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Peptide Receptor Radionuclide Therapy versus Capecitabine/ Temozolomide for the treatment of Metastatic Pancreatic Neuroendocrine Tumors

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BACKGROUND

Peptide Receptor Radionuclide Therapy (PRRT) and Capecitabine/Temozolomide (CAPTEM) are cornerstones of systemic therapy for metastatic pancreatic neuroendocrine tumors (PNETs). The best sequence of systemic therapies in PNETs is poorly understood. Herein we compare the efficacy of PRRT vs. CAPTEM as second line and beyond systemic therapies.

METHODS

Clinicopathologic, radiographic, and genomic data were captured for metastatic PNET patients seen at the University of Chicago between 2013 and 2023. The primary outcome was progression free survival (PFS) with PRRT/CAPTEM after progression on at least one prior line of systemic therapy. The secondary outcomes were objective response rate (ORR), time to response (TTR), and overall survival (OS). Outcomes were analyzed using Kaplan Meier estimations and Cox proportional hazards regression.

RESULTS

59 patients were included and median follow-up was 31.7 months. There was no difference in PFS between the PRRT (n = 29) and CAPTEM (n = 30) groups (21.90 months vs. 20.03 months; HR, 0.99; 95% CI, 0.56 – 1.74; p = 0.97). On subgroup analysis, PRRT had longer PFS in cases without extrahepatic metastases (n = 20; 26.47 months vs. 17.67 months; HR, 0.31; 95% CI, 0.10 – 0.92; p = 0.03) and cases with mutations in the *MEN1, DAXX*, and/or *ATRX* genes (n = 19; 28.43 months vs. 18.67 months; HR, 0.22; 95% CI, 0.06 – 0.85; p = 0.03). CAPTEM had longer PFS in patients with grade 3 disease (n = 13; 16.33 months vs. 7.83 months; HR, 0.13; 95% CI, 0.02 – 0.67; p = 0.02) and trended towards longer PFS in cases with bone metastases (n = 20; 28.60 months vs. 17.87 months; HR, 0.35; 95% CI, 0.11 – 1.18; p = 0.09). ORR did not vary significantly (PRRT, 8/23, 34.78%; vs. CAPTEM, 9/22, 40.91%; p = 0.67). CAPTEM responders showed shorter TTR (6.03 months vs. 11.15 months; log-rank p = 0.03). In patients who received both (PRRT first = 11; CAPTEM first = 12), OS did not vary based on the sequence (48.57 months vs. 50.07 months; HR, 1.20; p = 0.75).

CONCLUSIONS

PFS, ORR, and OS are similar when using PRRT vs. CAPTEM as 2nd line and beyond therapy for patients with metastatic PNETs. However, patients with *MEN1, DAXX,* and/or *ATRX* mutations or without extrahepatic metastases might further benefit from PRRT and patients with grade 3 disease from CAPTEM. Candidates for surgical debulking or those with tumor-induced symptoms may benefit from initial treatment with CAPTEM due to shorter TTR.

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