

ctDNA testing in treatment response monitoring of patients with metastatic colorectal cancer: the DOLPHIN study

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Background & objectives

Accurate monitoring of clinical response is important for treatment decision-making in patients with metastatic colorectal cancer (mCRC). Currently, imaging-based assessment of changes in tumor size is used to determine clinical response. However, the number of images per patient per year is high and accompanied by an increasing workload at the radiology department. Detection of circulating tumor DNA (ctDNA) in liquid biopsies is indicative for viable neoplastic cells and may offer a complementary approach to monitor treatment response. Analysis of cell-free DNA (cfDNA) fragmentation patterns may offer a sensitive, affordable and broadly applicable ctDNA-test for treatment response monitoring in an extra mural setting.

The DOLPHIN study aims to investigate the clinical added value of longitudinal ctDNA-testing in treatment response monitoring of mCRC patients.

Methods

DOLPHIN is a prospective, observational study within the Prospective Dutch ColoRectal Cancer cohort (PLCRC). Clinical data, images and blood samples will be collected from 400 mCRC patients treated with systemic therapy in 8-10 hospitals in the Netherlands. Blood samples will be collected longitudinally every 8-12 weeks in conjunction with regularly scheduled imaging. If patients undergo local treatment after induction systemic therapy, blood samples will be collected at follow-up appointments every 3-6 months. Plasma cfDNA will be analyzed for tumor-specific fragmentation patterns and used to establish a tumor fraction score: DELFI-TF. Droplet digital PCR ctDNA-testing of RAS/RAF hotspot mutations will be performed as reference, when feasible. The primary endpoint is the correlation between ctDNA changes and clinical response. The secondary endpoints are the correlation between ctDNA changes and biochemical and radiological response according to RECIST at various time points during

systemic treatment, lead time of ctDNA-testing compared to imaging to detect progressive disease, and the prognostic value of longitudinal ctDNA-testing.

Results

The DOLPHIN study is currently open for patient accrual (February 2023).

Conclusion

The DOLPHIN study will assess the added clinical value of ctDNA-testing in treatment response monitoring of mCRC patients and whether imaging can be complemented and/or (partly) replaced by ctDNA-testing. This may result in better clinical outcome and will facilitate transfer of disease monitoring to the home living environment.