Aim: Knowledge about somatic driver mutations in cancer is crucial for decision-making in personalized therapy. Samples with low tumor content cannot be sequenced reliably with traditional methods. We have developed a complete pipeline to sequence more than 550 cancer-relevant genes in parallel using next-generation sequencing of FFPE or frozen tumor tissue. Interpretation of somatic mutations yields a medical report for the oncologist to support treatment decision.

Methods: FFPE or frozen tumor sections are macrodissected and DNA is extracted from tumor material and patient’s blood. Enrichment for more than 550 cancer-relevant genes is performed using a specially designed custom enrichment kit and the samples are sequenced to a very high depth. Somatic mutations are detected with very high sensitivity by comparison of sequencing data from the tumor and the blood sample. Clinical interpretation of mutations is performed by a team of scientists and medical doctors. A medical report listing actionable mutations, potentially beneficial targeted drugs and contraindications, as well as clinical trials the patient may wish to participate in.

Results: Sensitive and specific detection of somatic mutations is achieved with this diagnostic sequencing panel, even in samples with a tumor content as low as 20%. A majority of patient samples contains actionable mutations, allowing personalized treatment. In addition, the panel allows the classification of CUP as metastasis of previous cancer. The analysis is also able to assign the source of metastasis to one of multiple primary tumors, where histology was not informative. In addition, the panel allowed the classification of CUP as metastasis of a previous cancer and assignment of metastases to one of multiple primary tumors, when histology was not informative.

Conclusions: Comprehensive molecular profiling using panel-based next-generation sequencing can identify therapeutic targets in tumor patients. This helps to decide on an optimized therapy and to clarify the source of metastases. Early sequencing can also save costs and provide an advantage to the patient by excluding therapies that will likely have no benefit.

Disclosure: M. Menzel: Employee of CeGaT; S. Armeanu-Ebinger: Employee of CeGaT; M. Feldhahn: Employee of CeGaT; S. Biskup: Founder and director of CeGaT.