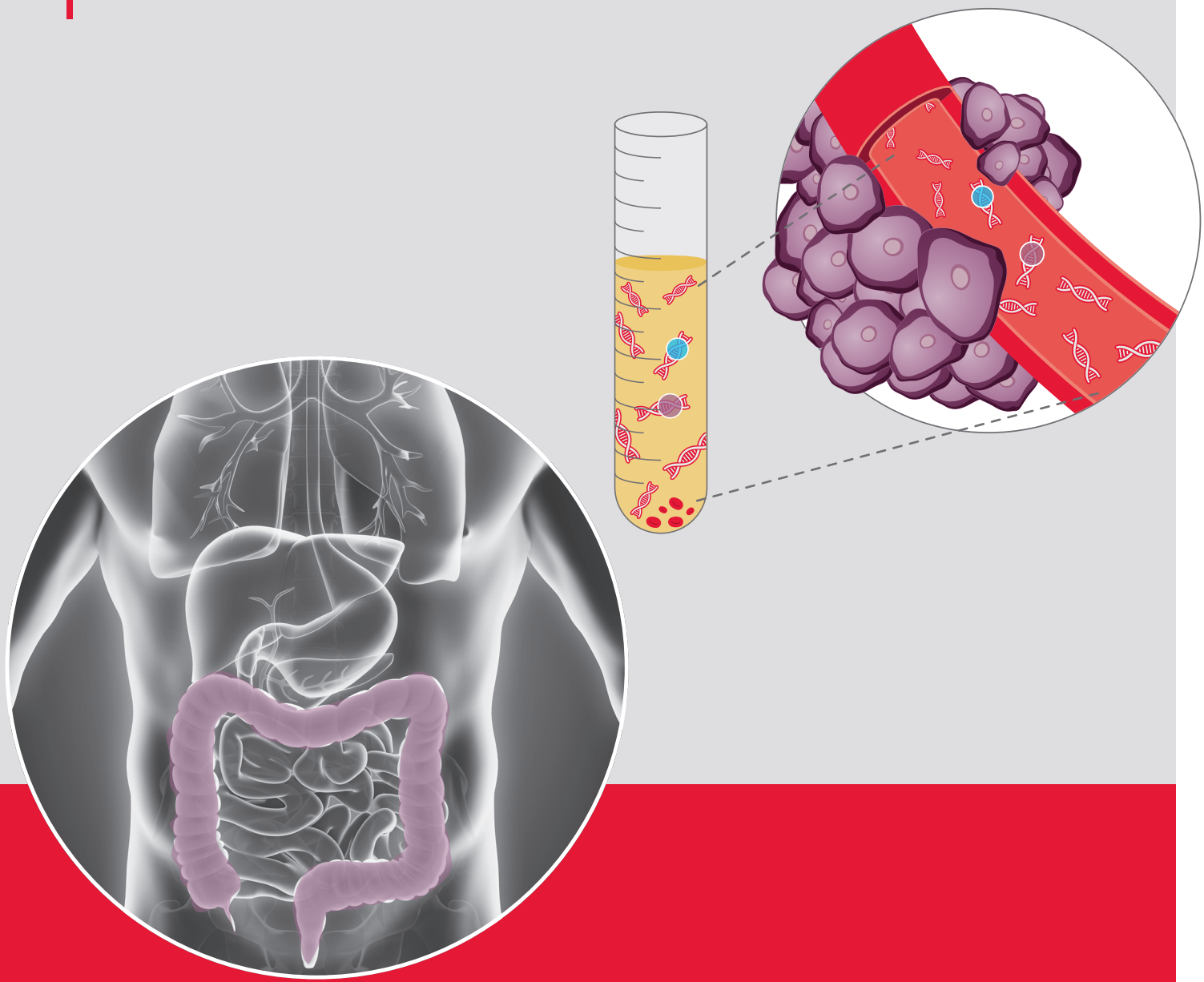
Institute for
Hematopathology
Hamburg

MRD status in patients with solid tumors

Circulating tumor DNA as biomarker for treatment decisions
Focus: Colon cancer



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Circulating tumor DNA for therapy management in solid tumors

In patients with CRC (colorectal cancer), the recommendation for adjuvant therapy is primarily based on TNM status, which can lead to overtreatment (1, 2) or undertreatment (3) in localized and resected CRC. This raises a number of open questions:

- Are the adjuvant therapy regimens for the treatment of colon cancer still up to date?
- Are the established risk factors sufficient to guide the intensity and duration of adjuvant therapy?
- Do we have meaningful biomarkers to decide for or against starting adjuvant therapy?

In particular, only about 3-5% of unselected stage II patients with CRC benefit from adjuvant chemotherapy (4), while the proportion is slightly higher at about 7% in patients with high-risk factors (5).

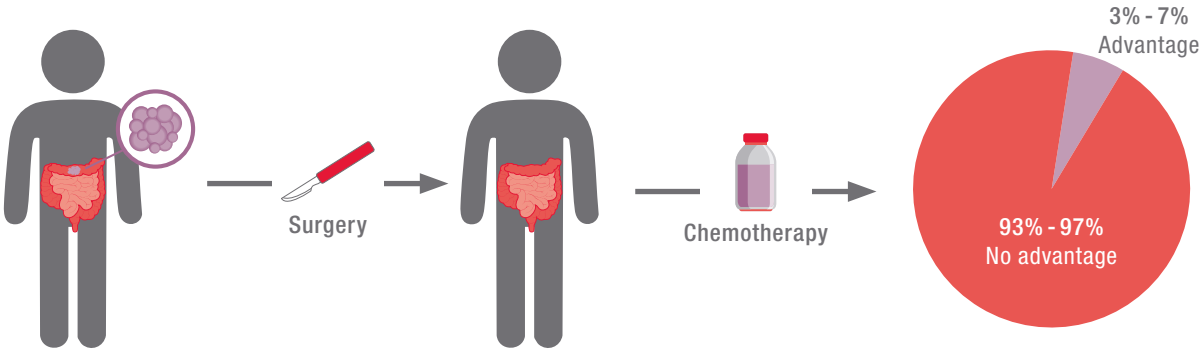
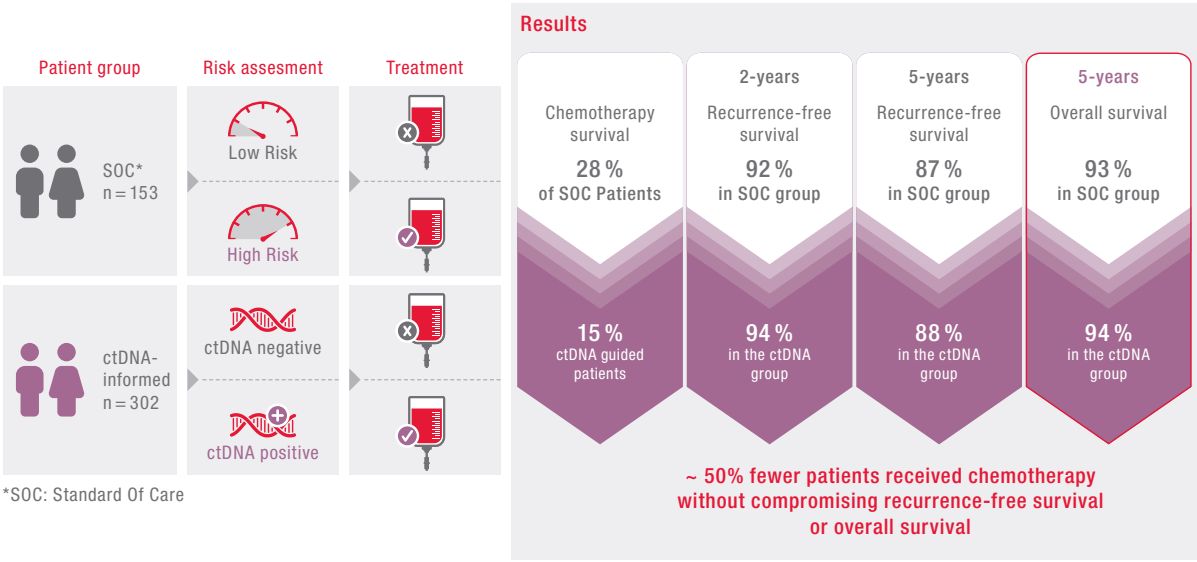


Figure 1: Benefits of adjuvant therapy for patients with stage II CRC

DYNAMIC study: clinical benefit of MRD testing for guiding adjuvant therapy

The DYNAMIC study investigated whether ctDNA-based MRD testing can help to select patients who require adjuvant therapy in a more targeted manner and whether it can also be used during the course of therapy to identify patients who can forego adjuvant therapy without increasing the risk of recurrence (6).

The results of the study showed that ctDNA-guided therapy reduced the use of adjuvant chemotherapy in stage II CRC by approximately 50% without compromising recurrence-free survival at 2 years (6). The results of the 5-year follow-up study confirmed the results for recurrence-free survival and showed comparable overall survival data between the patient groups with and without ctDNA-guided therapy (7).



*SOC: Standard Of Care

Figure 2: Summary of the design and results from the DYNAMIC study and data from the 5-year follow-up to the DYNAMIC study

Highly sensitive MRD detection: Tumor informed and personalized testing of ctDNA

In the DYNAMIC study, a next-generation sequencing (NGS) panel with 15 defined markers was used for MRD monitoring from peripheral blood (PB) by measuring circulating tumor DNA (6). The test methodology was further developed, significantly increasing the sensitivity of the MRD assay established by HPH. Based on the mutation profile of the individual tumor, a patient-specific ctDNA test is developed for each tumor and patient, which can detect approximately 50 tumor-specific somatic mutations that were previously identified by whole genome sequencing (WGS) of DNA of DNA from tumor tissue (FFPE) and peripheral blood of the patients.

This method enables the detection of a tumor fraction of only 0.0005% based on the measurement of circulating tumor DNA in relation to normal DNA.

This test is used to determine the patient-specific tumor burden in an initial test (MRD baseline test) and in the further course of the disease as a liquid biopsy from peripheral blood (MRD monitoring test).

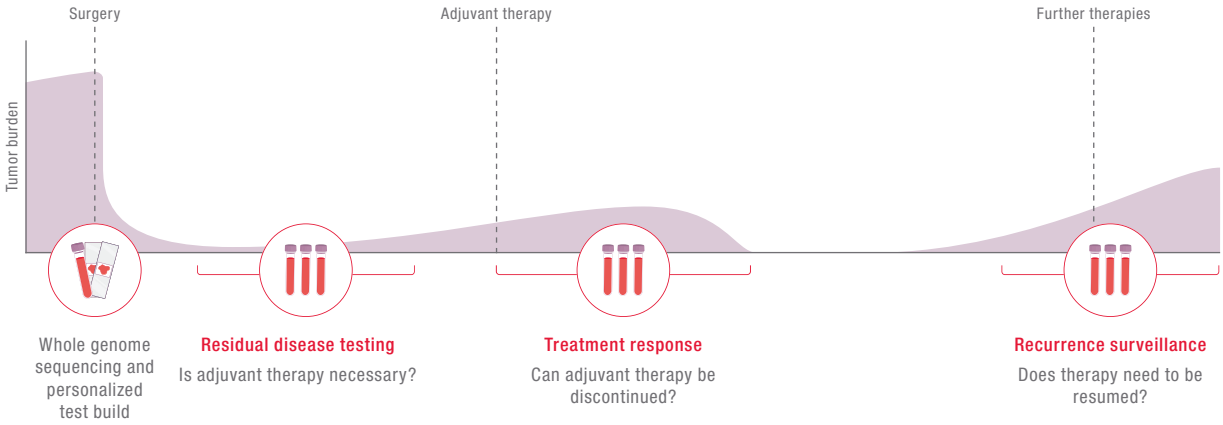


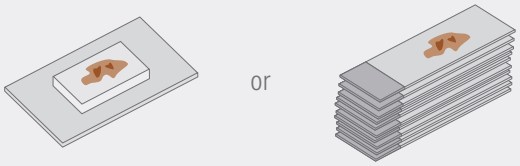
Figure 3: Schematic representation of tumor burden over the course of treatment.

Sample material and test request

1. Development of a patient-specific MRD test and MRD baseline testing:

- Tumor material (FFPE): Block (preferred) or sections (alternative)
- 3x 9 ml peripheral blood (Streck tube)

FFPE-Material



Block: preferred or Sections: alternative

+

peripheral blood

Streck tube

2. MRD monitoring

For all MRD measurements (baseline and progression), we require 3 x 9 ml of peripheral blood in Streck tubes.

peripheral blood

Streck tube

3. Test request and shipping of Streck tubes

To request the MRD assay, please contact us at: **mrd@hp-hamburg.de**.

We will be happy to inform you about test request options, sample logistics processes, and shipment of the Streck tubes.

4. MRD testing for other tumor entities

In addition to therapy stratification in colon cancer, MRD testing is becoming increasingly important for numerous other tumor entities such as NSCLC, breast cancer, urothelial carcinoma, pancreatic carcinoma, and melanoma for early detection of recurrence, stratification of adjuvant therapy, and as a predictive marker for therapeutic response and monitoring. Please feel free to contact us to discuss the testing options.

References

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