

## Identification of Therapeutically Targetable Genomic Alterations in a cohort of patients with CUP using a Hybrid-Capture based Next Generation Sequencing Assay

### Background:

Carcinomas of unknown primary (CUP) comprise a heterogeneous group of advanced cancers that pose a serious diagnostic as well as therapeutic challenge. Patients present with metastatic disease, while the anatomic location of the primary tumor remains unidentified. These cancers represent excellent candidates for multi-gene panel molecular profiling, which can help resolve tumor origin while also providing insights for personalized treatment.

### Methods:

At NEO New Oncology GmbH (Cologne, Germany), we have developed hybrid-capture based next generation sequencing assays capable of detecting clinically relevant genomic alterations in solid tumors, such as point mutations, small insertions and deletions, gene fusions and copy number alterations from limited starting material. The NEOliquid™ assay is specifically designed for liquid biopsies and covers a panel of more than 30 tumor related genes, whereas the NEOplus™ panel is optimized for formalin-fixed paraffin-embedded (FFPE) tumor tissue and covers more than 90 clinically relevant cancer genes.

Here we describe an ongoing project consisting of a series of 36 CUP patients with available FFPE and/or blood samples, that were analyzed with NEOplus and/or NEOliquid, following the acquisition of patient informed consent.

### Results:

With reference to the current samples, a driver mutation was identified in 58%. Most commonly affected genes included *PIK3CA*, *TP53*, *KRAS*, *ARAF*, *ERBB2*, *EGFR*, *PIK3CA*, *IDH2* and *MET*. In 18 patients the alteration could be matched to one or more approved targeted or experimental therapies. Several cases harbored genomic alterations with clinical implication. These included tumors positive for microsatellite instability-high, *ERBB2* amplifications, *EGFR* activating mutations and *MET* exon 14 skipping mutations. Few of the identified mutations also provided a genomic hint with reference to the origin of the tumor.

### Conclusion:

The number of potential therapeutic targets identified in this series of CUP cases analyzed with NEOliquid and NEOplus is noteworthy and highlights the significant role of hybrid-capture based next generation sequencing assays in the diagnostic work-up of this challenging tumor entity.