SCLC

HIGH FREQUENCY OF THERAPEUTICALLY RELEVANT GENOMIC ALTERATIONS IN ADVANCED SMALL CELL LUNG CANCER DETECTED BY TARGETED NEXT-GENERATION SEQUENCING FROM SMALL BIOPSY SAMPLES

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Aim: The information regarding therapeutically relevant genomic alterations in advanced small cell lung cancer (SCLC) is not well developed due to the lack of suitable tumor specimens for integrative genomic analysis. We assessed the potentially actionable genomic alterations in advanced SCLC using a next-generation sequencing-based genomic profiling assay from biopsy samples.

Methods: Genomic DNA extracted from biopsy samples were subjected to the 1.499 Mb custom target capturing panel including all exons of 244 cancer-related genes. Targeted sequence enrichment was performed using the Agilent SureSelect Target Enrichment Kit (Agilent Technologies). Ninety SCLC samples were applied to the target sequencing.

Results: The demographics of the 90 patients were as follows: median age 67 years (range: 37-85); male 71 (79%); history of smoking 88 (98%) and clinical stage II/III/IV=1/26/63. We repeatedly confirmed the high prevalence of inactivating mutations in TP53 (81%) and RB1 (44%). Additionally, genetic alterations in the PI3K/AKT/mTOR pathway were detected in 28 (31%) of the tumors: PIK3CA 3%, PTEN 7%, AKT2 1%, AKT3 1%, TSC1 2%, TSC2 11%, RPTOR 3%, RICTOR 3% and mTOR 3%. Alterations in targetable receptor tyrosine kinase (RTK) genes were also identified in the present study: EGFR 4%, ERBB2 3%, KIT 6%, PDGFRA 9%, ALK 11%, ROS1 12%, and RET 6%. Many of them were potentially targetable with currently available drugs.

Conclusions: Sequencing-based molecular profiling of SCLC is feasible from clinically available small biopsy samples. Advanced SCLC harbored frequent genomic alterations in PI3K/AKT/mTOR pathway and in targetable RTK genes. We are planning clinical trials targeting for these alterations.

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