

Retreatment with peptide receptor radionuclide therapy (PRRT) in patients with neuroendocrine tumors (NET): Spanish clinical experience from SEPTRALU national registry [1157P]



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BACKGROUND

- PRRT is widely used in patients with gastroenteropancreatic NET, supported by the evidence of NETTER-1 and NETTER-2 studies [1,2]. Optimal position of PRRT in the NET therapeutic sequence remains unknown.
- Repetition of a previous succesful therapeutic line in the treatment of patients with NET has been explored in trials like RESUNET, were rechallenge with sunitinib seems active and safe [3]. Currently, PRRT retreatment (rePRRT) has arise as an option for patients with previous clinical benefit to first PRRT (PRRT1).
- Standardized protocols for the optimal efficacy, safety and rePRRT schedule administration remain undefined across centers. Onoling clinical trials are exploring optimal duration and position of rePRRT in NET therapy.
- SEPTRALU is a collaborative spanish national registry for NET patients treated with PRRT. Currently comprises over 500 patients [4]. The aim of the present study is to explore rePRRT outcomes in NET population included in SEPTRALU registry.

REFERENCES

1-Strosberg J, El Haddad G, Wolin E, et al. Phase 3 Trial of 177Lu-Dotatate for Midgut Neuroendocrine Tumors. N Eng J Med 2017; 376:125-135
2-Singh S, Halperin D, Myrnesaug S, et al. [177Lu]Lu-DOTA-TATE plus long-acting octreotide for the treatment of newly diagnosed, Advanced grade 2-3, well-differentiated, gastroenteropancreatic neuroendocrine tumors (NETTER-2): an open-label, randomised, phase 3 study. The Lancet 2024; 403:2007-2017
3-Granda E, Espinosa-Olano P, Serrano R, et al. RESUNET (GETNE-2016-01): A phase II study to evaluate the efficacy and safety of the challenge with sunitinib in G1/G2 pancreatic neuroendocrine tumors (pNET). A Spanish Task Force Group in neuroendocrine and endocrine tumors (GETNE) study. Ann Oncol 31 (suppl4): S777-S778
4-Mitjavila M, Jimenez-Fonseca P, Bello P, et al. Efficacy of [177Lu]Lu DOTATATE in metastatic neuroendocrine neoplasms of different locations: data from the SEPTRALU study. Eur J Nucl Med Mol Imaging. 2023;50(3):2480-2500.

METHODS

- All patients included in SEPTRALU spanish registry were reviewed. All patients with more than 4 cycles of PRRT were considered for analysis.
- Clincal, pathological and PRRT outcomes variables were collected. Univariate analysis was performed with X².

	SEPTRALU (n=522)	RePRRT (N=71)	P
Sex			
Female	208 (39,8%)	29 (59,15%)	0,87
Male	314 (60,2%)	42 (40,85%)	
Age (median)	60	55	
Functioning tumor	169 (32,4%)	25 (35,21%)	0,54
Primary tumor location			0,95
Pancreas	182 (34,86%)	25 (35,21%)	
Small intestine	148 (28,35%)	24 (33,8%)	
Gastric/Colon/Rectum	60 (11,49%)	5 (7,04%)	
Unknown	-	8 (11,26%)	
Pulmonary	56 (10,72%)	5 (7,04%)	
Other	-	4 (5,63%)	
Ki67 (median)	5%	10%	
WHO Grade			0,67
Grade 1	178 (34,1%)	26 (36,62%)	
Grade 2	292 (55,9%)	35 (49,3%)	
Grade 3	52 (9,9%)	10 (14,08%)	

rePRRT	N=71
Time from PRRT1 to rePRRT (months)	29,3
Number of rePRRT cycles	
1	24 (33,8%)
2	30 (42,25%)
3	5 (7,04%)
4	12 (16,9%)
Best radiological response	
PD	8 (11,26%)
SD	28 (36,43%)
PR	12 (16,9%)
NA	23 (32,39%)
ORR (%)	16,9%
PFS (months)	NR
10m PFS	78%

Table 1 (left).Patients characteristics

Table 2 (up). RePRRT characteristics and outcomes
PD: Progressive disease; SD: Stable disease; PR: Partial response; ORR: Overall response rate; PFS: Progression free survival. NR: Not reached.

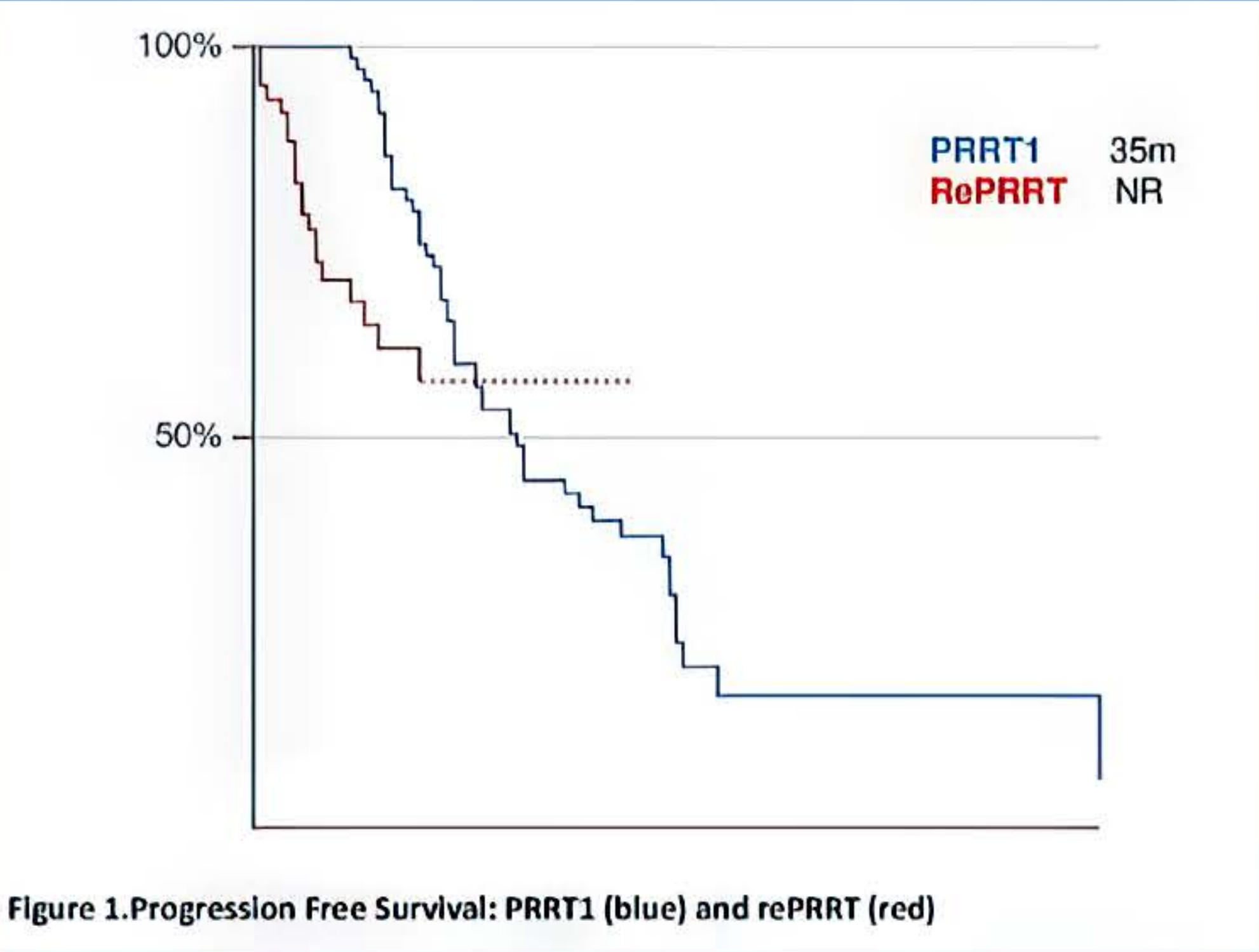


Figure 1.Progression Free Survival: PRRT1 (blue) and rePRRT (red)

RESULTS

- 71 rePRRT patients were included. Baseline characteristics are presented in **Table 1**.
- PRRT1 was administered mainly in 2nd (35,5%) and 3rd line (27%) and all patients received 4 doses. Overall response rate (ORR) and progression free survival (PFS) of PRRT1 was 61,7% and 35 months, respectively (**Fig1**).
- Characteristics and outcomes of rePRRT are included in **Table 2**. After 10 months of follow up, rePRRT PFS was not reached (**Fig1**). Considering only rePRRT patients with available radiological evaluation (n=48), ORR was 25%. Main reason for rePRRT discontinuation was disease progression (18%)
- Univariate analysis identified predictors of rePRRT radiological response: **Previous PRRT1 radiological response** (p 0.004), **Ki67 >30%** (p 0.033) and **WHO Grade 3** (p 0.035).

CONCLUSIONS

- RePRRT offers a viable therapeutic strategy for patients with SSTR+ NET, mainly in those with previous benefit to PRRT1.
- Outcomes of rePRRT are limited compared to PRRT1. Radiological responses could be achieved, especially in patients with more agresive NET and those who responded to the PRRT1.
- Ongoing rePRRT trials will help to understand optimal duration and its role in therapeutic algorithms.