

OUTLIVE-CRC: Improvement of prognosis of young colorectal cancer patients through multimarker models and nutritional medical intervention – focus on liquid biopsy-based ctDNA genomics

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Background & objectives

Colorectal cancer (CRC) steadily increases in incidence among younger people and has a 5-year survival rate of 65% with a recurrence rate of about 10-40%. Lifestyle criteria such as physical activity and diet are important risk factors.

OUTLIVE-CRC aims at prevention and/or early detection of recurrences and the improvement of the prognosis and quality of life of young CRC patients (<50 years) using combined approaches from multi-omics analysis and nutritional medicine.

Methods

Using liquid biopsy-based analytical methods (genomics, proteomics and metabolomics) and artificial intelligence we aim to develop a biological age (BA) based multimarker risk panel including both clinical parameters and multi-omics data from blood and stool samples. It will serve to detect CRC recurrence at an early stage and/or to identify individuals at increased risk of recurrence. Furthermore, novel nutritional interventions will be tested for their effect on transformation, metabolism and proteome of personalized 3D colon organoids.

Results

For the subproject focusing on liquid biopsy genomics a deep scale Next generation sequencing (NGS) cancer panel as well as multiplexed digital droplet PCR (ddPCR) assays to detect CRC-specific changes in circulating tumor DNA (ctDNA) have been designed and

are currently being validated. They will allow 1) detection of CRC-specific mutations, 2) surveillance of MRD, 3) surveillance of resistance development and 4) validation of the performance of fusion genes. In phase 1, patients who cannot be treated curatively are initially included for clinical validation. We will enroll 150 CRC patients (<50 y) with 150 plasma samples obtained at time of diagnosis and before starting treatment or at time of relapse or progression after treatment. In phase 2 we will focus on patients with intended curative treatment. We will analyze 75 plasma samples from 25 CRC patients at time of diagnosis before starting treatment, after completion of treatment and at time of relapse. Furthermore, 25 healthy controls will be analyzed in each phase for validation.

Conclusion

OUTLIVE-CRC aims to establish a novel tertiary prevention approach combining liquid biopsy-based blood testing with nutritional interventions. The project is managed by central biobanking and data structures and intensive patient participation is key.