

## Detection of an EGFR kinase domain duplication in a lung adenocarcinoma patient by liquid biopsy using hybrid capture-based next generation sequencing

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### Introduction

EGFR kinase domain duplications are a rare but targetable alteration, driving lung cancer. Only limited patient data has been published on the detection of the kinase duplications. This molecular alteration has been shown to lead to the activation of EGFR and is thought to be predictive for response to treatment with EGFR inhibitors. Using a hybrid capture-based next generation sequencing method, we describe here the initial detection of the EGFR kinase domain duplication in an FFPE sample from the primary tumor (NEOplus) and the subsequent detection in a liquid biopsy (NEOliquid) sample.

### Method

A 72-year-old patient was diagnosed with a lung adenocarcinoma. Initial routine tests were negative for genomic alterations in known targetable lung cancer genes. Therefore, the patient was treated with 3 cycles of chemotherapy, but the patient continued to progress.

Recently a tissue sample and a liquid biopsy was analyzed by NEO New Oncology (Cologne, Germany) using NEOplus and NEOliquid. The assay uses a hybrid capture-based next generation sequencing 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 90 genes for FFPE material or 30 genes for liquid biopsies.

### Results

Hybrid capture-based NGS assays were able to identify an EGFR kinase domain duplication. Based on the identification of the duplication, the patient was put on second line treatment with the EGFR inhibitor Afatinib. Despite a response of the primary tumor and the metastasis in lymph nodes and adrenal gland, a recent scan revealed that the metastasis in the brain and liver progressed. The discordance in response might depict the tumors heterogeneity or drug transportation and metabolism to the metastatic foci.

## **Conclusion**

Here we describe the detection of a rare EGFR kinase domain duplication using the NEO assay. Interestingly, when treated with Afatinib, some of the patient's distant metastases continued to progress. Novel technologies capable of detecting rare genomic alterations, in the routine setting, further stresses on the urgent need to develop and identify drugs to treat patients harboring these rare mutations.