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Comparative Outcomes of Second Line Topoisomerase I Inhibitor-Containing Therapies on Extrapulmonary Neuroendocrine Carcinoma



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BACKGROUND: Extrapulmonary neuroendocrine carcinomas (NEC) are rare and aggressive tumors with limited therapeutic options. After first-line platinum-based chemotherapy, no further guideline treatment has been established. This investigation aims to assess the outcomes for second-line therapies.

METHODS: With IRB approval, we conducted a retrospective study of extrapulmonary NEC patients that progressed on first-line platinum chemotherapy from 2008-2018. Demographic data and treatment related characteristics were collected and represented as descriptive statistics. The primary endpoint include overall survival (OS) and progression-free survival (PFS). OS and PFS were estimated and stratified by site of primary (gastroenteropancreatic vs non-GI) and type of second-line therapy (irinotopotecan vs others). Log-rank test and Kaplan-Meier curves were used to compare survival distributions between groups. Therapy discontinuation or death was used as surrogates for PFS.

RESULTS: Forty-seven patients met eligibility, with median age 65 (range 31-82), 62% male, and 83% White. Of these, 22 were gastroenteropancreatic while 25 were non-GI primary. Thirty patients (63.8%) received second-line therapy where 11 received irinotecan/topotecan (ir/to), while 19 received other agents (temozolomide, other platinum agents, gemcitabine, paclitaxel, pembrolizumab, and sunitinib). The median OS was 10.3 months in the ir/to group versus 13.4 months for other therapies, $p=0.10$.

The median PFS for ir/to therapy compared to other therapies was 2.0 months versus 1.8 months, respectively, $p=0.72$. The OS and PFS with and without ir/to were not significantly different by the primary site ($p=0.61$ and $p=0.21$).

CONCLUSION: A significant proportion of extrapulmonary NEC patients undergo second-line therapies. Interestingly, outcomes for ir/to-containing second-line therapies were not statistically different from other agents, regardless of the site of primary. With approval of new second-line therapies for small cell lung cancer, further research in therapeutic options is needed for this aggressive disease.

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