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Non-invasive genotyping and MRD monitoring by circulating tumor DNA in patients with solid tumors patients receiving targeted treatment within molecular tumor boards

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Introduction: Molecular tumor boards (MTB) stratify personalized targeted treatment for patients with rare and advanced cancers. Treatment response is assessed by CT/MRI, though limited by suboptimal sensitivity and specificity. Circulating tumor DNA (ctDNA) from blood plasma has emerged as a promising biomarker for noninvasive profiling of tumor mutational landscapes and disease monitoring. This study applied an ultra-sensitive next-generation sequencing (NGS) technology to evaluate ctDNA for tumor genotyping, early response prediction, and characterization of clonal heterogeneity in patients receiving targeted therapies within MTBs.
Methods: A custom-targeted NGS panel (ExTARGET) covering 266 genes across 540 kb, was applied to 167 plasma samples from 60 patients at distinct disease milestones. 24 healthy plasma samples were used to assess specificity. Digital droplet PCR (ddPCR) was used to assess concordance with NGS.
Results: In a pilot cohort of 21 patients, mutations were detected in 100% of pretreatment samples (median: 12 mutations/patient, range: 1-25). Target mutations guiding treatment initiation within MTBs, were identified in 80.9% (17/21 patients). Frequently mutated genes were *BRAF* (76%), *KRAS* (47%), *ROS1* (61%) and *TP53* (42%). NGS and ddPCR allele frequencies showed significant correlation (R^2=0.62, p<0.0001). Longitudinal tracking during therapy revealed that early ctDNA increases (4/4 cases) predicted disease progression at later timepoints. ctDNA dynamics reflected tumor burden and predicted progression in select patients.
Conclusion: We developed and implemented a NGS-based ctDNA profiling pipeline for patients with solid tumors within MTBs. Plasma genotyping identified targetable mutations in most cases. Monitoring ctDNA mirrors tumor burden and may enable early prediction of disease progression.

Preferred type of presentation

Primary authors: RANGANATHAN, Lavanya (Deutsches Krebsforschungszentrum); Dr KUEHN, Julia (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany)

Co-authors: Dr KLINGLER, Christian (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Mrs BLEUL, Sabine (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Ms PHILIPP, Ulrike (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Mr HUMMEL, Fabian (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Mr WEINSCHENK, Samuel (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Dr DEUTER, Max (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg,

Germany); Dr PAULI, Thomas (Institute of Medical Bioinformatics and Systems Medicine, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany); Dr METZGER, Patrick (Institute of Medical Bioinformatics and Systems Medicine, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany); RAPP, Julian; WINTER, Christof (TUM Klinikum); SÜLTMANN, Holger (Deutsches Krebsforschungszentrum); TINHOFER-KEILHOLZ, Ingeborg; LASSMANN, Silke (University Medical Center Freiburg); WERNER, Martin (Institute for Surgical Pathology, University Medical Center Freiburg); BÖRRIES, Melanie (Institute of Medical Bioinformatics and Systems Medicine, Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany 5 Faculty of Biology, University of Freiburg, Freiburg, Germany); Prof. PETERS, Christoph (Comprehensive Cancer Center Freiburg, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany); Dr MIETHING, Cornelius (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); Prof. BECKER, Heiko (Department of Medicine I, Medical Center- University of Freiburg, Faculty of Medicine, Freiburg, Germany); DUYSTER, Justus (University Medical Center Freiburg); SCHERER, Florian (Uniklinik Freiburg)