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## Are there any clinical factors associated with PRRT-refractoriness in NET patients?

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### BACKGROUND

Peptide receptor radionuclide therapy (PRRT) with Lutetium-177 DOTATATE (LUTATHERA) is an effective treatment option for somatostatin receptor (SSTR) positive metastatic gastroenteropancreatic neuroendocrine tumors (NETs) and has also demonstrated antitumor activity in SSTR positive NETs from other primary sites. While the median progression free survival (mPFS) is around 29 months, there is a subset of patients who are refractory to PRRT and demonstrate progression within one year of treatment completion. Since literature from United States on Lutetium-177 DOTATATE refractory disease is limited, we specifically wanted to study clinicopathological factors that may correlate with primary PRRT-refractory disease.

### METHODS

Retrospective analysis of 163 patients with NETs who underwent PRRT at University of Kentucky between January 2018 until December 2022 was performed. Sixty-one progressors were identified and 39 were included in the final analysis. Primary PRRT-refractoriness was defined as radiographic progression within 12 months of last PRRT treatment. Univariate and multivariate analysis using logistic regression were performed to determine if tumor grade, primary tumor origin, carcinoid syndrome, number of metastatic sites, metastatic peritoneal disease, prior systemic therapies, history of surgical debulking, prior chemotherapy, prior liver directed therapy (LDT) and prior tumor resection were associated with PRRT-refractoriness. Subgroup analyses were also performed to explore the aforementioned associations.

### RESULTS

Patients who had unknown cause of death (n=14), demonstrated clinical progression but no radiographic progression (n=2) or received less than 3 doses of PRRT (n=6) were excluded from the final analysis. There were 21 patients in the primary PRRT-refractory group and 18 patients in the PRRT-sensitive group. The median time to progression (TTP) was 163 days and 624 days in the PRRT-refractory group and PRRT-sensitive group, respectively. No statistically significant ($p<0.05$) associations were found between the studied clinicopathological factors and PRRT-refractoriness. On subgroup-analysis performed several different ways including patients with tumor grade 2 or higher, lung/pancreatic primary, no history of surgical debulking, presence of peritoneal metastasis, lines of prior systemic treatment more than or equal to 3 and prior chemotherapy did not reveal significant associations.

## CONCLUSIONS

This study did not identify any association between pre-specified clinicopathological factors and PRRT-refractoriness in NET patients. Larger multi-center studies are needed to further explore this clinical question.

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