Cross-Platform Biomarker Program for Establishment and Validation of Liquid Biopsy for Clinical Decision Making in resectable Gastrointestinal Stromal Tumour (GIST)

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Background & objectives

In GIST, risk of relapse after resection is assessed using Armed Forces Institute of Pathology (AFIP) criteria (tumor size, localization, mitotic index). Individual risk of relapse within AFIP high risk patients is 34% to 90%. However, biomarkers for individual risk assessment are lacking. Liquid biopsy allows detection of tumor specific mutations in circulating tumor (ct)DNA. We have demonstrated that ctDNA can be detected in plasma samples of patients with localized and metastatic GIST (Meier et al, 2013) and that ctDNA level indicates disease activity and response to treatment (Jilg and Rassner et al, 2019).
In this prospective, explorative, multicentre biomarker trial (Helios Klinikum Bad Saarow, Helios Klinikum Berlin-Buch, Universitätsklinikum Dresden, Westdeutsches Tumorzentrum Essen, UMM Mannheim, Universitätsklinikum München, Medizinische Hochschule Hannover, UKSH Schleswig-Holstein, UniversitätsKrebszentrum Göttingen, Sarkomzentrum Universitätsklinikum Erlangen) we investigate whether presence of ctDNA after surgery indicates individual risk of relapse in 100 high risk GIST patients. Our study is conducted in cooperation with the German Interdisciplinary Sarcoma Group and funded by the H.W. & J. Hector Stiftung zu Weinheim.

Methods

CtDNA is analysed in peripheral blood plasma samples by digital droplet (dd)PCR and next generation sequencing (NGS). Furthermore, we perform proteomic analysis and radiomic methodology for risk stratification. Inclusion criteria are localised, locally advanced or limited metastatic GIST, finding of cKIT or PDGFRA mutation in tumor tissue, planned complete resection and high AFIP risk score. Blood samples are taken around surgical procedure or institution of systemic treatment and at regular follow-up intervals for 5 years. The primary endpoint is the rate of ctDNA positivity after surgery. Secondary endpoints include decrease of ctDNA after neoadjuvant treatment and surgery, ctDNA negative-to-positive conversion rate, specificity/sensitivity of ctDNA test, risk stratification after proteome analysis and radiomics methodology.

Results

Currently, study is initiated in Lübeck, Mannheim, Berlin-Buch and Bad Saarow and is recruiting.

Conclusion

We prospectively investigate whether the amount of mutant ctDNA at different timepoints is informative concerning risk of relapse, response to neoadjuvant therapy, progression-free and overall survival. Furthermore, we study secondary mutations in ctDNA at relapse to investigate the impact of clonal heterogeneity and further possibilities for risk stratification (proteomics, radiomics).