

## Successful AZD9291 Therapy Based on NEOliquid Detection of Circulating T790M in a Liquid Biopsy Sample

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### **Background:**

Research in the field of molecular cancer profiling has allowed for the detection of cell free tumor DNA to identify disease using patient blood. Therefore, liquid biopsies that can detect cancer specific driver mutations as well as emerging resistance mutations have the potential to revolutionize cancer treatment of the future.

### **Methods:**

At NEO New Oncology AG (Cologne, Germany), we have developed a ctDNA-based assay called NEOliquid®. NEOliquid® is a hybrid-capture and next-generation based sequencing assay that covers clinically relevant genomic alterations, such as mutations, gene fusions and copy number alterations in more than 30 genes.

Here we describe a 50-year-old never-smoker who was diagnosed with metastatic lung adenocarcinoma harbouring an activating EGFR exon 19 deletion and no T790M resistance mutation in 2012. The disease remained in remission under erlotinib for one year. In 2014, the patient was diagnosed with brain metastasis and was subjected to whole brain radiotherapy. The disease was stable under afatinib treatment for 6 months, followed by progression.

### **Results:**

Previous attempts to detect a T790M resistance mutation by sequencing in re-biopsied tumor material failed. Following consent, NEOliquid® analysis was performed on the patient's plasma. A T790M mutation was found (allele frequency 39%), along with the previously described exon 19 deletion (allele frequency 28%). Based on the detection of the T790M resistance mutation, the patient was given AZD9291 on compassionate use. Within a few days, the patients' clinical condition improved. Further blood samples under AZD9291 therapy in intervals of 2 weeks were analysed using the NEOliquid® technology, showing gradual decrease of the T790M allele frequency. After 6 weeks, the T790M mutation was detected at an allele frequency of only 0.03%, with no indication of the exon 19 deletion anymore. Currently, AZD9291 therapy is ongoing, tolerability is excellent, and there is no evidence of tumor progression.

In summary, we describe the successful detection and monitoring of a T790M resistance mutation in a patient not suitably for biopsy, even at very low allele frequencies, using our sensitive and reliable NEOliquid® assay. The ability to detect residual disease and resistance mutations, non-invasively, using liquid biopsies will greatly influence cancer treatment in the future.