NEOliquid: Detection of *KIF5B-RET* fusions in liquid biopsy samples

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Background

Research in the field of molecular cancer profiling made sequencing of cell-free tumor DNA to identify targetable genomic alterations using patient blood possible. Therefore, liquid biopsy assays that can reliably detect cancer specific driver mutations in clinical routine have the potential to revolutionize cancer treatment of the future.

Methods

At NEO New Oncology AG (Cologne, Germany), we have developed a liquid biopsy assay called NEOliquid. NEOliquid is a hybrid-capture and next-generation sequencing based assay that covers clinically relevant genomic alterations, such as point mutations, small insertions and deletions, selected gene fusions and copy number alterations within a panel of more than 30 genes.

Here we describe a 65-year-old patient who was diagnosed with an adenocarcinoma of the lung with liver metastasis, tested negative for *ALK*, *EGFR*, *KRAS*, and *ROS1* mutations. The patient was pre-treated with chemotherapy, EGFR inhibitor and radiation therapy, but still progressed after therapy before being tested with NEOliquid. The second patient is a 45-year-old male, diagnosed with pulmonary adenocarcinoma. The patient was pre-tested negative for mutations in *ALK*, *BRAF*, *EGFR*, *KRAS*, *MET*, *PIK3CA, ROS1*, *TP53* before NEOliquid testing was performed.

Results

Following patient consent, NEOliquid analysis was performed on the patients' blood samples to identify oncogenic driver mutations. In both cases, a *KIF5B* (exon 1-15)-*RET* (exon 12-20) fusion was detected in the blood samples, with differences in the individual intronic breakpoints. These *KIF5B-RET* fusions result in the retention of the kinase domain of RET and the coiled-coil domain of KIF5B. The coiled-coil domain of KIF5B induces homodimerization, thereby activating the kinase of the *KIF5B-RET* fusion.

Conclusion

Using hybrid-capture based next generation sequencing, we identified therapeutically relevant gene fusions (*KIF5B-RET*) in two patients previously tested negative for mutations in a selection of genes. Patients harboring this fusion may potentially benefit from treatment with tyrosine kinase inhibitors (i.e. cabozantenib or vandetanib).