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Genomic Profiling of Responders and Non-responders to Checkpoint Inhibition in Neuroendocrine Carcinoma

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BACKGROUND: The role of immune checkpoint inhibitors (ICI) in the treatment of neuroendocrine carcinoma (NEC) has yet to be established. While objective responses have been observed, it is still unknown which patients are likely to derive benefit. We investigated the genomic profiles of patients who did and did not respond to ICI.

METHODS: This is a retrospective series of patients with extrapulmonary NEC. RECIST 1.1 criteria were used to categorize patients as responders (CR, PR, or SD) vs non-responders (PD). The electronic medical record was reviewed to identify patients who had genomic panels performed, and results were extracted for analysis.

RESULTS: Of 31 patients eligible for RECIST assessment, 19 had genomic panels available (9 responders - 4 SD, 5 PR and 10 non-responders - PD). Of those with a NEC histology specified, 9 were small cell, 1 combined large and small cell, 3 were large cell. All tumors were microsatellite-stable. All but one (with TMB = 25) of 16 tumors with TMB status available were < 10 m/MB. Of the responders, 67% had both TP53 and RB1alterations, compared with only 10% in the non-responders; this was statistically significant (p = 0.0198, Fisher exact). Of 7 total tumors with TP53+RB1alteration, 4 were specified as small cell carcinoma. Half of non-responders showed alterations in CTNNA1or CTNNB1, compared to only one of the responders, but this did not reach significance (p= 0.1409, Fisher exact).

CONCLUSION: In this small series, the small cell lung cancer-like genomic signature of TP53and RB1mutations was significantly more frequent in responders to ICI compared to non-responders. Further study is warranted to determine whether the presence of having simultaneous TP53and RB1mutations predicts response to ICI in NEC.

ABSTRACT ID: 131