OeGHO - Förderpreis Onkologie 2023

Targeting CDK6-regulated growth and transcription in therapy resistant EGFR-mutated lung adenocarcinoma

Lung cancer is among the most commonly diagnosed cancers worldwide and represents the first cause of cancer-related death in Europe and the United States. Non-small cell lung cancer (NSCLC) accounts for 85% of all lung cancers and is often diagnosed at an advanced stage with treatment options being limited. Patients with advanced NSCLC and somatic activating mutations of the tyrosine kinase (TK) domain in the epidermal growth factor receptor (EGFR) gene represent a biologically distinct population with exquisite sensitivity to the EGFR TK inhibitors (TKI). EGFR TKIs have been shown to be superior over chemotherapy in terms of response rate, progression-free survival and quality of life in this specific entity. Osimertinib, an irreversible EGFR TKI, represents the standard care for patients with $EGFR^{+}$ advanced tumors and for those progressed on EGFR TKI. Despite long-lasting disease control upon osimertinib, patients inevitably develop resistance via heterogeneous mechanisms. A systems-level understanding of secondary mechanisms of resistance status is crucial to define the best management of patients in progression to osimertinib.