Background

- Current clinical guidelines in the Netherlands recommend adjuvant chemotherapy treatment (ACT) following resection of the primary tumor for all stage III colon cancer patients.
- Only 15-20% of the patients benefit from ACT; around 55% of stage III colon cancer patients are cured by surgery alone and are being overtreated, and 30% will relapse despite ACT.
- Prognostic biomarkers may improve ACT decisions and reduce futile treatment in this group of patients by identifying the patients at a higher risk of recurrence that could benefit from ACT.

Post-surgery circulating tumor DNA (ctDNA) detection indicates presence of minimal residual disease, and it is a strong prognostic factor in stage II and III colorectal cancer.

Goal of the study

Investigate the prognostic value of post-surgery ctDNA testing for disease recurrence in ACT treated stage III colon cancer patients.

Experimental approach: PROVENC3 study

- PROVENC3: (PROgnostic Value of Early Notification by ctDNA in Colon Cancer stage III).
- PROVENC3 is an observational study within the Prospective Dutch Colorectal Cancer Cohort (PLCRC, https://plcrc.nl/for-international-visitors).
- 26 Participating hospitals in PROVENC3.

Experimental approach: ctDNA detection method

Tumor-informed detection of plasma ctDNA through integrated whole genome sequencing (WGS) analyses:

- ctDNA+: 7.7 months (95% CI: 4.0, 11.4).
- ctDNA-: 13.3 months (95% CI: 9.4, 17.2).

Clinicopathological characteristics and ctDNA MRD results

Results for 114 patients with post-surgery ctDNA analyzed and clinical follow up (FU) information about recurrence available. Median FU 31 months, IQR: 18 months.

41% of the patients that experienced a recurrence had detectable minimal residual disease (MRD) post-surgery, and 30% of the ctDNA+ patients were likely cured by ACT:

Conclusions

- Post-surgery ctDNA testing improves the stratification of stage III colon cancer patients for disease recurrence on top of current clinicopathological risk factors.
- Approximately one third of the ctDNA-positive patients seem to benefit from ACT.

Next steps

- Complete sample analysis and clinical data collection.
- Based on the results of this study, design of an interventional study towards implementation of ctDNA testing for stage III colon cancer patients.