Hybrid-capture based sequencing assays to detect novel alterations in BRAF from tissue and liquid biopsies

Judith N Müller1, Sotirios Lakis1, Erika Mariotti1, Petra Schneider1, Christian Gloeckner1, Svetlana Leenders1, Annina F. Hube1, Giuseppe Gullo3, John Crown3, Frank Griesinger2, Johannes M. Heuckmann1, Lukas C. Heukamp1, Roopika Menon1

1NEO New Oncology GmbH, Cologne; 2Pius Hospital, Oldenburg; 3St Vincents University Hospital, Dublin

Abstract ID: #2761

**TECHNOLOGY:**
- Proprietary NEO assay: 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 95 genes for FFPE samples and 39 genes for liquid biopsies

**THE ASSAY:**
- 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 95 genes for FFPE samples and 39 genes for liquid biopsies

**CASE 1:**
Patient history:
- 46-year old male patient
- Metastasized hepatocellular carcinoma
- No molecular diagnostics performed

NEO findings:
- Liquid biopsy detected activating mutations in CTNNB1 and an in-frame deletion in the conserved β3-αC loop of the kinase domain of BRAF

**CASE 2:**
Patient history:
- 57-year old female patient, never smoker
- Adenocarcinoma of the lung
- Tested negative for EGFR, KRAS mutations and ROS1 translocations
- Relapsed under chemotherapy

NEO findings:
- Molecular analysis of tissue detected a SMURF1-BRAF fusion (SMURF1 Exon 17 - BRAF Exon 10)
  - Hybrid capture-based NGS identified novel fusions in BRAF (SMURF1-BRAF and CALD1-BRAF), that structurally resemble known alterations identified in several tumor entities (REF.3,4)
  - The alteration results in a loss of the auto-inhibitory N-terminal RAS binding domain and might lead to constitutive activation of BRAF

**CASE 3:**
Patient history:
- 52-year old male patient
- Melanoma with metastasis to the lung
- Identified as BRAF V600E negative by COBAS®
- Treated with chemotherapy + Bevacizumab

NEO findings:
- Molecular analysis of tissue detected a SMURF1-BRAF fusion (SMURF1 Exon 17 - BRAF Exon 10)
- Hybrid capture-based NGS identified novel fusions in BRAF (SMURF1-BRAF and CALD1-BRAF), that structurally resemble known alterations identified in several tumor entities (REF.3,4)
- The alteration results in a loss of the auto-inhibitory N-terminal RAS binding domain and might lead to constitutive activation of BRAF

**REFERENCES:**

www.newoncology.de