Abstract #3278

Prognostic value of post-surgery liquid biopsy cell-free circulating tumor DNA in stage III colon cancer patients - PLCRC-PROVENC3 study

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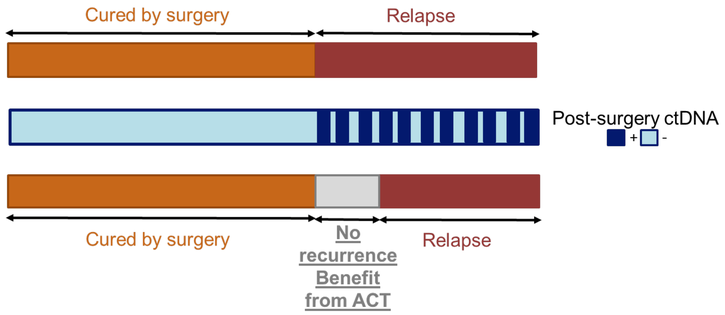
Background

- Current clinical guidelines in the Netherlands recommend ACT following resection of the primary tumor for all stage III colon cancer patients.
- Only **11%** of the patients benefit from ACT[1,2,3]
- **Prognostic biomarkers** are urgently needed



- Post-surgery circulating tumor DNA (**ctDNA**) detection indicates minimal residual disease and is a strong prognostic factor: around 30% of the patients that develop a recurrence are ctDNA+ at this timepoint [4,5].

Goal of the study

Investigate whether ctDNA testing could avoid futile adjuvant chemotherapy (ACT) for stage III colon cancer patients

Research questions

Primary research questions:

- Determine what proportion of stage III colon cancer patients has a post-surgery ctDNA-positive test.
- Determine recurrence rates in both post-surgery ctDNA-negative and post-surgery ctDNA-positive ACT-treated patients.
- Determine the optimal strategy to apply ctDNA-guided personalized treatment, to improve disease management of (subsets of) stage III colon cancer patients.

Secondary research questions:

- Determine whether pre-surgery ctDNA mutant allele fractions have prognostic value for disease recurrence.
- Determine the lead time of ctDNA detection compared to clinical imaging-based detection of disease recurrence.

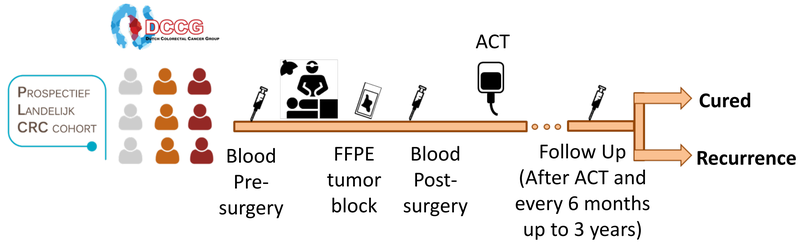
Study population

- **267 Stage III colon cancer** patients that received **ACT**
- Consent to use FFPE tumor
- Estimated distribution of patients:
  - 40 ctDNA-positive
  - 227 ctDNA-negative

Experimental approach: PROVENC3 study

PROVENC3: (**PRO**gnostic **V**alue of **E**arly Notification by **C**tdna in Colon Cancer stage **3**).

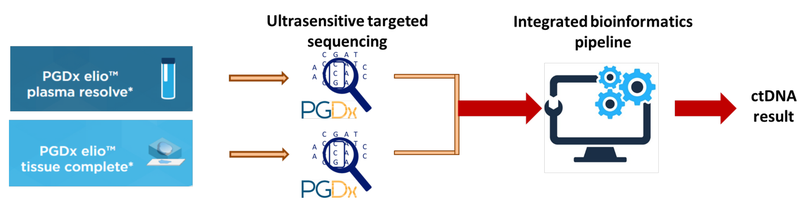
- PROVENC3 is an **observational** study within the Prospective Dutch Colorectal Cancer Cohort (PLCRC, https://plcrc.nl/for-international-visitors).
- 25 Participating hospitals in The Netherlands.



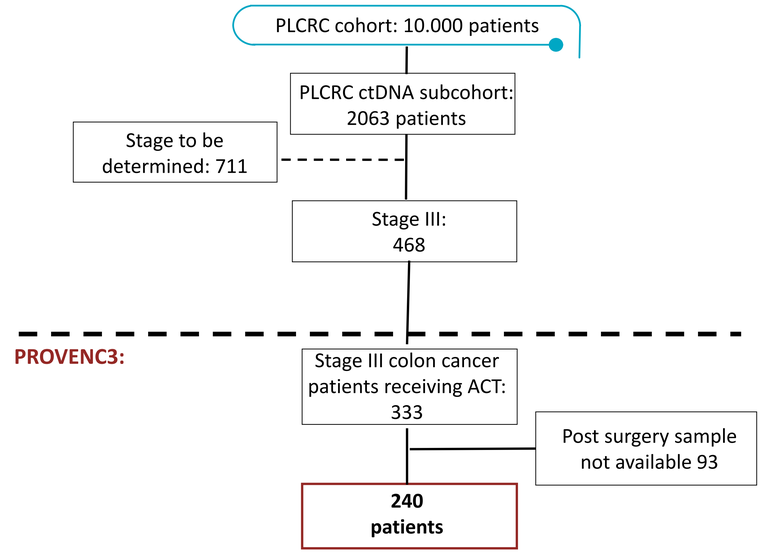
- Post-surgery blood sample is collected from day 4 after surgery.
- All biosamples are sent to a central location (The Netherlands Cancer Institute).
- Clinical data is collected by PLCRC team and The Netherlands Cancer registry.

Tissue-guided ctDNA detection (PGDx technology)

- Tissue-guided plasma ctDNA analysis for improved sensitivity and specificity compared with analyzing plasma-only:
  - Detection of down to 2 ctDNA molecules in cfDNA.
  - False positives due to clonal hematopoiesis can be excluded.



Current patient accrual



Next steps and future plans

- Complete clinical data collection
- Tumor Blocks request via the Dutch Public Pathology Database ("Pathologisch-Anatomisch Landelijk Geautomatiseerd Archief" palga)
- Sample analysis:

Ultrasensitive targeted sequencing	WGS Shallow-Seq	Tissue microarrays generation
• ctDNA detection • Characterization of the primary tumor (point mutations).	• Copy number analysis • Breakpoints detection	• Immunohistochemical validation of predictive and prognostic biomarkers

- Integration and data analysis: cBioPortal FOR CANCER GENOMICS, health RI

References

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FUNDED BY Dutch Cancer Society, Maarten van der Weijden foundation, Health~Holland

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