Circulating tumor DNA guided treatment-monitoring in advanced lung cancer - a randomized interventional study

Precise treatment monitoring is essential in order to reduce ineffective, costly treatments and consequent needless adverse events. The precision of conventionally radiologic evaluation scans have been challenged by immunotherapy-induced recruitment of immune-cells resembling increment in tumor-size, named “pseudo-progression”. Liquid biopsy has the potential to overcome these challenges by measuring molecular changes with high precision, distinguishing circulating tumor DNA (ctDNA) from normal DNA in a dynamic manner in consecutive plasma samples, enabling a precise treatment monitoring.

In our recent real-life explorative study, we found that ctDNA measurements could potentially reduce 33% of likely inefficient treatment cycles, and could help in clarifying 79% of non-conclusive CT-scans. These findings underline the potential of liquid biopsy to change clinical practice. Based on these promising results, a randomised interventional study is planned, including patients from Region Zealand, Region of Southern Denmark and North Denmark Region to explore the benefit of treatment monitoring by liquid biopsy.

Purpose

1) To investigate if ctDNA measurements can reduce the numbers of treatment cycles without decreasing Overall Survival (OS)

2) To explore if ctDNA measurements can lead to more precise treatment management

Study design

A total of 160 patients with advanced non-small cell lung cancer eligible for immunotherapy, will be randomised between Computed Tomography (CT) scan evaluation (Arm A) and ctDNA-based evaluation (Arm B). In Arm B patients exhibiting decreasing ctDNA measurements to Limit of Detection (LoD) within 6 months of treatment will be proposed discontinuation of treatment and follow-up by sequential ctDNA measurements in order to investigate if standard 2 years of immunotherapy can be reduced.

Quality of Life assessments by EORTC (The European Organization for Research and Treatment of Cancer) QLQ-C30-LC13 and EQ-5D-5L questionnaires, adverse event monitoring, and numbers of treatment-cycles together with overall survival data will be the foundation for cost-utility and cost-effectiveness analyses to evaluate ctDNA measurements as a novel method of treatment monitoring.

The results of this study are expected to pave the way for clinical implementation of liquid biopsy monitoring for advanced cancer patients and to spare health cost of inefficient treatments.