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Cell-free DNA fragmentomes for treatment response monitoring in patients with metastatic colorectal cancer: the DOLPHIN study

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Introduction

- Accurate monitoring of treatment response in patients with metastatic colorectal cancer (mCRC) is essential for optimizing therapeutic strategies
- Currently, treatment response is determined by imaging
- Analysis of cell-free DNA (cfDNA) fragmentation patterns may offer a sensitive, non-invasive, and tissue agnostic approach to monitor treatment response in mCRC patients[1]

Study aim

Evaluate the clinical added value of DELFI-TF to conventional imaging-based response monitoring in patients with mCRC

Methods

- **DOLPHIN is a prospective, observational study within the Prospective Dutch ColoRectal Cancer cohort[2] (PLCRC)**

Patient population

- Patients diagnosed with mCRC who receive systemic treatment +/- local therapy
- PLCRC informed consent, including additional blood withdrawal
- Inclusion before start second line of therapy

Blood and image collection

- Blood collection every 8-12 weeks aligned with imaging.
- Samples are collected within a 14-day window around each scan and sent to The Netherlands Cancer Institute.
- Images are centrally collected via Health-RI XNAT

ctDNA analysis

- DELFI tumor fraction (DELFI-TF)
- ddPCR

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Study design

DOLPHIN: DNA-testing **O**f **L**iquid biopsies for **P**atient care close to **H**ome **I**n the **N**etherlands.

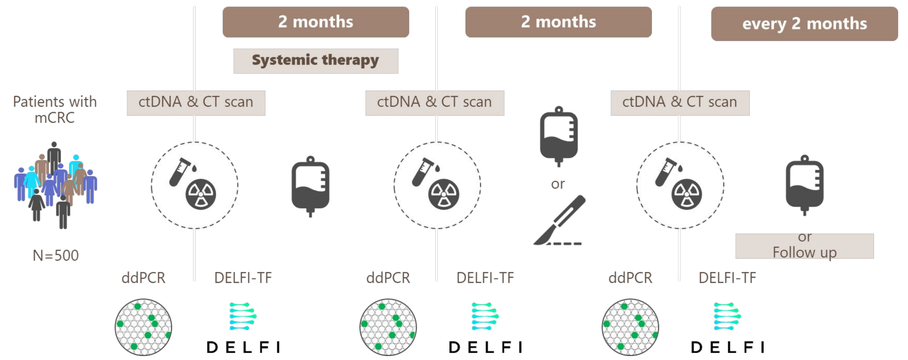

Figure 1. The DOLPHIN study design

Results

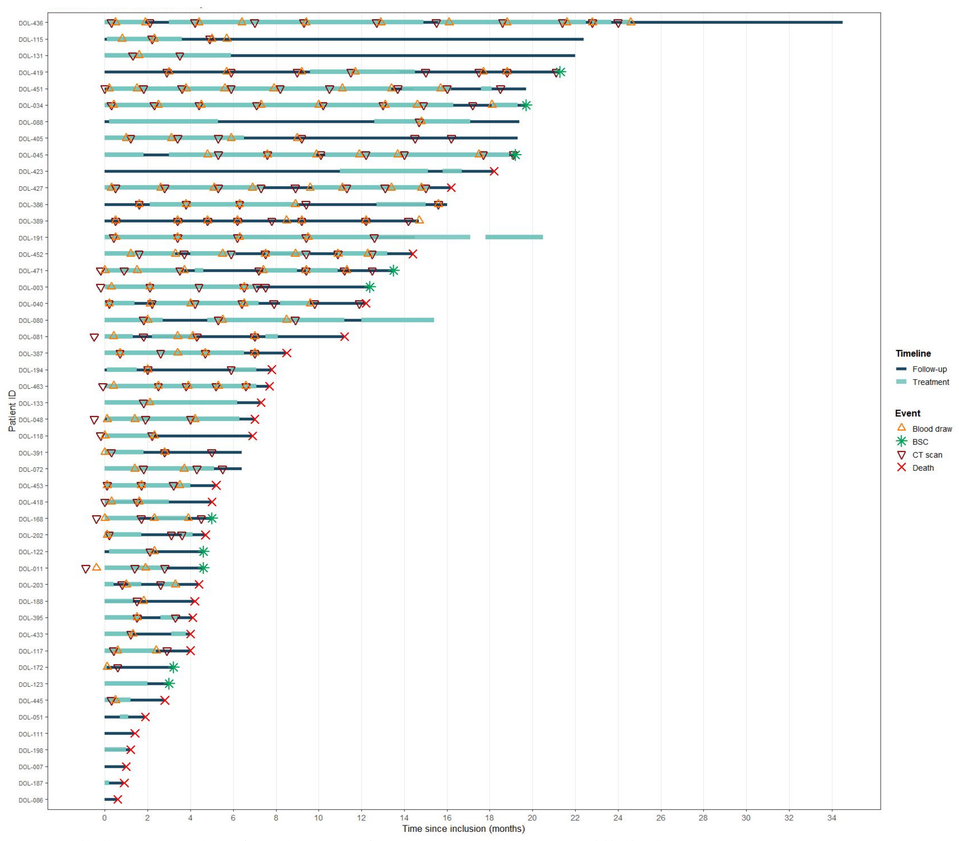

Figure 2. Swimmer plot of a subgroup of patients included in the DOLPHIN study, showing treatment duration, follow-up time, and clinical events. Symbols indicate computed tomography (CT), blood draws, surgery, best supportive care (BSC), and death.

	Overall (N=504)
Age at inclusion	
Mean (SD)	64.1 (11.6)
Median [Min, Max]	62.0 [22.0, 90.0]
Sex	
Male	285 (56.5%)
Female	219 (43.5%)
Sidedness	
Right	38 (7.5%)
Left	30 (6.0%)
Rectum	32 (6.3%)
Rectum + right (double)	2 (0.4%)
Unknown	402 (79.8%)
Time of mCRC development	
Metachronous	35 (6.9%)
Synchronous	67 (13.3%)
Unknown	402 (79.8%)
BRAF	
MT	59 (11.8%)
WT	337 (67.1%)
Unknown/ not determined	106 (21.1%)
KRAS	
MT	230 (45.8%)
WT	201 (40.0%)
Unknown/ not determined	71 (14.1%)
NRAS	
MT	17 (3.4%)
WT	333 (66.3%)
Unknown/ not determined	152 (30.3%)
MMR/MSI status	
MSS	434 (86.4%)
MSI	45 (9.0%)
Unknown/not determined	23 (4.6%)
Primary tumor resection	
Resected	60 (11.9%)
Not resected	43 (8.5%)
Missing/unknown	401 (79.6%)
Organs involved at DOLPHIN inclusion	
Liver only	13 (2.6%)
Lymph node only	2 (0.4%)
Lung only	2 (0.4%)
Peritoneum only	4 (0.8%)
Multiple	75 (14.9%)
Missing	408 (80.9%)

Table 1. Overview of the baseline clinical and molecular characteristics of the DOLPHIN patients included to date (N= 504).

Conclusions

Patient inclusion has been successful and a strong alignment of blood samples with CT scans is observed.

Next steps

- Sample analysis : ddPCR and DELFI-TF
- Health technology assessment
- Processed data regarding the DOLPHIN clinical trial will be stored in cBioPortal

References

1. van 't Erve, I., Alipanahi, B., Lumbard, K. et al. Cancer treatment monitoring using cell-free DNA fragmentomes. Nat Commun 15, 8801 (2024). https://doi.org/10.1038/s41467-024-53017-7
2. https://plcrc.nl/project/dolphin-dna-testing-of-liquid-biopsies-for-patient-care-close-to-home-in-the-netherlands