

Is First-Line PRRT in GEP-NETs
the Standard of Care?
Yes (within reason)

Daniel M. Halperin, MD

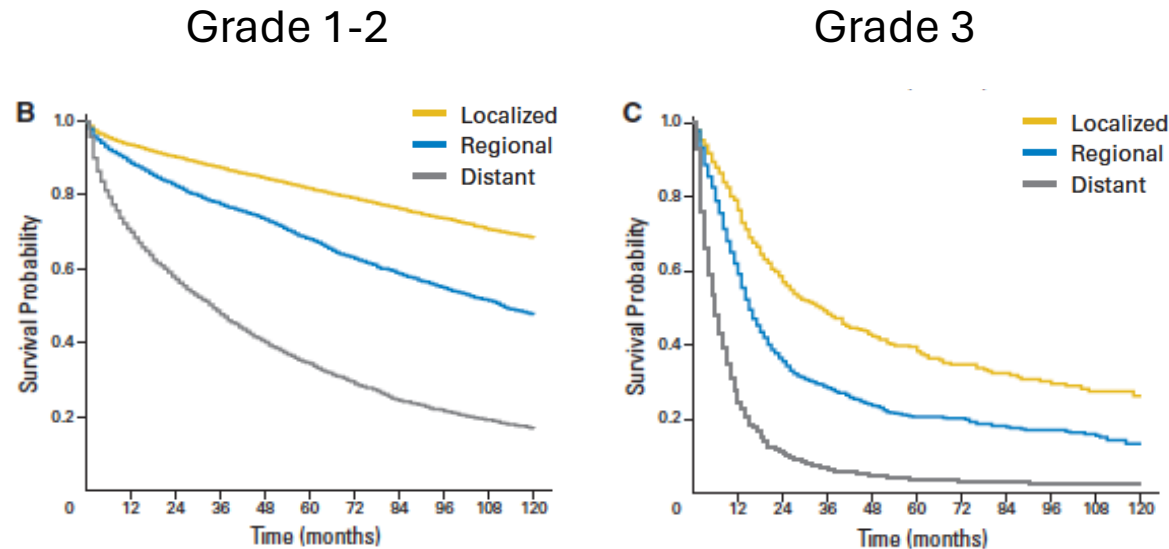
Disclosures (24 months)

- Consultant for Exelixis, Harpoon Therapeutics, ITM, Novartis, Crinetics, Amryt, Camurus, Alphamedix, Chimeric Therapeutics.
- Research funded by Genentech, ThermoFisher Scientific, ITM, AAA/Novartis, Camurus, RayzeBio.
- I **will not** discuss off-label and/or investigational use.

Take Home Points

- NETs are highly heterogeneous, and not universally indolent
 - A universal 1L SoC for all NET is as rational as a universal 1L SoC for all adenocarcinoma
- PRRT has PFS and ORR benefit in 1L for high G2/3 GEP-NET
- PRRT is therefore a reasonable 1L option for patients with high G2/3 NET in whom delaying progression or accelerating response is desirable.

Grade, Stage, Primary Site

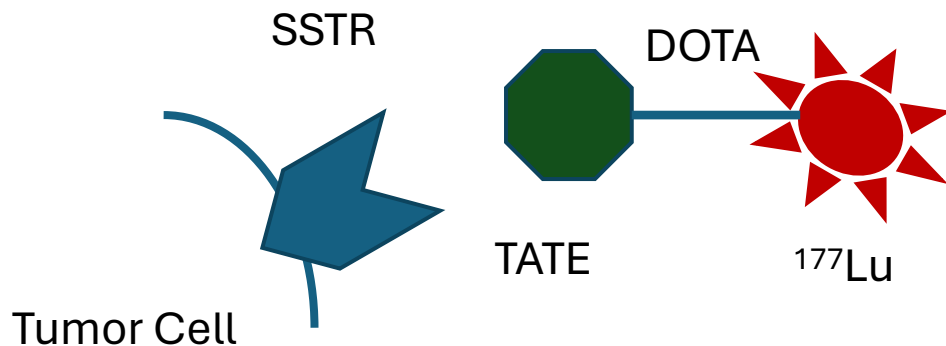


Metastatic Grade 1-2 NET

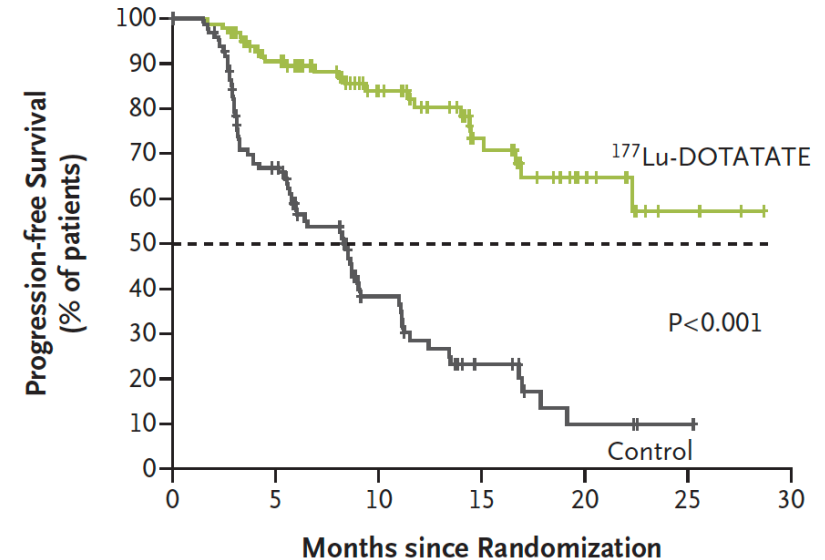
Primary Tumor Site	Median Survival (months)
Appendix	NA
Cecum	98
Colon	14
Lung	24
Pancreas	60
Rectum	33
Small Intestine	103
Stomach	29

Peptide Receptor Radionuclide Therapy (PRRT) in midgut NET

- NETTER-1
- ^{177}Lu -DOTA-Octreotate (DOTATATE): a radioactive isotope conjugated to somatostatin analogue.
- Patients with G1-2 midgut NET, PD on octreotide LAR 30, somatostatin-avid.
- DOTATATE vs. octreotide LAR 60mg.
- Notable SSTR-mediated myelotoxicity including MDS/AML in ~3% at 3-5 years.



A Progression-free Survival

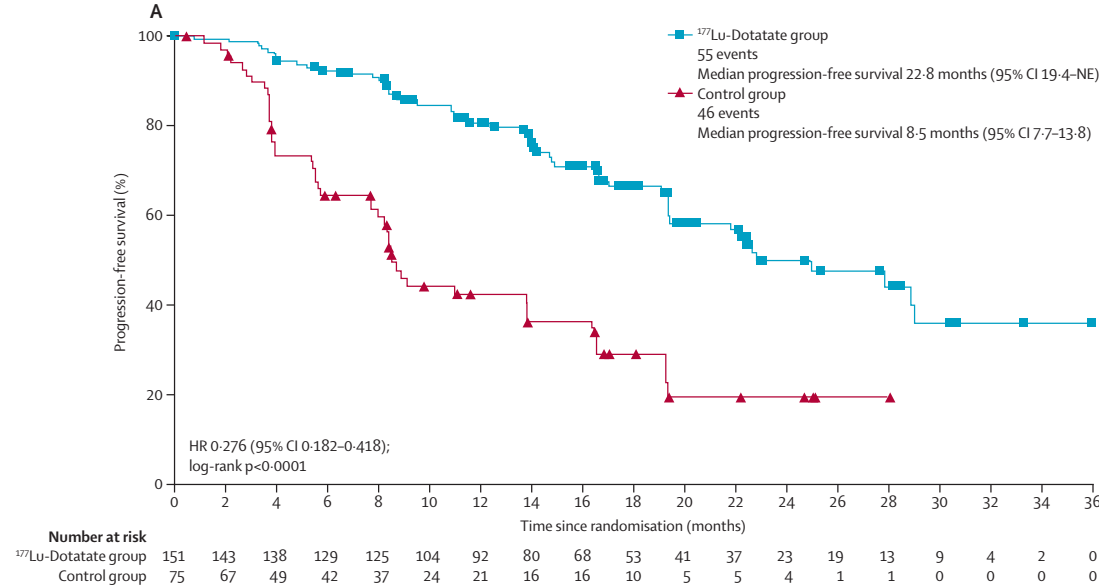


No. at Risk

	0	5	10	15	20	25	30				
^{177}Lu -DOTATATE group	116	97	76	59	42	28	19	12	3	2	0
Control group	113	80	47	28	17	10	4	3	1	0	0

PFS HR 0.209 [95% CI 0.129-0.33]

1L ¹⁷⁷Lu-DOTATATE Improves PFS in G2/3 GEP-NET



	HR (95% CI)	¹⁷⁷ Lu-Dotatate plus octreotide 30 mg LAR (n=151)	High-dose octreotide 60 mg LAR (control group) (n=75)
Age, years			
<65 (n=134)	0.26 (0.16-0.45)	30/86 (35%)	30/48 (63%)
≥65 (n=92)	0.37 (0.20-0.71)	25/65 (38%)	16/27 (59%)
Sex			
Female (n=105)	0.30 (0.16-0.55)	26/70 (37%)	19/35 (54%)
Male (n=121)	0.32 (0.18-0.54)	29/81 (36%)	27/40 (68%)
Race			
White (n=165)	0.36 (0.22-0.59)	43/115 (37%)	27/50 (54%)
Asian (n=34)	0.14 (0.05-0.38)	10/23 (43%)	10/11 (91%)
Tumour grade			
Grade 2 Ki67 ≥10% and ≤20% (n=147)	0.31 (0.18-0.53)	29/99 (29%)	25/48 (52%)
Grade 3 Ki67 >20% and ≤55% (n=79)	0.27 (0.14-0.49)	26/52 (50%)	21/27 (78%)
Tumour origin			
Pancreas (n=123)	0.34 (0.20-0.56)	39/82 (48%)	27/41 (66%)
All non-pancreas (n=103)	0.23 (0.12-0.46)	16/69 (23%)	19/34 (56%)
Small intestine (n=66)	0.30 (0.13-0.74)	11/45 (24%)	10/21 (48%)
Serum chromogranin A before randomisation			
≤2 × ULN (n=67)	0.22 (0.09-0.49)	11/43 (26%)	14/24 (58%)
>2 × ULN (n=144)	0.33 (0.20-0.53)	39/100 (39%)	28/44 (64%)
Somatostatin receptor uptake per central review			
Score 3 (n=34)	0.31 (0.10-0.89)	9/24 (38%)	6/10 (60%)
Score 4 (n=185)	0.30 (0.19-0.47)	46/123 (37%)	38/62 (61%)

0.03125 0.0625 0.125 0.25 0.5 1
 ← Favours ¹⁷⁷Lu-Dotatate Favours control →

ORR With ¹⁷⁷Lu-DOTATATE Across Grade and Primary Site

Subgroup	Complete response, n (%)	Partial response, n (%)	Total responders/N	ORR (95% CI)	Odds ratio (95% CI)
NET grade: Grade 2					
¹⁷⁷ Lu-DOTATATE	6 (6.1)	34 (34.3)	40/99	40.4 (30.7, 50.7)	5.83
High-dose octreotide	0	5 (10.4)	5/48	10.4 (3.5, 22.7)	(2.12, 16.00)
NET grade: Grade 3					
¹⁷⁷ Lu-DOTATATE	2 (3.8)	23 (44.2)	25/52	48.1 (34.0, 62.4)	11.57
High-dose octreotide	0	2 (7.4)	2/27	7.4 (0.9, 24.3)	(2.48, 53.97)
NET origin: Pancreas					
¹⁷⁷ Lu-DOTATATE	5 (6.1)	37 (45.1)	42/82	51.2 (39.9, 62.4)	7.56
High-dose octreotide	0	5 (12.2)	5/41	12.2 (4.1, 26.2)	(2.70, 21.19)
NET origin: Small intestine					
¹⁷⁷ Lu-DOTATATE	1 (2.2)	11 (24.4)	12/45	26.7 (14.6, 41.9)	7.27
High-dose octreotide	0	1 (4.8)	1/21	4.8 (0.1, 23.8)	(0.88, 60.24)

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