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NSCLC, early stage

1180PD GENOMIC CHANGES IN LUNG CANCER PATIENTS WITH MULTIPLE LUNG RELAPSES

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Aim: Patients with early stage non-small cell lung cancer (NSCLC) undergo surgical removal of their tumors. However, in some individuals tumors can recur and are re-removed multiple times. We identified patients (pts) who underwent multiple serial surgeries for early stage NSCLC and evaluated genetic changes in their tumors over time.

Methods: Using an institutional database, we identified 15 pts that underwent surgical resection for stage I-II NSCLC with 2 or more recurrent tumors without intervening therapy. Among these, we selected 20 tumors from 6 pts with available tissue (median tumors/pt = 3 [3-4]) and their matched germline DNA. All pts provided informed consent. DNA extracted from archival FFPE samples and paired blood was analyzed by massively parallel sequencing (MPS) on an Illumina HiSeq 2500 using a targeted hybrid capture approach for 504 cancer-related genes. Sequencing was performed at high depth with a mean target coverage of 186x across all samples. We compared the somatic mutations and copy number variations (CNV) in the recurrent specimens to those in the primary tumor. We performed hierarchical clustering to compare the relapsed tumors to the primary tumors.

Results: In 2/6 pts, the genetic changes confirmed that all the tumors were related among relapses, while in 4/6 pts some tumors showed distinctive genetic changes consistent with a different lung cancer. In pts with recurrent tumors, the subsequent relapsed tumors contained either additional mutations or increased CNV, suggesting genomic evolution over time. In pts with 3 or more surgically removed tumors, the time to relapse shortened with each subsequent tumor. In 3 pts with EGFR mutant NSCLC, the relapsed tumors contained additional potential driver mutations including EGFR T790M, PIK3CA E542K, and TP53 C176F, suggesting that these genetic changes can evolve even in the absence of drug treatment.

Conclusions: Genomic changes in tumors from NSCLC pts with multiple recurrences evolve over time in the absence of systemic therapy. MPS helps to classify relapses vs. new primaries and reveals new insights in the biology and natural history of EGFR mutant lung cancer.

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