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Efficacy of Checkpoint Inhibitors in Combination with Chemotherapy in Patients with High-grade Extrapulmonary Neuroendocrine Carcinoma

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BACKGROUND: Most extrapulmonary neuroendocrine carcinomas (EP NECs) are metastatic at presentation and survival is poor. Platinum and etoposide (CTX) is the standard first-line therapy. Data on CTX and checkpoint inhibitors (CPIs) for patients with EP NECs are largely extrapolated from lung cancer data. The DART SWOG 1609 trial suggested a benefit of dual CPI therapy in patients with high-grade NENs but did not evaluate the combination of CTX and CPI. A randomized trial of CTX with and without CPI is in development but unlikely to yield results for several years.

METHODS: The study was approved by the Mayo Clinic IRB. The retrospective cohort included patients with a diagnosis of EP NEC at Mayo Clinic between 2000 and 2021. We matched patients according to age, sex, and primary site of tumor. Chi-squared (_2) and Fisher's exact tests were used to assess clinical and demographic factors.

RESULTS: We identified 57 patients with EP NECs treated with either CTX monotherapy or CTX + CPI as first line treatment. Thirty-eight were treated with CTX monotherapy and 19 with CTX + CPI. For patients treated with CTX monotherapy the median overall survival (OS) and progression free survival (PFS) of 11 months (95% CI: 9-22) and 6 months (95% CI: 5-11), respectively. Patients treated with CTX + CPI had a median OS and PFS of 9 months (95% CI: 6-not reached [NR]) and 4 months (2-NR) respectively. The overall response rate (ORR) and disease control rate (DCR) in patients treated with CTX monotherapy was

63.2% and 73.7%, respectively. The ORR and DCR in patients treated with CTX + CPI was 42.1% and 63.2%, respectively.

CONCLUSION: CTX + CPI therapy did not show benefit over CTX alone as first line therapy in patients with EP NECs. Further development of novel treatment is necessary to improve the prognosis.

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