Abstract: 5801

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

Study aim

Investigate the added clinical value of the DELFI-TF score compared to CT imaging for treatment response monitoring in patients with mCRC

Methods

- **DOLPHIN is a prospective, observational study within the Prospective Dutch ColoRectal Cancer cohort (PLCRC, https://plcrc.nl/for-international-visitors)**

Patient population

- Patients diagnosed with mCRC who are being treated with systemic treatment +/- local therapy
- All patients signed PLCRC informed consent, including additional blood withdrawal
- Inclusion before start second line of therapy

Blood and image collection

- Longitudinal blood collection: every 8-12 weeks in conjunction with imaging.
- Blood samples are aimed to be coupled to every CT scan and collected within a 14-days time window.
- All blood samples are being send to The Netherlands Cancer Institute.
- Images will be collected centrally using Health-RI XNAT

ctDNA analysis

- DELFI tumor fraction (DELFI-TF)
- ddPCR

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Results

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

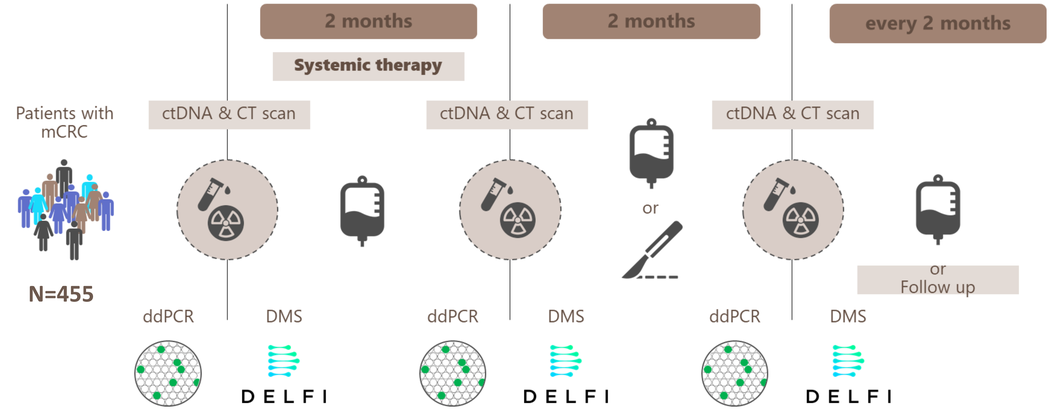

Figure 1. DOLPHIN study design

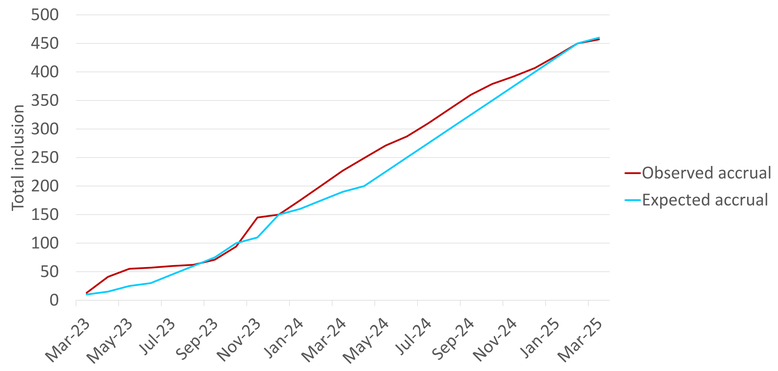

Figure 2. Graph showing the DOLPHIN accrual over time since the start of the study in March 2023.

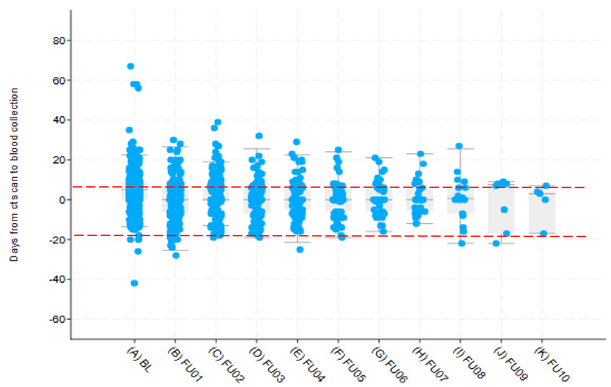

Figure 3. Boxplot showing the time difference between blood sample collection and CT scan across collection timepoints. CT scans were matched to 98% of samples, with 86.2% collected within 14 days (n = 1185).

	Overall (N=455)
Gender	
Male	252 (55.4%)
Female	200 (44.0%)
Missing	3 (0.7%)
Time of metastases	
Metachronous	155 (34.1%)
Synchronous	236 (51.9%)
Missing	64 (14.1%)
Inclusion timepoint	
Before 1st line	46 (10.1%)
Before 2nd line	152 (33.4%)
During 1st line	123 (27.0%)
Unknown	134 (29.5%)
Metastatic site at baseline	
Liver only	94 (20.7%)
LN only	13 (2.9%)
Lung only	9 (2.0%)
Peritoneum Only	24 (5.3%)
Other only	6 (1.3%)
Multiple	144 (31.6%)
Missing	165 (36.3%)
Primary Tumor Resected	
No	223 (49.0%)
Yes	231 (50.8%)
Missing	1 (0.2%)
KRAS	
MT	203 (44.6%)
WT	154 (33.8%)
Unknown	97 (21.5%)
Missing	1 (0.2%)
NRAS	
MT	17 (3.7%)
WT	250 (54.9%)
Unknown	186 (40.9%)
Missing	2 (0.4%)
BRAF	
MT	53 (11.6%)
WT	258 (56.7%)
Unknown	142 (31.2%)
Missing	2 (0.4%)
PIK3CA	
MT	60 (13.2%)
WT	128 (28.1%)
Unknown	265 (58.2%)
Missing	2 (0.4%)
MMR/MSI status	
MSI - Instable	40 (8.8%)
MSS - Stable	392 (86.2%)
Unknown/Not Determined	23 (5.1%)

Table 1. Overview of the baseline clinical and molecular characteristics of the DOLPHIN patients included to date (n = 455). MT = Mutant; WT = Wild-type; MSI = Microsatellite Instable; MSS = Microsatellite Stable; KRAS = Kirsten rat sarcoma viral oncogene homolog; NRAS = Neuroblastoma RAS viral oncogene homolog; BRAF = v-Raf murine sarcoma viral oncogene homolog B1; PIK3CA = Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

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

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