

Dynamic measurement of treatment response in advanced non-small cell lung cancer.

Background

Treatment resistance is one of the major challenges in treatment of advanced cancer. Lung cancer is the leading cause of cancer related death. The introduction of new therapies in treatment of advanced non-small cell lung cancer during recent years, such as immunotherapy and targeted/personalized treatment has bettered the prognosis. Though the response rates are widely varying due to primary or acquired resistance. Recent years of research have clarified some of the mechanisms of resistance, primarily focusing on genomic alterations.

Exploration of acquired resistance is challenging as it requires continuous information of the biological behaviour and alterations of the cancer during treatment, which can only be obtained by comprehensive genomic profiling of repeated biopsies and/or plasma samples (liquid biopsies).

Purpose and Methods

In this prospective exploratory study, we aim to identify resistance mechanisms and molecular therapeutically actionable targets. In addition, we aim to assess how the levels of circulating tumor DNA (ctDNA), measured in plasma, during treatment correlate to treatment response.

Patients with confirmed advanced NSCLC without targetable mutations, referred to Department of Oncology at Zealand University hospital, Aalborg University Hospital and Vejle Hospital (planned), are screened for eligibility. At diagnosis and before every treatment cycle a plasma sample is taken for quantification of ctDNA. At the time of diagnosis and at the time of progressive disease, a biopsy is taken. Comprehensive genomic profiling is performed on the tissue biopsy and on the plasma ctDNA.

Status and Perspectives

All relevant approvals have been obtained and inclusion is on going. We expect to include more than 200 patients.

A dynamic measurement of treatment-response through ctDNA will potentially lead to an early registration of treatment-failure. Ineffective, costly treatments with unnecessary toxicity are being avoided and the quality of life preserved.

A thorough exploration of the molecular alterations during treatment will improve the understanding of resistance mechanisms, giving the possibility to evolve treatment-regimens that target these mechanisms - potentially bettering the treatment response and the prognosis.

Based on the findings in this study, a national interventional study, randomizing patients to either CT-scan monitoring (standard) or ctDNA monitoring of treatment, is planned to investigate the clinical utility and significance of ctDNA monitoring in advanced NSCLC.