Preliminary Safety and Efficacy Data of [212Pb]VMT-α-NET in Somatostatin Receptor 2 (SSTR2) Expressing Neuroendocrine tumors (NETs) (NCT05636618)

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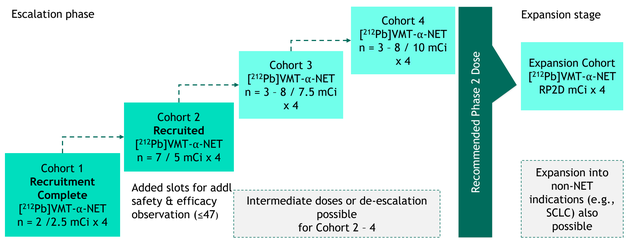
Background

- Neuroendocrine tumors are heterogenous
- >80% overexpress somatostatin receptor 2 (SSTR2)
- Despite the availability of [177Lu]Lu-DOTATATE, there remains a high unmet medical need for novel therapies
- [212Pb]VMT-α-NET is a modified SSTR2 binding peptide with proprietary chelation technology for 203Pb, 212Pb and 212Bi allowing for optimized delivery and retention of the payload in the tumor microenvironment
- [212Pb]VMT-α-NET, a novel targeted alpha radionuclide therapy (TAT) to the SSTR2, is being investigated for safety and efficacy in PRRT-naïve patients with SSTR2-expressing tumors

Trial Parameters

Escalation Stage Population	Key Study Features	Study Endpoints
• Advanced/Unresectable or metastatic NETs • Progressive disease on prior therapy • PRRT naïve • FDA approved SSTR2 PET/CT avid disease	• Bayesian mTPI-2 design • Dosimetry to be assessed during screening period by [203Pb]VMT-α-NET SPECT/CT	• Primary: DLTs, MFD, RP2D • Secondary: ORR, DOR, PFS, OS by RECIST v1.1 • Exploratory: absorbed radiation doses estimates for[212Pb]VMT-α-NET

Trial Design



Patient Characteristics (All Treated Patients = 9)

Age (years)	
Median	63
Range	37,78
Sex, n (%)	
Female	4 (44)
Male	5 (56)
Race, n (%)	
White	8 (89)
Asian	1 (11)
Tumor Type, n (%)	
Pancreatic NET	3 (33)
Non-pancreatic NET	6 (66)
Grade, n (%)	
G1	3 (33)
G2	6 (66)
Time since diagnosis (months)	
Mean	70
Median	37
Range	12, 181
Number of prior systemic therapies	
Median	1
Range	0, 2
Prior systemic therapies (patients with each)	
Somatostatin analogues	7
Capecitabine, temozolomide	1
Small molecule (sunitinib, everolimus)	2
ECOG Performance Status, n (%)	
0	8 (89)
1	1 (11)
Disease at Baseline, median (range)	
RECIST median sum of target lesions (cm)	6.7 (2.9, 8.7)
SUV max SUV mean	41.5 (18, 162) 30 (12, 102)

Data cutoff 10/31/24

Patient Disposition & Exposure (all patients as treated)

Cohort	Subject	Subject Status	Weight (kg)	Adm Activity (mCi)	Adm Activity per Weight (μCi/kg)	C1D1	C2D1	C3D1	C4D1
1	103-101	Follow-Up	53	2.5	50.1	✓	✓	✓	✓
1	103-102	Follow-Up	61	2.5	40.8	✓	✓	✓	✓
2	103-103	Follow-Up	157	5	31.7	✓	✓	✓	✓
2	109-103	Progressive disease	78	5	63.9	✓			
2	102-101	Follow-Up	91	5	54.5	✓	✓	✓	✓
2	103-104	Follow-Up[1]	59	5/2.5	84.5/42.3	✓	✓	✓	✓
2	102-103	Follow-Up	80	5	62.1	✓	✓	✓	*scheduled*
2	112-101	Follow-up	101	5	49.1	✓	✓	✓	✓
2	103-105	Follow-up	73	5	68.7	✓	✓	✓	✓

Green line denotes timepoint through which all post-cycle scans are available to the study team.

[1] Patient experienced syncope and dose was reduced for cycle 3 and cycle 4 to 2.5 mCi of administered activity
Additional notes: (1) 17 patients screened, (2) one patient (102-102) experienced a decline in renal function prior to administration of [212Pb]VMT-α-NET and was not treated.
Data cutoff 10/31/24

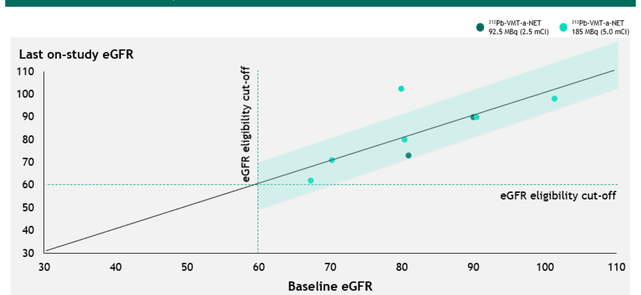
Treatment Emergent Adverse Events

Incidence of TEAEs	[212Pb]-VMT-a-NET 92.5 MBq (2.5 mCi) (N=2)			[212Pb-VMT-a-NET 185 MBq (5.0 mCi) (N=7)			Total (n=9)		
Grade	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
AEs by Preferred Term and Grade Reported by Patient [No patients with AE (% of pts treated per cohort)]									
Most Common (Occurring in ≥ 2 patients and/or grade ≥ 2									
Fatigue	1 (50)	1 (50)	-	3 (43)	2 (28)	-	4 (44)	3 (33)	-
Alopecia	2 (100)	-	-	4 (57)	-	-	6 (66)	-	-
Lymphocyte count decreased	-	1 (50)	-	2 (29)	3 (42)	-	2 (22)	4 (44)	-
Nausea	-	1 (50)	-	4 (57)	1 (14)	-	4 (44)	2 (22)	-
Anaemia	-	2 (100)	-	3 (43)	-	-	3 (33)	2 (22)	-
Diarrhoea	2 (100)	-	-	2 (29)	1 (14)	1 (14)	4 (44)	1 (11)	1 (11)
Haematocrit decreased	1 (50)	1 (50)	-	2 (29)	-	-	3 (33)	1 (11)	-
Red blood cell count decreased	1 (50)	1 (50)	-	2 (29)	-	-	3 (33)	1 (11)	-
White blood cell count decreased	2 (100)	-	-	-	-	-	2 (22)	-	-
Abdominal pain	-	-	-	2 (29)	-	-	2 (22)	-	-
Haemoglobin decreased	-	-	-	2 (29)	-	-	2 (22)	-	-
Hyperglycaemia	-	-	-	2 (29)	-	-	2 (22)	-	-
Blood alkaline phosphatase	-	-	-	2 (29)	-	-	2 (22)	-	-
Constipation	-	-	-	2 (29)	-	-	2 (22)	-	-
Haematuria	-	-	-	2 (29)	-	-	2 (22)	-	-
Headache	1 (50)	-	-	1 (14)	-	-	2(22)	-	-
Lethargy	1 (50)	-	-	1 (14)	-	-	2(22)	-	-
Aspartate aminotransferase incr'd	1 (50)	-	-	1 (14)	-	-	2(22)	-	-
Dizziness	1 (50)	-	-	1 (14)	-	-	2(22)	-	-
Presyncope	-	-	-	-	1 (14)		-	1 (11)	
Syncope	-	-	-	-	-	1 (14)	-	-	1 (11)
Amylase increased	-	1 (50)	-	-	-	-	-	1 (11)	-
Hypercalcemia	-	1 (50)	-	-	-	-	-	1 (11)	-
Weight decreased	-	-	-	-	1 (14)	-	-	1 (11)	-

Note: no renal insufficiency or dysphagia were observed.

Data cutoff 10/31/24

Estimated GFR, Most Recent vs Baseline

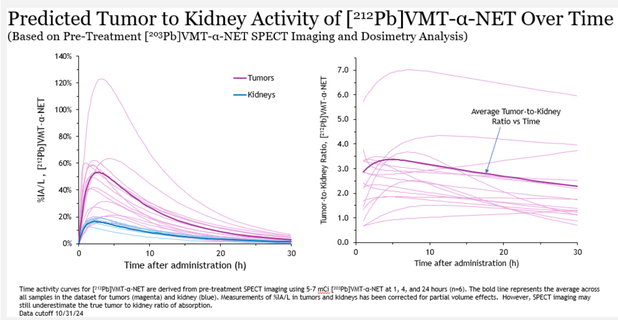


Data cutoff 10/31/24

Summary of Adverse Events

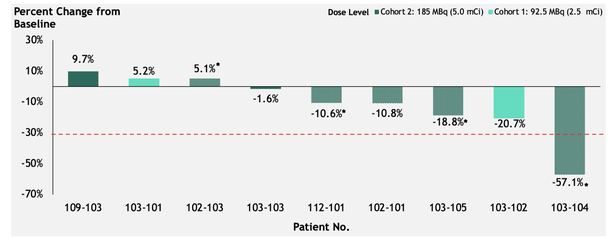
- No DLTs were observed in either cohort
- No grade 4, grade 5 or serious AEs were observed
- No decline in renal function was observed
- Hematologic AEs were few in number and low grade
- No dysphagia was observed
- No treatment discontinuations due to AE have occurred

Dosimetry



Time activity curves for [212Pb]VMT-α-NET are derived from pre-treatment SPECT imaging using 5-7 mCi [212Pb]VMT-α-NET at 1, 4, and 24 hours (n=6). The bold line represents the average across all samples in the dataset for tumors (magenta) and kidney (blue). Measurements of %IA/L in tumors and kidneys has been corrected for partial volume effects. However, SPECT imaging may still underestimate the true tumor to kidney ratio of absorption.
Data cutoff 10/31/24

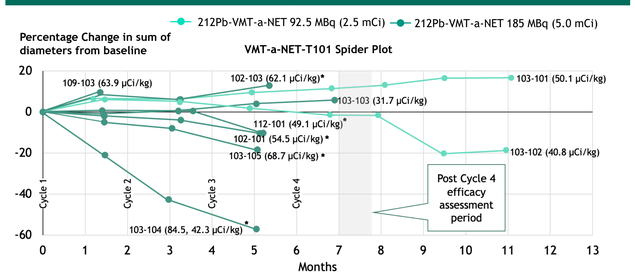
Preliminary Response Assessment by RECIST v1.1



Data cutoff 10/31/24

* The full sets of scans following cycle 4 are not yet available to the study team for five patients.
Note: Patient 109-103 experienced progressive disease by unambiguous progression of non-target lesions

Kinetics of Treatment Response



* The full sets of scans following cycle 4 are not yet available to the study team for five patients.
Notes: Patients had progressive disease prior to enrollment on study, and patient 109-103 experienced progressive disease by unambiguous progression of non-target lesions
Data cutoff 10/31/24

Acknowledgment

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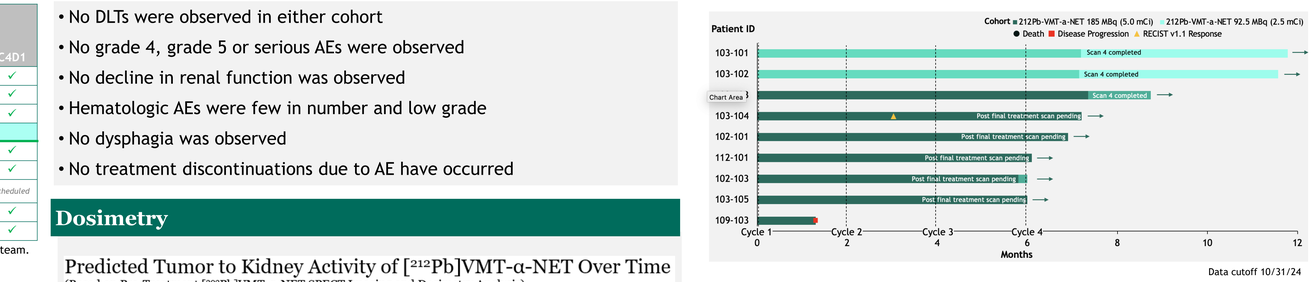
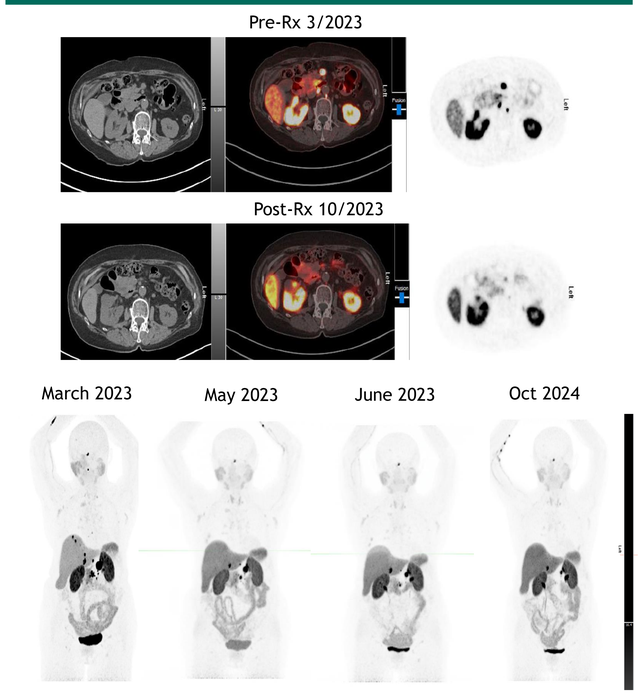
Preliminary Assessment of Disease Control Durability



Data cutoff 10/31/24

Patient with PR after [212Pb]VMT-α-NET



Conclusions

[203Pb]VMT-α-NET and [212Pb]VMT-α-NET were well-tolerated	• No DLTs were observed • No grade 4, grade 5 AEs or SAEs were observed • No decline in renal function was observed • Hematologic AEs were low in number and low grade • No treatment discontinuations due to AE have occurred
Appreciable activity was been observed with treatment at this early timepoint in the study	• 8 of 9 (89%) patients had durable control of disease • Analysis of cohort 1 and 2 at this early stage already shows clear signs of clinical activity • The study will continue to define the RP2D with further dose escalation cohorts

The Safety Monitoring Committee has recommended dose escalation which will be considered with FDA

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