Efficacy and Safety of Peptide Receptor Radionuclide Therapy in Metastatic Neuroendocrine Tumour: Malaysian Single-Institution Retrospective Analysis

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INTRODUCTION

Peptide Receptor Radionuclide Therapy (PRRT) has been recommended as a treatment option in metastatic somatostatin receptor (SSTR) positive gastroenteropancreatic-neuroendocrine tumours (GEP-NETs), thoracic-NETs and pheochromocytomas/paragangliomas.

METHODOLOGY

Seventy-three NET patients who received either 177Lu-DOTA-TATE or 90Y-DOTA-TOC in a single institution in Malaysia from March 2018 to March 2020 were evaluated for treatment outcome. Patients were either local (Malaysian residents) or from South-East Asian and East Asian countries (Table 1).

Progression of tumour response to treatment cycles were determined using Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 analysis criteria.

Toxicities and side effects in each patient resulting from each treatment cycle were assessed using Common Terminology Criteria for Adverse Events.

		N = 73
Age	mean	49.5 (27 – 84)
Gender	M:F	39:35
Primary	Pancreas:	
	Non-functioning	33
	Insulinoma	2
	VIPoma	1
	GI:	
	Stomach	2
	Small bowel	6
	Rectum	16
	Lung/ mediastinum	4
	Thymic	2
	Pheo/ Paranganglioma	5
	Liver	1
	Unknown	1
Ki67	G1	14
	G2	44
	G3 Ki67=20%	9
	Unknown	6

		N= 73
Metatastic Site: Node; liver; bone; other organs	0	3
	1	27
	2	17
	3	16
	>3	10
Prior treatment	Nil	6
	Primary tumour resection	30
	Other tx to primary	2 RT; 1 alcohol
	Metastectomy	10
	Long-acting octreotide	34
	Everolimus	20
	TAE/ TACE/ RFA	13 (4 ≥ x3)
	CAPTEM	13
	Eto-Cis	5
	Other chemotherapy	4
	Sorefenib	3
	Sunitinib	10
	Sulfatinib	2
	MIBG	2
	PRRT	11

Table 1. List of known and unknown primaries in all patients, including known metastatic sites and Ki67.

RESULTS AND DISCUSSION

Sixty patients were diagnosed with GEP-NETs; six diagnosed with thoracic-NETs; five diagnosed with paraganglioma/pheochromocytomas; and two presenting with unknown primary disease. Most NETs presented are classified as either Grade 1 (low-grade tumour) at 19.2%, and Grade 2 (intermediate-grade tumour) at 60.3%. Twenty-nine patients (39.7% of cohort) received ≥ 1 medical therapy ± liver directed therapy prior to PRRT. Thirty-nine patients (53.4% of cohort) received 2-4 cycles of PRRT; whereas 34.2% of patients received more than 4 cycles of PRRT. Twelve (16.4%) patients received either 1 or 2 courses of PRCRT. Nearly 1/3 patients received alternating 177Lu-/90Y-PRRT (Table 1).

Objective response rate (ORR) in all NETs patients was 47.0%, whereas disease control rate (DCR) was 83.3%. In GEP-NETs, 55.6% patients achieved ORR and 88.9% achieved DCR (Table 2 & 3).

Table 2 & 3. Treatment response to PRRT in all NETs group and GEP-NETs group.

Outcome	All NETS, N = 73
Objective Response, ORR	31/66 (47.0%)
Disease Control, DCR	55/66 (83.3%)
Progression, PD	11/66 (16.7%)
Unable to assess	7 (4 discontinued after 1st cycle due to stroke; no uptake; high uptake in enlarged spleen; positive FDG) (3 loss follow-up)

Outcome	GEP-NETS, N = 59
Objective Response, ORR	30/54 (55.6%)
Disease Control, DCR	48/54 (88.9%)
Progression, PD	6/54 (11.1%)
Unable to assess	5 (3 discontinued after first cycle due to stroke; no uptake; high uptake in enlarged spleen) (2 loss follow-up)

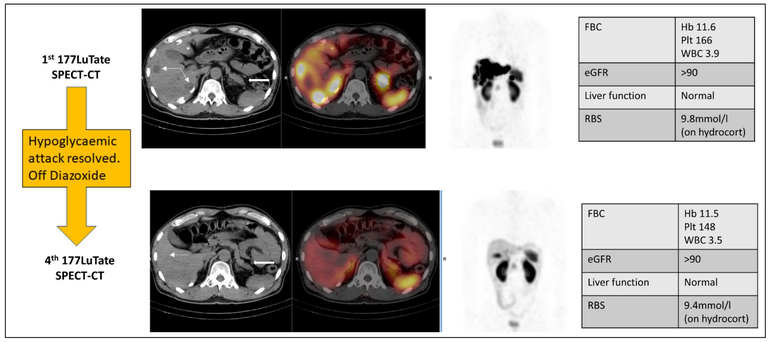

Figure 1. 55 year old male. Presented with persistent hypoglycaemia. Insulinoma with liver metastases. Ki67 = 15%. Patient undergoing everolimus prior to PRRT. He was then referred for PRRT and subsequently received 4 cycles of 177LuTate + everolimus.

With regards to adverse effect, only one patient developed Grade 3 bicytopaenia who required transfusion and thrombopoietin (Table 4). No renal toxicity was identified including 4 patients initially presented with Stage 2 and 3 CKD. One patient developed Grade 3 liver toxicity but recovered after symptomatic treatment. Three (4.1%) patients developed transient vomiting during radiopharmaceutical infusion. No carcinoid and hypertensive crisis observed.

CONCLUSION

PRRT demonstrates high ORR and DCR in these parts of South East Asian/East Asian population. PRRT is also seen to be well tolerated with minimal to no side effects.

In the follow up periods, no renal toxicities were observed, with the exception of a single rare incidence of Grade 3-4 haematological toxicity.

Table 4. Haematological toxicity

Short term adverse effect	N= 73	Remark
Anaemia,		
Grade 1	8	
Grade 2	4	
Grade 3	1	Require transfusion
Grade 4	0	
Thrombocytopaenia,		
Grade 1	13	
Grade 2	2	
Grade 3	1	Require thrombopoietin
Grade 4	0	
Neutropaenia		
Grade 1	14	
Grade 2	3	
Grade 3	0	
Grade 4	0	

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