Hybrid-capture based sequencing assays to detect novel alterations in BRAF from tissue and liquid biopsies

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Background:

In recent years advances in translational cancer research have led to the characterization of oncogenic drivers and to the development of their respective targeted inhibitors.

Melanomas harbouring the activating BRAF V600E mutation, for example, exhibit high sensitivity towards site-directed inhibitors, translating into a beneficial clinical response.

In contrast to standard PCR or FISH- based diagnostics, limited to detect specific, well-established mutations or translocations, NEO is a comprehensive molecular diagnostics platform, capable of detecting genomic alterations including point mutations, small insertions and deletions (InDels), copy number alterations and translocations from both, liquid biopsy (NEOliquid) and tumor tissue (NEOplus) samples.

Methods:

NEO New Oncology is able to detect clinically relevant genomic alterations from clinical specimen with high sensitivity and specificity using a hybrid-capture based NGS technology.

NEOliquid is specifically designed for detection genomic alterations from cell-free DNA of liquid biopsies and covers a panel of more than 30 cancer-related genes. NEOplus is applied to FFPE tumor tissue and can detect somatic alterations in more than 90 clinically relevant cancer genes.

Results:

Using the NEO platform we were able to detect previously unidentified alterations in *BRAF* from tissue specimen and liquid biopsies, which would have remained undetected by current routine diagnostics. A likely activating in-frame kinase-domain deletion was detected in a liquid biopsy from a kidney cancer, a tumor entity not commonly linked to alterations in *BRAF*. Additionally, we detected novel genomic rearrangements involving the *BRAF* gene locus in a lung cancer and strikingly in a pre-diagnosed BRAF(V600E)-negative melanoma sample. Patients harbouring these atypical *BRAF* alterations might potentially benefit from treatment with pan-*BRAF* or *MEK* inhibitors.

Conclusion:

In addition to the reliable and comprehensive detection of known hot-spot alterations routinely tested in cancer diagnostics, the NEO platform is efficient in detecting novel and potentially targetable alterations even in already established, well-defined oncogenes.