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Efficacy of 2nd-line Chemotherapy in Patients with Poorly Differentiated, High Grade Extrapulmonary Neuroendocrine Carcinoma (PD NEC)

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BACKGROUND: A platinum/etoposide doublet is standard 1st-line therapy for PD NEC, however evidence to guide treatment beyond 1st-line regimens is lacking. Second-line small cell lung cancer (SCLC) regimens are commonly used, but despite morphological similarities, extrapulmonary PD NEC is genetically distinct from SCLC. This study aimed to evaluate the efficacy of 2nd-line regimens in PD NEC.

METHODS: We performed a retrospective analysis of patients treated with 2nd-line chemotherapy for PD NEC. Inclusion criteria were previous 1st-line therapy with platinum/etoposide, extrapulmonary PD NEC, and follow-up data. The primary end points were overall survival (OS) and progression-free survival (PFS) following 2nd-line therapy. Secondary end-points included OS and PFS from 1st-line therapy.

RESULTS: Sixty-four patients were included. The median OS from initiation of 2nd-line therapy for all regimens was 6.2 months [95% CI 4.9–8.9]. The median PFS was 2.3 months [95% CI 2.0–3.2]. No 2nd-line regimen showed a statistically significant difference in OS or PFS, though irinotecan-containing regimens had the longest OS (7.8 months [3.3–14.8]) and paclitaxel-containing regimens (without topotecan) had the longest PFS (2.7 months [1.3–6.4]). Multiple-agent regimens showed a nonsignificant increase in both OS (6.2 months [3.7–10.8]) and PFS (2.3 months [1.8–4.6]) compared to singlets (OS 5.8 months [4.9–11.3];

PFS 2.2 months [1.4–4.1]). Tumors of unknown primary site had the longest PFS from 2nd-line, but this was nonsignificant. There was a significant increase in OS for cisplatin 1st-line regimens compared to carboplatin (17.0 months [12.5–22.6] vs 11.7 months [8.0–14.0]). These patients were younger (median age 54 vs 63), but the effect persisted when controlling for age.

Conclusion: The efficacy of current 2nd-line therapy in PD NEC is poor. No 2nd-line regimen showed statistically significant superiority. Cisplatin was associated with a longer OS regardless of 2nd-line regimen or age. However, unmeasured confounders such as performance status or comorbidities may explain some of this effect.