Comparison of genomic alterations derived from matched tumor tissue and liquid biopsy

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TECHNOLOGY:

- Proprietary NEO assay
- DNA extracted from FFPE or blood
- Hybrid capture-based NGS technology
- Parallel detection of point mutations, InDels, copy number changes and gene fusions
- Reliable analysis also on small amounts of material (fine needle biopsies, blood)
- Provides nucleotide resolution for every genomic lesion
- Identifies novel fusion partners
- Comprehensive testing of 94 genes for FFPE samples and 39 genes for liquid biopsies

ASSAY:

- Hybrid capture Next Generation Sequencing (NGS)
- Detection of genomic alterations

PROJECT:

- Total cohort of matched tumor tissue and liquid biopsy of 80 patients with NSCLC of non-squamous histology
- After exclusion of patients with M0 and those with >50 days between tissue excision and blood withdrawal, final analysis was performed on 57 patients
- Analysis of concordance, sensitivity and positive predictive value was performed for:
  - Tumor associated alterations such as activating mutations (point mutations, InDels, translocations, copy number alterations) in ALK, BRAF, CNTNB1, EGFR, ERBB2, HRAS, IDH1/2, KRAS, PIK3CA, NRAS, MET, RET, ROS1 and inactivating alterations in PTEN, RB1 and TP53
  - Targetable alterations such as translocations in ALK, RET and ROS1 and activating mutations in BRAF, EGFR (excluding exon 20 insertion), ERBB2 and MET
- Calculations are based on the assumption that FFPE-based molecular profiling serves as a gold standard

RESULTS:

- The analysis in the cohort revealed a concordance of 76% with a sensitivity of >68% and a PPV of >85% for tumor associated alterations, and a concordance of 82% with a sensitivity of >72% and a PPV of >94% for targetable alterations when comparing tissue and blood samples.
- Focused analysis for EGFR revealed a concordance of >92%, a sensitivity of >85% and a PPV of 100%

CONCLUSION:

- Liquid biopsy provides a powerful diagnostic tool to detect genomic alterations with high concordance to tissue diagnostics

Patients with lung carcinoma of non-squamous histology

| Time between tissue and liquid biopsy: 50h; M1a, M1b |

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<tr>
<th>Concordance</th>
<th>Sensitivity</th>
<th>PPV</th>
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<td>Targetable mutations</td>
<td>EGFR mutations</td>
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- Discordant alterations in liquid biopsy result from:
  - Examples of discordant alterations detected in liquid biopsies can provide an added value to display the tumor heterogeneity (in setting of resistance)
  - Indicate additional primary tumors (activating IDH1 mutation)
  - Provide molecular diagnostics when tissue material is limited (KIF5B-RET fusion not detected in <10% tumor cell content)

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