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Assessment of genetic tumor profiles and clonal evolution by liquid biopsy: The Augsburg Longitudinal Plasma Study (ALPS)

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Background: Analyzing circulating tumor DNA (ctDNA) from liquid biopsy (LBx) allows diagnostic, prognostic and predictive assessment and disease course monitoring of malignancies. However, the routine clinical application of ctDNA assessment is still limited. ALPS is a prospective interventional trial and an LBx-banking resource that aims at bridging the gap of LBx from translational research to routine clinical practice by investigating key questions: (a) the concordance of LBx and tissue biopsy (TBx); (b) the relevance of LBx for follow-up and disease progression; (c) the applicability of LBx to display clonal heterogeneity and evolution upon treatment and progression.

Methods: ALPS is a prospective interventional study recruiting patients (pts) with metastatic cancer undergoing systemic treatment without curative intent. At enrollment, tumor TBx and LBx from peripheral blood (PB) are obtained. Serial PB samples are collected every 3 months or concurrently with standard staging evaluations. Circulating cell free DNA (ccfDNA) is analyzed using CAPP-seq based gene panels. Genomic characterization of tumor TBx is performed by whole exome sequencing (WES). Enrolled patients are thoroughly characterized by clinical annotation within an electronic record file system.

Results: Recruitment started in April 2021. As of April 2023, 340 patients have been enrolled. Median age is 67 years (range 29-89), 36% are women. Pts with NSCLC represent the largest sub-cohort (n=88), followed by SCLC (n=33), colorectal cancer (n=27), CUP (n=18), pancreatic cancer (n=15), and other entities. In total, 969 LBx and 425 TBx were collected. Up to 11 LBx per patient were collected with a mean of 2,7 LBx per patient. For 24% of patients, a second TBx was obtained upon tumor progression. Sequencing of ccfDNA from the first 48 pts yielded 46 to 68 M reads with an on-target rate of 40-80% and a detection sensitivity of 0.1%. Cancer-related mutations and copy number variations were identified in all samples. Updated recruitment numbers and sequencing results will be presented at the conference.

Conclusion: Here we describe a study and infrastructural resource (ALPS) for the systematic evaluation of LBx in metastatic tumors. In the pilot phase, we demonstrate that ccfDNA can be obtained in sufficient quantity and quality for successful genomic analyses in patients with various metastatic malignancies. ALPS is suitable to evaluate questions relevant to routine clinical application of LBx.

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