Discrepancies Between ALK FISH and Capture Based NEOplus Diagnostics

Rafał Dziadziuszko¹, Martin Reck², Sylvie Lantuejoul³, Frank Griesinger⁴, Federico Cappuzzo⁵, Wilfried E. E. Eberhardt⁶, Markus Tiemann⁷, Roopika Menon⁸, Lukas C. Heukamp⁸, Johannes M. Heuckmann⁸

¹Medical University of Gdansk, PL, ²LungenClinic Grosshansdorf, DE, ³CHU de Grenoble, FR, ⁴Pius-Hospital Oldenburg, DE, ⁵Istituto Toscano Tumori, IT, ⁶University Hospital Essen, DE, ⁷Haematopathology Hamburg, DE, ⁸NEO New Oncology AG, DE

**Technology:**

- Fluorescence In Situ Hybridization (FISH)
- Proprietary NEOplus Assay

**Fluorescence In Situ Hybridization (FISH)**

- Technology to indirectly visualize structural genomic alterations
- Sensitive to fixation artifacts
- Does not provide information about specific breakpoints and fusion partners
- Long hands-on time by pathologists
- One assay per analysis

**Proprietary NEOplus Assay**

- Hybrid capture based NGS technology
  - Detects point mutations, Indels, copy number alterations and gene fusions in one sample
  - Provides nucleotide resolution for every breakpoint
  - Identifies even novel fusion partners
  - Comprehensive testing of 72 genes

**Conclusion:** Here, we describe a selection of tumor samples with discrepant results for fusion detection using FISH and NEOplus. In all of the cases for which clinical response data was available, tumor sensitivity was in line with the initial diagnosis generated by the NEOplus assay.

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**Patient 1:**
- 58 year old patient
- Lung adenocarcinoma
- Never smoker

**FISH analysis:**
- Fusion negative

**NEOplus analysis:**
- DML4 ALK fusion positive

**Response data:**
- Baseline; treatment with Crizotinib suggested
- Post treatment with Crizotinib

**Patient 2:**
- 58 year old patient
- Lung adenocarcinoma
- Initially ALK FISH positive
- Progressive post Crizotinib
- Uninterpretable follow-up cytology FISH

**FISH analysis:**
- Fusion negative

**NEOplus analysis:**
- DML4 ALK fusion positive

**Response data:**
- Baseline; treatment with Crizotinib suggested
- Post treatment with Crizotinib

**Patient 3:**
- 41 year old patient
- Metastatic mucinous adenocarcinoma
- Ex smoker
- EGFR and ALK tested negative

**FISH analysis:**
- Fusion negative

**NEOplus analysis:**
- ALK IHC positive EML4 ALK fusion breakpoint

**Response data:**
- Baseline; treatment with Ceritinib suggested
- 12 weeks of Ceritinib

**Patient 4:**
- 13 year old patient
- Myofibroblastic sarcoma
- ALK IHC positive

**FISH analysis:**
- Fusion negative

**NEOplus analysis:**
- ALK CARS negative

**Response data:**
- Baseline; treatment with Ceritinib suggested
- 6 weeks of Ceritinib
- 12 weeks of Ceritinib
- 18 weeks of Ceritinib

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