Circulating tumour cells & circulating tumour dna in patients with resectable colorectal liver metastases – a prospective cohort study (the miracle)

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Abstract

Background. Recurrence risk after curative surgery for colorectal liver metastases (CRLM) remains high, underlining the need to identify prognostic markers enabling more individualised treatment approaches. Objective. The aim of this study was to determine the association between recurrence-free survival (RFS) at one year and the detection of circulating tumour cells (CTCs) or circulating tumour DNA (ctDNA) before and after curative local treatment.

Methods. In the MIRACLE, a prospective, observational biomarker study, a total of 188 patients with isolated, resectable CRLM without (neo)adjuvant chemotherapy were included between October 2015 and December 2021. Blood samples were collected before surgery (T0) and three weeks (T3) after surgery. ctDNA before surgery was measured by next generation sequencing (NGS) using a targeted panel (Oncomine Colon cfDNA assay) and postoperatively by digital PCR (dPCR) on genetic variants found pre-operatively with the NGS panel. CTCs were enumerated using the FDA-approved CellSearch system.

Results. ctDNA was detected in 117 out of 187 patients (63%) at baseline, and 28 out of 104 evaluable patients (27%) still had detectable ctDNA at T3. CTC enumeration resulted in positivity for 37 out of 182 patients (20%) at baseline and 14 out of 158 patients (9%) at T3. No association was found between 1-year RFS and the presence of CTCs or ctDNA at baseline. In contrast, patients with postoperative undetectable ctDNA had a significantly improved 1-year RFS compared to patients with postoperative ctDNA (54% vs 25%, log-rank $p = 0.001$). Similarly, patients with postoperative detectable CTCs at T3 had a significantly shorter 1-year RFS compared to patients without postoperative CTCs (15% vs. 52%, log-rank $p < 0.001$). Also in multivariable analysis, both detectable ctDNA and CTCs after surgery remained independently associated with a shorter 1-year RFS (HR 2.10; $p = 0.007$ and HR 2.65; $p = 0.002$, respectively).

Conclusion. This is the first study conducted in patients with resectable CRLM without (neo)adjuvant chemotherapy, which demonstrates the impact of detectable circulating tumour load after surgery on 1-year RFS. Postoperative ctDNA and CTC detection both represent strong, independent predictors for a shorter RFS after local treatment, as opposed to preoperative ctDNA or CTC detection.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.