1. Introduction

Molecular testing in blood-transmitted therapies has revolutionized cancer treatment, particularly in the field of lung cancer. NSCLC-ALK fusion biomarker analysis is a promising method for non-invasive diagnosis in patients with advanced NSCLC.

2. EML-ALK Detection

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

3. Assay Performance on Clinical Data

Clinical Samples: From a large cohort of plasma samples from patients with known ALK+ tissue status by FISH, we selected two groups of samples defined to be true positive and true negative using EML4-ALK assay.

- **ALK Positive**: samples were defined as samples with FISH+ ALK+ that had received one prior ALK inhibitor. Patients were either not currently under treatment with ALK inhibitor or had progressive disease at the time of blood draw. Circulating EML4-ALK was considered to be detectable during treatment.

- **ALK Negative** samples: selected as samples with FISH- ALK- that were also EGFR- or KRAS- due to the limited sensitivity of the FISH-ALK assay.

4. Methods Comparison

ExoDx Lung(ALK) Liquid biopsy on Plasma

- **Plasma-based assay overcomes the challenges of tissue sample scarcity and heterogeneity**
- **Reproducible PCR-based analysis**
- **Analysis of single high-quality qPCR to detect EML-ALK mutation with high sensitivity**
- **Detects distinct fusion transcripts (v1, v2, v3, v4) with high specificity; increasingly important for treatment selection**
- **Liquid biopsy enables non-invasive, longitudinal monitoring to determine molecular response to therapy and prediction of resistance**

5. Conclusions

- **Liquid biopsies, in contrast to tissue testing (FISH, IHC), represent a non-invasive and low-risk method for detecting the predictive biomarker EML-ALK in plasma of NSCLC patients, with the added benefit of variant detection.**
- **The ExoDx Lung(ALK) test can be used both at baseline to help guide treatment choice, and longitudinally to display patient progress during therapy.**
- **Here we demonstrate the capability of our diagnostic test to determine variant-specific expression of rare EML-ALK fusion transcripts in low volumes of patient samples.**
- **The initial clinical results suggest a high sensitivity and specificity of ExoDx Lung(ALK) in patients suspected to be positive for ALK-translocations.**
- **The ExoDx Lung(ALK) test is now available as a laboratory developed test for clinical use from the Exosome Diagnostics CLIA laboratory.**