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Peptide Receptor Radionuclide Therapy Improves Survival in Patients Who Progress After Resection of Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND

Peptide Receptor Radionuclide Therapy (PRRT) is effective for gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) and received FDA approval after demonstrating improved progression-free-survival (PFS) in advanced midgut NETs. We investigated a two-decade experience with PRRT, hypothesizing that PRRT confers PFS and overall-survival (OS) advantages in patients who progress after surgery.

METHODS

A single-institutional NET database was reviewed for patients who had resection and/or cytoreduction of GEP-NETs and later had disease progression according to RECIST 1.1 criteria. The Kaplan-Meier method assessed PFS and OS, calculated from progression after surgery for the no-PRRT group or start of PRRT for PRRT recipients. Cox regression with time-dependent covariates controlled for immortal time bias and other confounders.

RESULTS

Among 237 patients identified, 95 received PRRT while 142 did not. There were no differences in sex, T- or N-stage, tumor grade/differentiation, primary site, or time to first progression; 94% of PRRT patients had metastases at diagnosis vs. 77% in the non-PRRT group. Among PRRT recipients, 60 received PRRT soon after first progression ("Upfront", median 4.6 months) while 35 received later PRRT ("Delayed" as 2nd - 4th line therapy at median 24.5 months). Median PFS from the start of PRRT was longer for both groups (32.0 and 34.3 months, respectively) compared with the no-PRRT group (11.0 months, $p<0.001$). Importantly, median OS was longer for the Upfront PRRT group (53.7 vs. 38.4 months in the no-PRRT group; $p=0.01$), and in both pancreatic (PNET) and small bowel-primary (SBNET) subgroups (Table). Time-dependent covariate analysis revealed a lower risk of death associated with PRRT (HR=0.61; 95%-CI 0.39-0.95; $p=0.028$) after adjusting for sex, age, M-stage, tumor grade, and primary site.

Table: PFS and OS by treatment category in 237 GEP-NET patients progressing after surgery.

	Median PFS (months)	p-value*	Median OS (months)	p-value*
PRRT Upfront (n=60)	32.0	<0.001	53.7	0.01
PRRT Delayed (n=35)	34.3	<0.001	48.7	0.2
No PRRT (n=142)	11.0	---	38.4	---
SBNET PRRT (n=65)	32.0	<0.001	40.5	0.02
SBNET No PRRT (n=79)	12.4	---	29.8	---
PNET PRRT (n=27)	34.3	<0.001	123.4	0.08
PNET No PRRT(n=52)	10.6	---	56.6	---

SBNET=Small bowel NET; PNET=Pancreatic NET. *p-value by log-rank test compared with No PRRT.

CONCLUSIONS

The strategy of surgical resection and cytoreduction followed by PRRT after progression appears to confer superior PFS and OS in SBNET patients, and PFS in PNET patients. The PFS benefit of PRRT was seen whether it was given Upfront or Delayed after failure of other lines of therapy.

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