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## Clinical outcomes following salvage PRRT in patients with metastatic neuroendocrine tumors

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### BACKGROUND

Peptide receptor radionuclide therapy (PRRT) with $^{177}$Lu-DOTATATE prolongs survival in metastatic, well-differentiated, somatostatin receptor subtype 2 (SSTR2)-positive gastro-entero-pancreatic neuroendocrine tumors (NETs). Disease progression after initial PRRT remains a clinical challenge. PRRT retreatment has emerged as a potential strategy, with real-world data supporting its efficacy and tolerability. This study evaluated clinical outcomes following PRRT retreatment, including progression-free survival (PFS), overall survival (OS), and treatment-related toxicity.

### METHODS

We retrospectively analyzed patients with metastatic, well-differentiated NETs who received PRRT retreatment after progression following initial PRRT at Mayo Clinic sites between 2016 and 2025. Patients were eligible for retreatment if they had previously benefited from PRRT with good tolerance and had DOTATATE-avid, potentially treatable disease. Clinical records, imaging (Ga-68 DOTATATE PET/CT), and laboratory results were reviewed. Toxicities were graded using CTCAE v5.0. Survival outcomes were estimated using the Kaplan-Meier method and Cox regression in RStudio, with multivariable adjustment for key clinical variables.

### RESULTS

Fifty-six patients underwent PRRT retreatment, receiving a median of 6 cycles in total (4 during initial therapy, 2 during retreatment). Most had small bowel (50%) or pancreatic (33.9%) primaries; 87.5% had a Krenning score of 4. The median interval between first cycle of initial PRRT and retreatment was 41.7 months. Over half received systemic therapies between PRRT courses. Median PFS and OS after retreatment were 14.5 and 31.8 months, respectively. The most common toxicities were Grade 1–2 thrombocytopenia (25%) and neutropenia (5.4%); no Grade ≥3 hematologic toxicities occurred. Three patients developed delayed hematologic events, including evolving myelodysplastic syndrome (n=1), acute myeloid leukemia (n=1), and prolonged myelosuppression (n=1). One patient experienced Grade 1 acute kidney injury.

In multivariable analysis, higher tumor grade and shorter time between PRRT courses were significantly associated with shorter PFS. Small bowel primary tumors and better ECOG performance status were associated with longer OS. Intervening therapies were not significantly associated with survival outcomes.

Five of the 56 patients in this cohort received an additional two cycles after progression from retreatment (total of 8 cycles). No acute toxicities were observed. Three progressed within 8 months; two remained progression-free at last follow-up (10.3 and 17.0 months)

## CONCLUSIONS

PRRT retreatment was well tolerated and associated with clinically meaningful PFS and OS in select patients with progressive, well-differentiated NETs.

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