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Opinion Article

Clinical Effects of Small Cell Bladder Cancer in Biomarkers Therapeutics

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DESCRIPTION

Small cell bladder cancer (SCBC) is a common histologic variation with a poor prognosis and also no unifying biomarkers. TP53 and RB1 gene mutations are very common in SCBC, according to the few publications on genomic sequencing, although the prognostic significance of these and other gene variants in SCBC is still unclear. In order to detect potential novel biomarkers, we performed targeted genome sequencing on a cohort of SCBC patients and compared genomic results with clinical outcomes. Less than 5% of bladder tumors are small cell carcinomas, which are a rare histologic subtype of bladder cancer. Small cell lung cancer (SCLC) is used as a model for extrapolating treatment paradigms, and patients with advanced illness have a poor prognosis. Radical cystectomy patients with no metastatic, limited-stage small cell bladder cancer have a worse prognosis than those with more common muscle-invasive urothelial (MIUC) of the bladder. When possible, definitive treatment regimens incorporating chemotherapy are advised because they likely improve outcomes.

Small cell bladder cancer's (SCBC) pathogenesis is still poorly understood. Neuroendocrine cells can combine with normal urothelium to form tumors, although SCBC frequently appears in mixed tumors made up of other histologist, such as conventional urothelial carcinoma. Genetic analyses have found similar anomalies in small cell and urothelial carcinomas starting to emerge from mixed tumors from the same patient, suggesting a shared clonal origin could occur. We have also previously seen in xenografts, cell lines, and patients that the variants of bladder cancer may have stem cell origins. Small cell and urothelial bladder carcinoma share certain overlapping genomic abnormalities, but there are also some different patterns, including a higher prevalence of TP53 and RB1 mutations in SCBC, according to the limited data on genomic profiling.

A comprehensive genomic investigation of lung small cell carcinomas reveals that TP53 and RB1 mutations occur commonly. However, the underlying pathogenic markers vary depending on the place of origin, with SCBC being distinguished from SCLC by the presence of APOBEC-mediated mutagenesis. Although a particular genetic biomarker has not even been discovered in small cell bladder cancer, the presence of mutant RB1 has been found to correlate with increased responsiveness to chemotherapy and survival in advanced SCLC. We wanted to do genomic analysis on a cohort of SCBC patients in order to uncover possible biomarkers and novel treatment targets in this study due to the dismal prognosis of patients with SCBC and the absence of validated biomarkers. Small cell carcinoma regions were identified using tumor sequencing, which was helped by immunohistochemistry for the neuroendocrine markers synaptophysin and chromogranin. Before DNA extraction, tumor samples from 31 individuals that included small cell carcinoma underwent micro dissection. These samples were then sequenced utilising a Next Generation Sequencing (NGS) technology. The small cell carcinoma component of tumors with mixed histology was micro dissected for examination.

Genomic evaluation in this group, 339 genes had pathogenic mutations. 52 (15.3%) of the identified genes with mutations occurred solely in the pure small cell carcinoma specimens, while 196 (57.8%) occurred exclusively in the dissected mixed histology tumors. The most frequent genetic changes linked to tumors Mutations in chromatin remodeling genes are less commonly observed in small cell lung cancer (SCLC) but are classically associated with urothelial carcinoma.

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