: 3 patients with ctDNA detection <2 months post-recurrence counted as false negatives as all ctDNA results post-recurrence are censored. 3 patients experienced recurrence >1 year after the last ctDNA result.
ACT = Adjuvant chemotherapy, NAT = Neoadjuvant therapy, CT = Computed tomography

Risk of recurrence

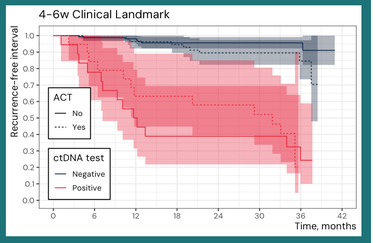
- Confounder adjusted hazard ratios (HR) with 95% CI for ctDNA positive versus negative on the rate of RFI
- Overall: **HR 38.5** (18.73-79.17)
- Colon cancer: **HR 33.78** (13.46-84.75)
- Rectal cancer: **HR 93.51** (19.89-439.62)
- Patients with ctDNA detected following curative intent treatment had a **significantly higher risk of recurrence**

Clinical landmark (4-6w post-surgery)



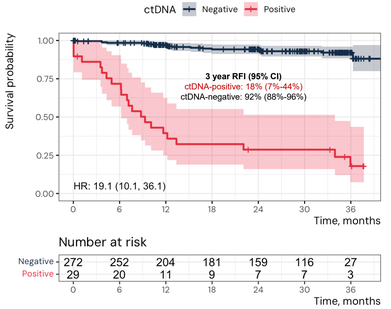
- 42.5% of positives at clinical landmark were in the ultrasensitive range (<100 ppm)

Clinical landmark (4-6w post-surgery) stratified by adjuvant chemotherapy (ACT)



- Recurrence risk was markedly higher in ctDNA positive patients who did not receive ACT
- ctDNA can help guide ACT treatment decisions

First sample after definitive treatment



Surveillance post-definitive therapy

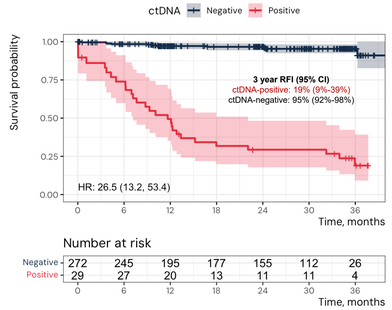


Figure 4. Kaplan Meier curves with estimated recurrence-free interval (RFI) from time of surgery.

Future Directions

- Conducting a randomized trial using ultrasensitive SV-based ctDNA detection for decision making in the neoadjuvant and adjuvant setting in CRC

Acknowledgements

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