1. Introduction

Molecular profiling to direct targeted treatment has revolutionized cancer treatment, particularly in the field of lung cancer. The EML4-ALK fusion, which is present in about 5% of lung adenocarcinomas, provides a potential therapeutic target for ALK inhibitor treatment. The fusion is often present in approximately 40% of patients with ALK-positive tumors, and the expression of EML4-ALK is used in the diagnosis and management of patients for targeted therapy. Clinical trials have demonstrated the feasibility of detecting the EML4-ALK fusion in plasma from patients known to be positive by tissue biopsy. Here, we present clinical performance data for a diagnostic assay that can provide a valuable alternative to tissue-based testing and provide a straightforward option for identifying and monitoring EML4-ALK positive NSCLC patients.

We determined the variant-specific expression profile of EML4-ALK fusion transcripts in a large cohort of NSCLC patients with known ALK status. The ExoDx EML4-ALK technology represents a valuable diagnostic test for non-surgical treatment guidance and longitudinal monitoring of patients positive for EML4-ALK ALK-positivity.

2. EML4-ALK Detection

Current determination of EML4-ALK fusion (for frequency of variants, see Figure 2) relies on tissue biopsies and fine-needle aspirations — techniques constrained by surgical complications, availability of tissue, and sample heterogeneity.

To address the shortcomings of current technology and to streamline the diagnostic procedure for NSCLC patients, Exosome Diagnostics developed the ExoDx Lung(ALK) assay to rapidly detect fusion transcripts in plasma (Figure 3).

3. Assay Performance on Clinical Data

Clinical Samples: From a large cohort of plasma samples from patients with known ALK status by FISH, we selected two groups of samples defined by its low and true negative and true positive samples based on clinical review.

ALK Positive samples (null): were defined as samples with FISH ALK merged that were either not currently under treatment with ALK-inhibitor or had progressive disease at the time of blood draw. Circulating exRNA signal was not expected to be detected during ALK inhibitor treatment.

ALK Negative samples (null): were defined as samples with FISH ALK that were also EGFR- or HER2-NSCLC patients. Due to the limited sensitivity of the ALK assay, positivity for any driver mutation (mutually exclusive to ALK translocation) was considered a better standard for a true-negative sample status.

Sample characteristics:

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• ALK detection: A highly-specific and sensitive assay for detection of ALK fusion

Figure 1: Fusion transcript of three EML4-ALK variants in NSCLC

Figure 2: Frequency of EML4-ALK fusion variants in NSCLC patients

Figure 3: Assay workflow for detection of EML4-ALK fusion variants in plasma using ExoDx Lung(ALK)

ExoDx Lung(ALK) Clinical Results

ExoDx Lung(ALK) Clinical Samples Results

ExoDx Lung(ALK) Clinical Results

ExoDx Lung(ALK) CLIA Laboratory

4. Methods Comparison

ExoDx Lung(ALK) Liquid Biopsy on Plasma

Presentation 2591

5. Conclusions

• Liquid biopsy, in contrast to tissue testing (FISH, IHC), represents a rapid, low-invasive and low-risk method for detecting the predictive biomarker EML4-ALK fusion

The ExoDx Lung(ALK) test can be used both as baseline to help guiding treatment choice, and longitudinally to display patient progress during therapy.

Here we demonstrate the capability of our diagnostic test to determine specific expression of rare EML4-ALK fusion transcripts in two volumes of patient plasma.

The initial clinical results suggest a high sensitivity and specificity of ExoDx Lung(ALK) in patients with ALK fusion positive for ALK translocations.

The ExoDx Lung(ALK) test has been validated in the Exosome Diagnostics CLIA laboratory.

Liquid Biopsy

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