UCCSH NGSP: Improvement of molecular tumor board decisions with a ctDNA-based deep scale cross-entity NGS panel

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Background & objectives

Genomic profiling of tissue is the method of choice to aid in decision-making for genomics-driven therapy. However, several fundamental limitations hamper its success in clinical routine including invasiveness and risks of sample collection, limited tissue availability as well as quality and lack of reflection of tumor heterogeneity. Next-generation-sequencing (NGS) of circulating tumor DNA (ctDNA) gains increasing importance for genomic profiling of solid and hematological cancers. The non-invasiveness, ease, reproducibility and repeatability of liquid biopsy collection as well as the full reflection of tumor heterogeneity together with novel technological developments are important advantages over tissue-based profiling. However, its implementation in clinical routine and molecular tumor board therapy decisions is still pending.

The goal of the UCCSH NGSP project is the prevention and/or early detection of recurrence and resistance development and the improvement of the prognosis of cancer patients across a broad range of both solid and hematological cancer entities.

Methods

A targeted capture high-throughput sequencing deep scale Next generation sequencing (NGS) panel to detect cancer-specific mutational changes has been designed and is currently being validated on a pilot study cohort. From each gene, the complete coding sequence as well as the most prominent mutational hot spot regions are sequenced.

Results

This pilot study cohort includes tissue as well as singly or longitudinally collected plasma samples with or without known primary tumor. In most cases tissue samples have already been analyzed by whole exome sequencing (WES) or transcriptome analysis to serve for validation. A comprehensive panel of digital droplet (dd)PCR assays will be used for validation of NGS results in liquid samples. The UCCSH NGSP will allow in parallel 1) detection of carcinogenic mutations across a broad range of different entities, 2) surveillance of minimal residual disease (MRD), 3) surveillance of resistance development and 4) validation of the performance of fusion genes (NTRK, ALK, RET, ROS1 and FGFR) in liquid biopsy-based ctDNA diagnostics. The current NGS panel includes 110 genes and 400kb of covered coding sequences. The UCCSH NGSP will be used to analyze samples both from the molecular tumor board and from several clinical studies, e.g. OUTLIVE-CRC, MELB, ELIAS, EXLIQUID, CAN.HEAL.

Conclusion

In conclusion, with the UCCSH NGSP we aim to pave the way for including liquid biopsy-based genomic analyses of ctDNA in clinical routine. Furthermore, we aim to improve patient outcome by offering a non-invasive and fast-paced surveillance tool to increase success of molecular tumor board-decided cancer therapies.