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THE ROLE OF SSA AT PROGRESSION – TO CONTINUE OR NOT?

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December 2022

CONFLICT OF INTEREST AND FUNDING

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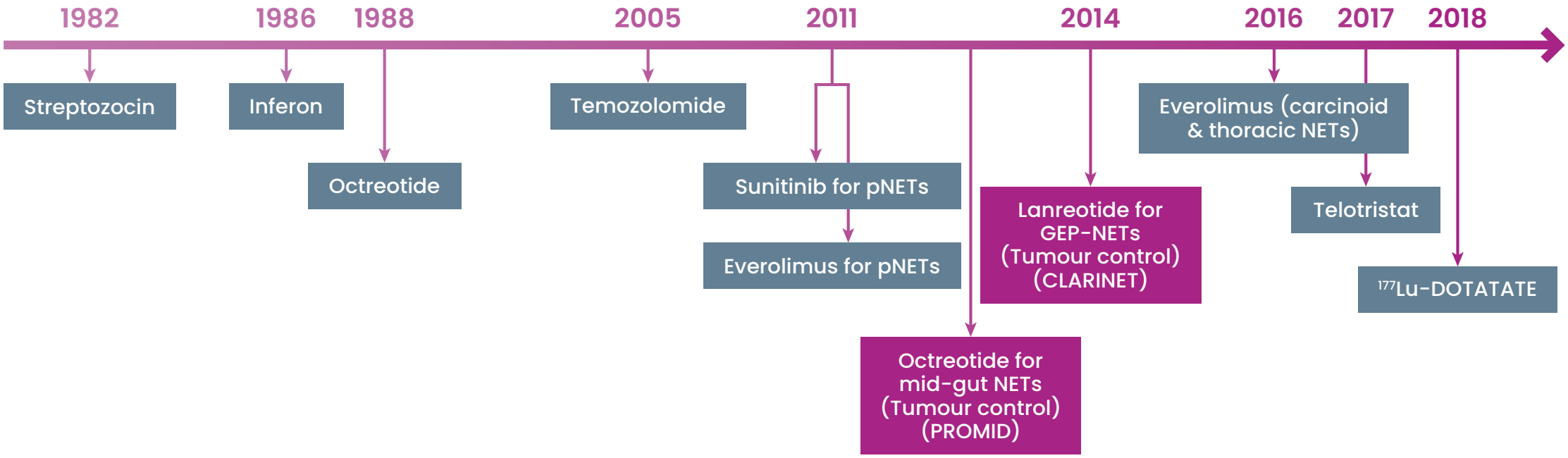
- **Prof. Martyn Caplin** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: AAA - Novartis, Chiasma, Ipsen, Pfizer
- **Dr Aman Chauhan** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: BMS, Clovis, EMD Serono, Nanotherapeutics, Ipsen, Lexicon, TerSera, Novartis/AAA

THERAPIES APPROVED FOR THE TREATMENT OF NEUROENDOCRINE TUMOURS



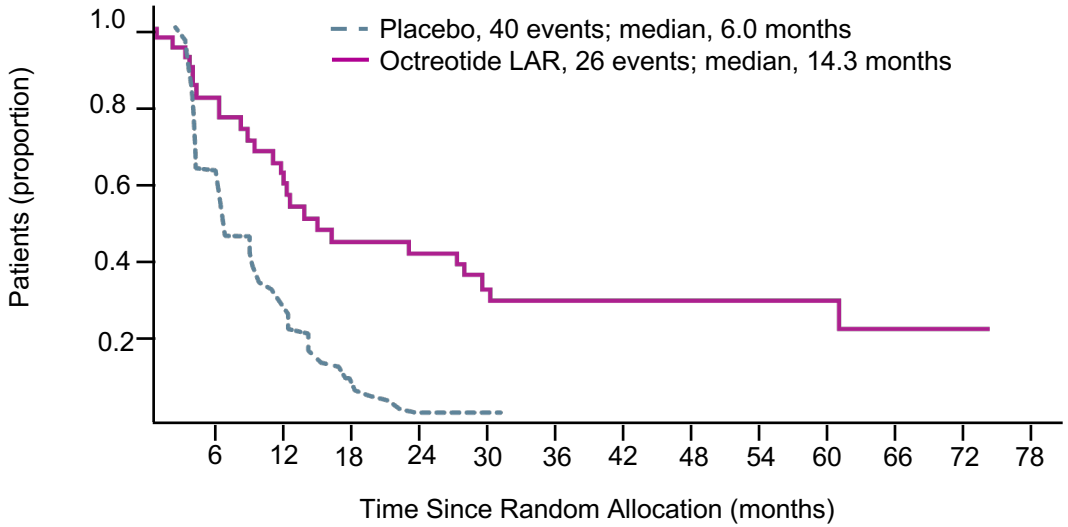
GEP, gastroenteropancreatic; NET, neuroendocrine tumour; p, pancreatic

Chauhan A, et al. Cancers 2022;14:5248

PROMID: EFFICACY

OCTREOTIDE VS PLACEBO IN MID-GUT NET

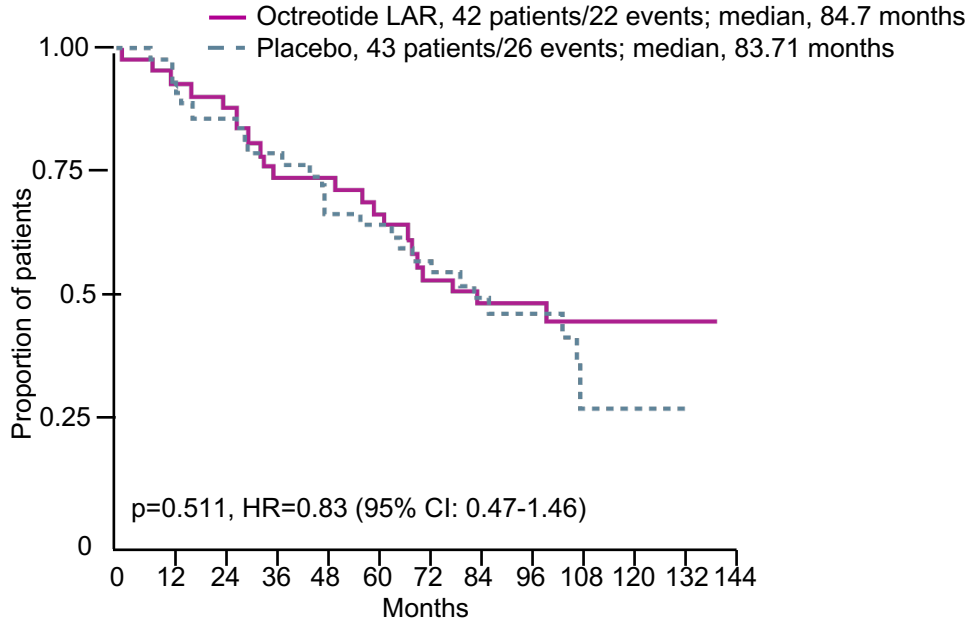
PRIMARY ENDPOINT: TTP[1]



No. of patients at risk														
Placebo	43	21	9	3	1	1	0	0	0	0	0	0	0	0
Octreotide LAR	42	30	19	16	15	10	10	9	9	6	5	3	1	0

Lon-rank test stratified by functional activity: p=0.000072, HR=0.34 (95% CI, 0.20 to 0.59)

SECOND PRIMARY ENDPOINT: OS[2]



Patients at risk												
Octreotide LAR	42	40	38	32	31	27	22	20	16	11	6	3
Placebo	43	42	36	33	31	27	24	18	14	8	3	1

CI, confidence interval; HR, hazard ratio; LAR, long-acting release; NET, neuroendocrine tumour; OS; overall survival; TTP, time to tumour progression

1. Rinke A, et al. J Clin Oncol. 2009;27:4656-63; 2. Rinke A, et al. Neuroendocrinology. 2017;104:26-32

PROMID: SAFETY

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SERIOUS ADVERSE EVENTS

	Octreotide LAR (N=42)	Placebo (N=43)
Serious adverse events	11	10
Affecting GI tract	6	8
Affecting haematopoietic system	5	1
Affecting general health status (fatigue and fever)	8	2
Treatment discontinuation due to AEs	5	0

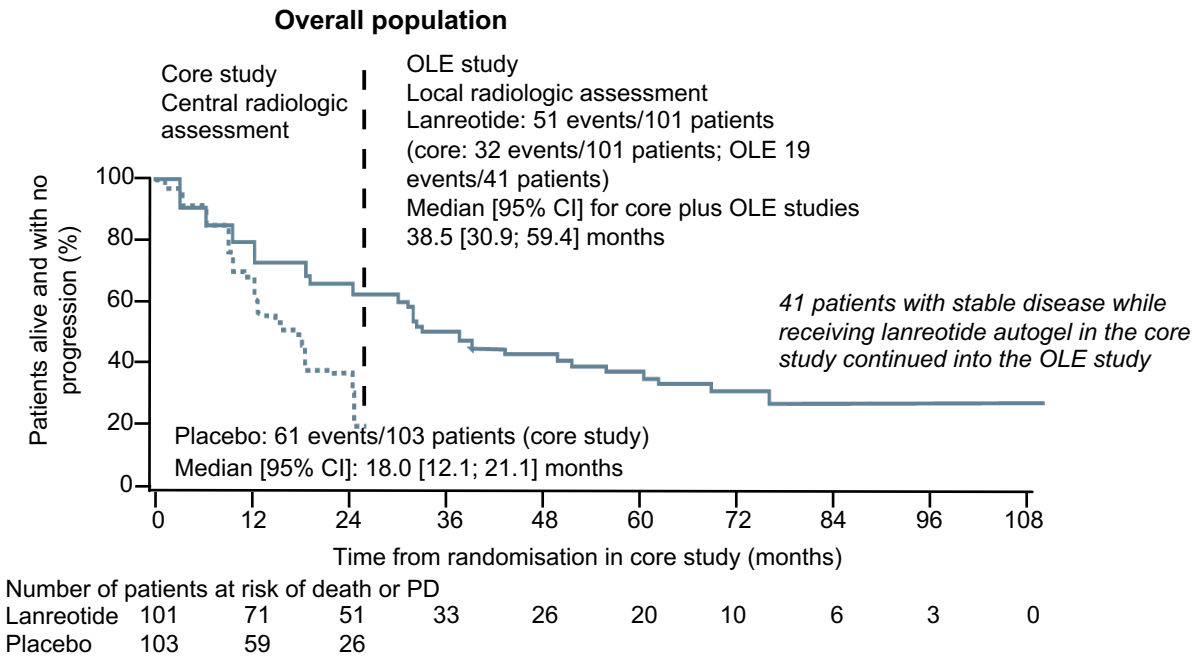
AEs, adverse events; GI, gastrointestinal; LAR, long acting release

Rinke, et al. J Clin Oncol 2009;27:4656-63

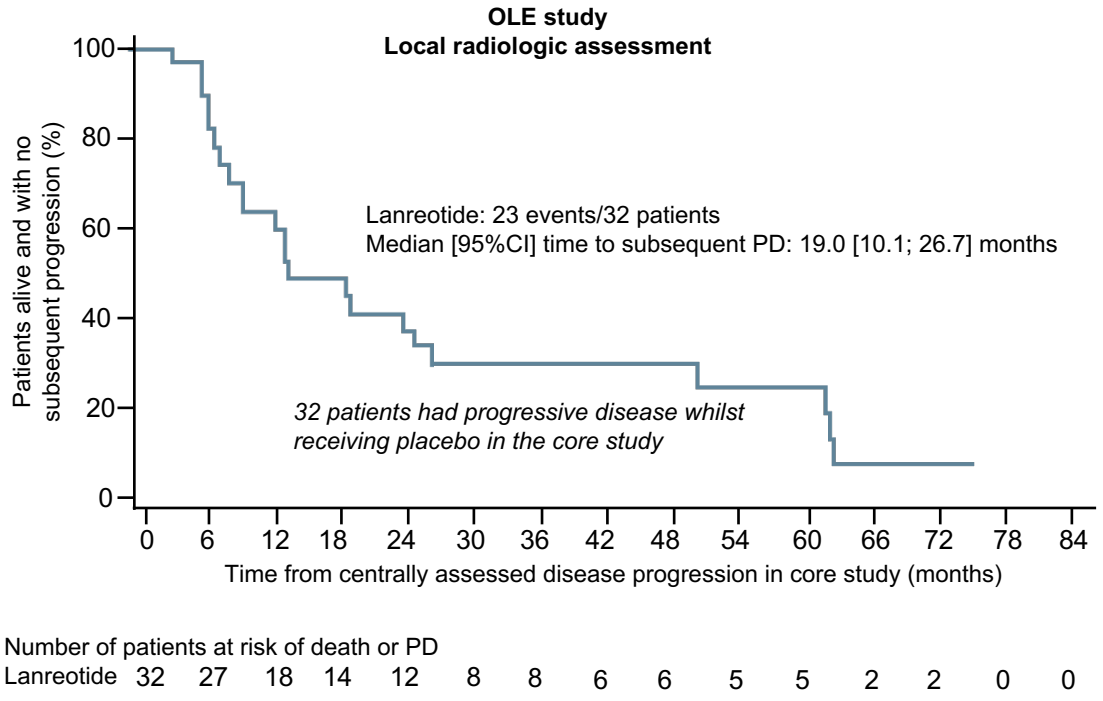
CLARINET: EFFICACY

LANREOTIDE VS PLACEBO IN GEP-NET

PRIMARY ENDPOINT: PFS



SECONDARY ENDPOINT: TIME TO DEATH OR SUBSEQUENT PD



PFS centrally assessed according to RECIST. OS accordingly to investigator follow up of patients

CI, confidence interval; PD, progressive disease; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumours

Caplin, et al. Endocrine 2021;71:502-13

CLARINET: SIDE EFFECTS

ADVERSE EVENTS (SAFETY POPULATION)

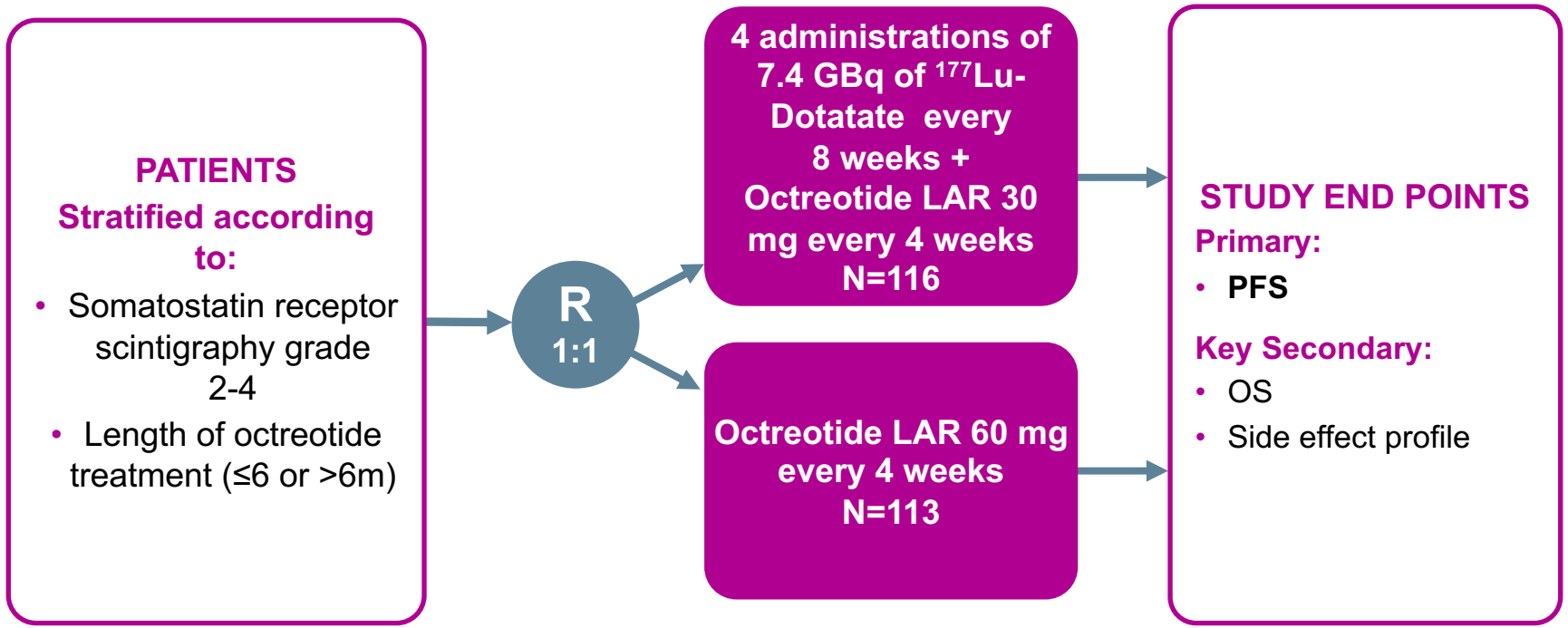
Event	Lanreotide (N=101)	Placebo (N=103)
	Number of patients (%)	
Any adverse event	89 (88)	93 (90)
Any adverse event related to study treatment	50 (50)	29 (28)
Any adverse event according to intensity		
Severe	26 (26)	32 (31)
Moderate	44 (44)	44 (43)
Mild	17 (17)	17 (17)
Any serious adverse event	25 (25)	32 (31)
Serious adverse event related to study treatment	3 (3)	1 (1)
Withdrawal from study because of any adverse event	3 (3)	3 (3)
Withdrawal because of adverse event related to study treatment	1 (1)	0

Caplin, et al. N Engl J Med 2014;371:224-33

CLINICAL EVIDENCE FOR CONTINUING SSA ON PROGRESSION

NETTER-1: STUDY DESIGN

Patient population: advanced, progressive, somatostatin-receptor positive mid-gut NETs



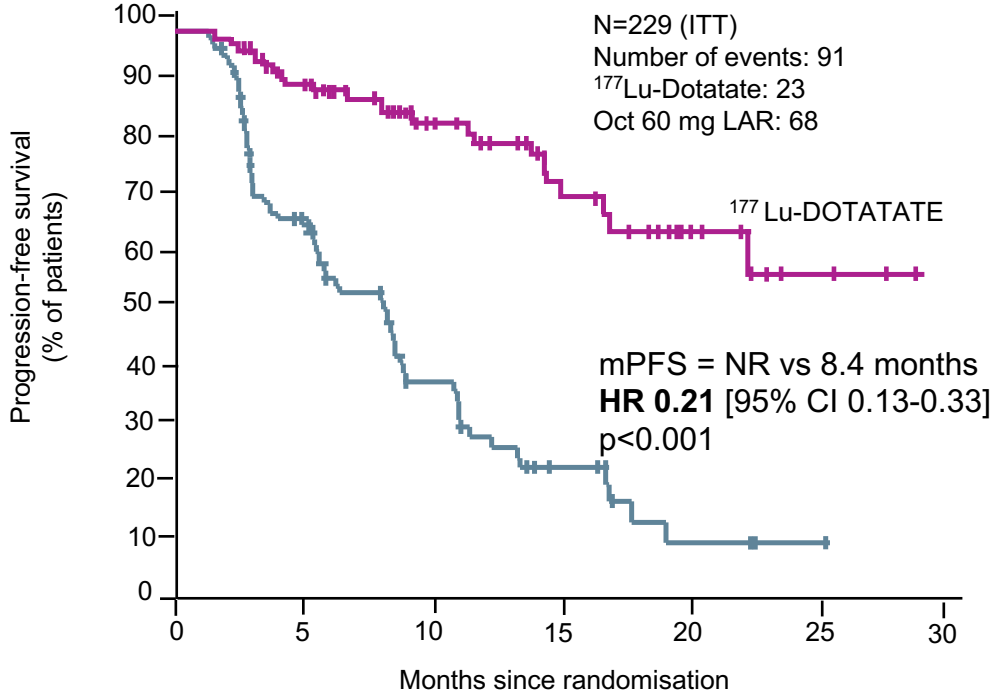
177Lu, lutetium-177; GBq, gigabecquerels; LAR, long-acting release; m, months; NET, neuroendocrine tumour; OS, overall survival; PFS, progression-free survival; R, randomisation

Strosberg, et al. N Engl J Med 2017;376:125-35

NETTER-1: EFFICACY

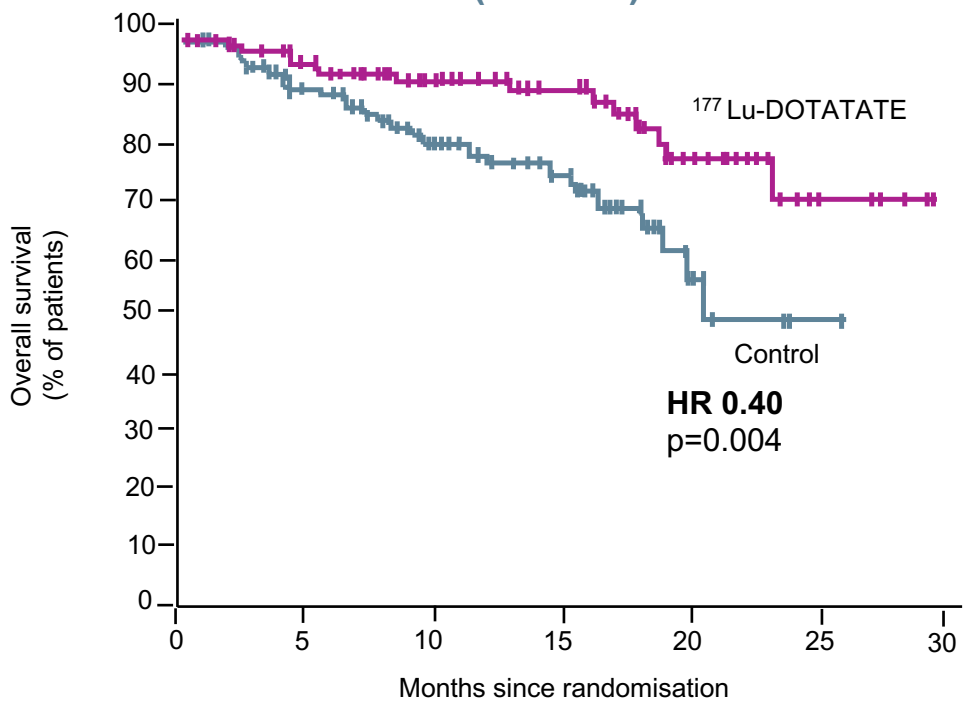
ALL STUDY PATIENTS CONTINUED HIGH DOSE OCTREOTIDE REGARDLESS OF FUNCTIONAL STATUS

PRIMARY ENDPOINT: PFS



No. at risk											
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

SECONDARY ENDPOINT: OS (interim)



No. at risk											
177 Lu-DOTATATE group	116	108	96	79	64	47	31	21	8	3	0
Control group	113	103	83	64	41	32	17	5	1	0	0

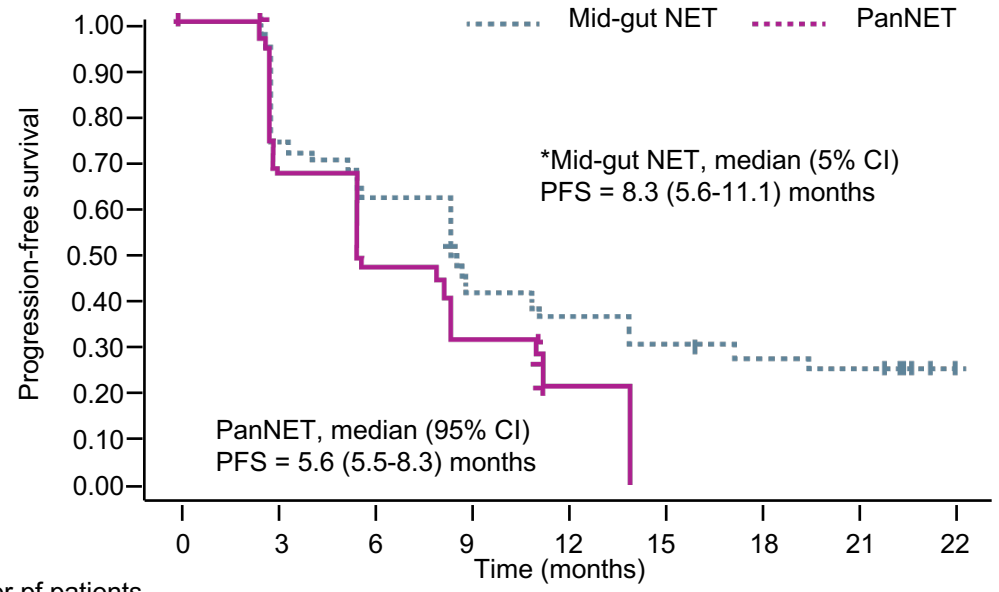
Primary analysis of NETTER-1 with interim analysis of overall survival
177Lu, lutetium-177; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; (m)PFS, (median) progression-free survival; NR, not reached; LAR, long-acting release; Oct, octreotide, OS, overall survival
Strosberg J, et al. N Engl J Med. 2017;376:125-35

CLARINET FORTE

INCREASE DOSING FREQUENCY BEFORE ESCALATION TO LESS WELL-TOLERATED THERAPIES

- High-dose lanreotide autogel (120 mg every 14 days) in patients with progressive pancreatic or mid-gut NETs following first-line standard-dose treatment (120 mg every 28 days)
- Reducing the dosing interval provided clinically meaningful PFS
- There were no safety concerns

PRIMARY ENDPOINT: PFS



Number pf patients									
Mid-gut NET at risk	51	36	30	19	17	14	12	11	0
Censor	0	2	2	3	3	3	4	4	15
Event	0	13	19	29	31	34	35	36	36
PanNET at risk	48	31	21	14	2	0	0	0	0
Censor	0	3	3	3	12	12	12	12	12
Event	0	14	24	31	34	36	36	36	36

CI, confidence interval; NET, neuroendocrine tumour; pan, pancreatic; PFS, progression-free survival

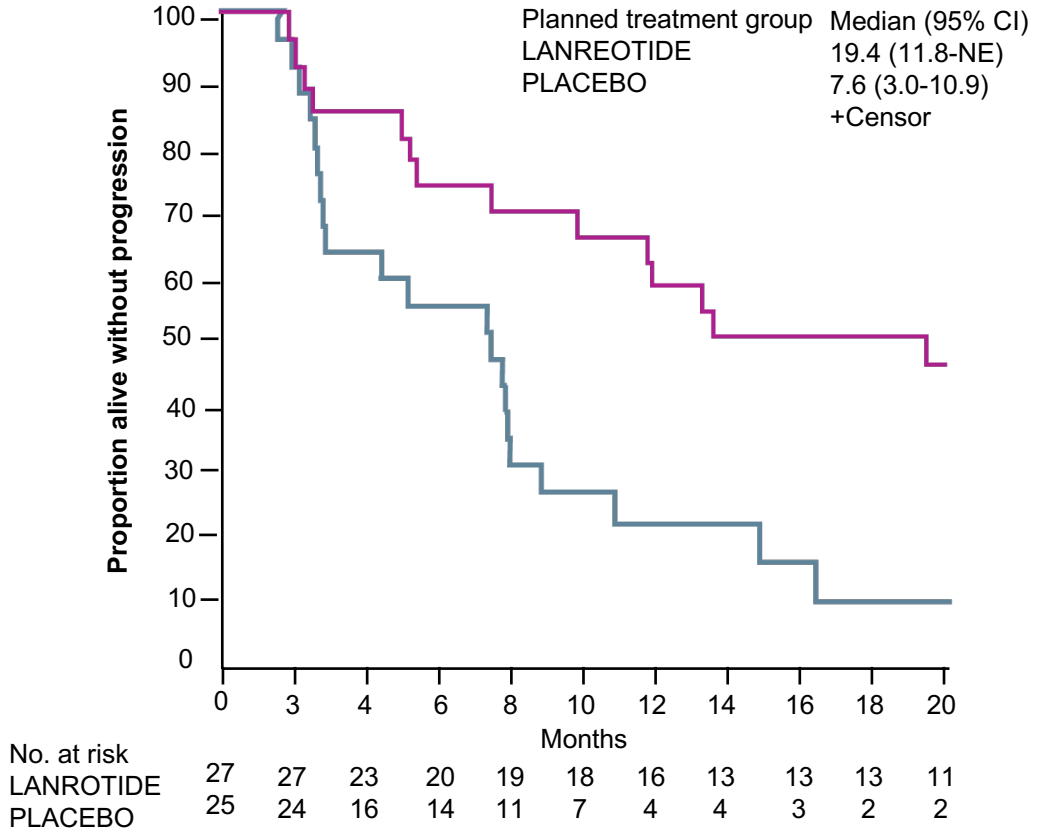
Pavel M, et al. Eur J Cancer. 2021;157:403-14

REMINET

MAINTENANCE TREATMENT WITH SSA IS FEASIBLE

- Lanreotide autogel (120 mg every 28 days) as maintenance treatment after ≥2 months of first-line treatment in aggressive G1/2 DP-NET
- Encouraging results as a maintenance treatment
- Treatment toxicity is reduced

PRIMARY ENDPOINT: PFS



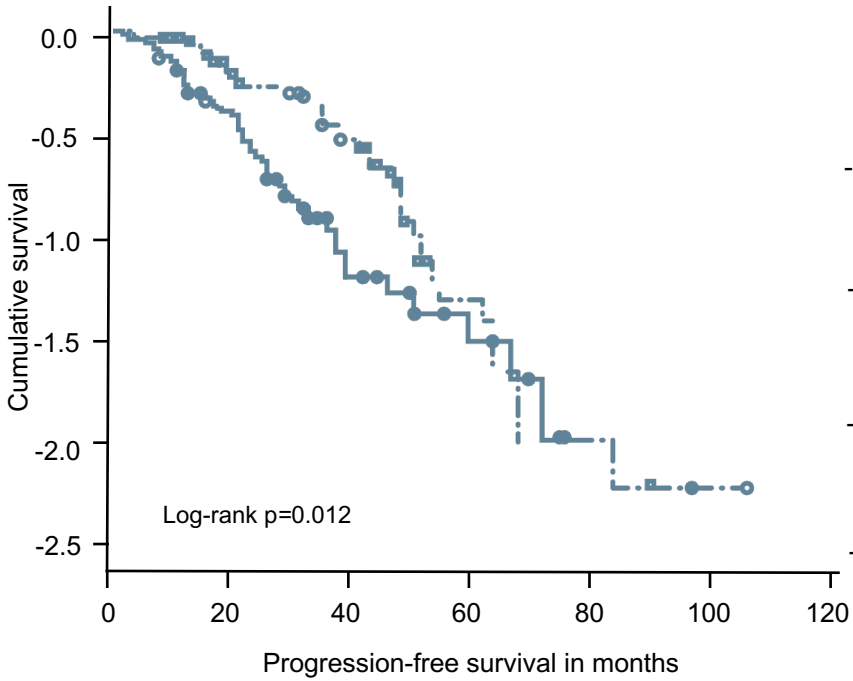
CI, confidence interval; DP-NET, duodeno-pancreatic neuroendocrine tumour; G, grade; NE, not estimable; PFS, progression-free survival; SSA, somatostatin analogue

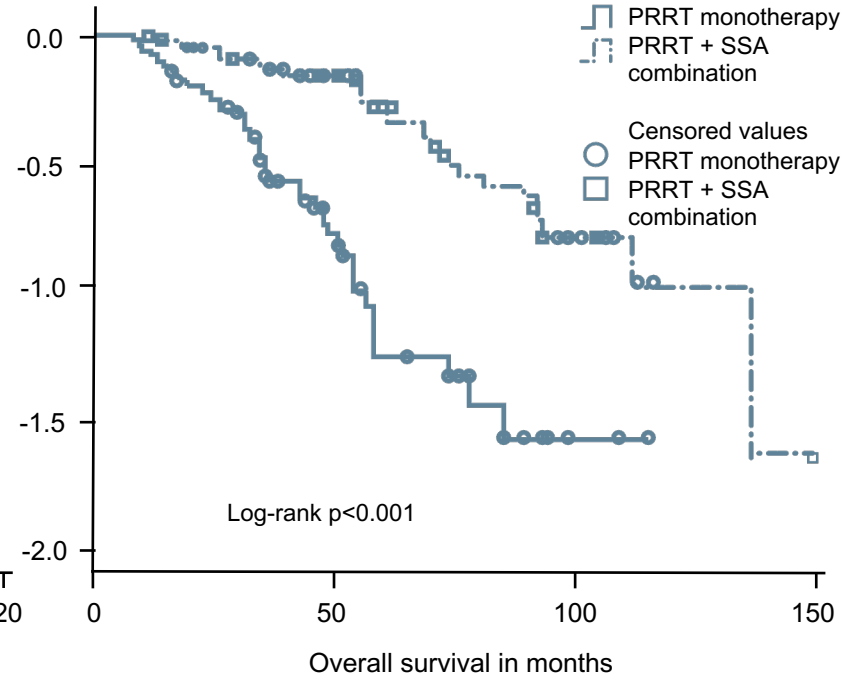
Lepage C, et al. Eur J Cancer. 2022;175:31-40

ADDING SSA TO PRRT AS COMBINATION AND/ OR MAINTENANCE THERAPY

BENEFIT OF COMBINATION/MAINTENANCE SSA WITH PRRT

- Retrospective analysis at the University Hospital Bonn, Bonn, Germany of survival benefit of adding SSA to PRRT as combination and/or maintenance therapy
- Patients with advanced GEP-NET
- Significantly better outcomes with SSA + PRRT vs PRRT alone





GEP-NET, gastroenteropancreatic neuroendocrine tumour; PFS, progression-free survival; PRRT, peptide receptor radionuclide therapy; SSA, somatostatin analogue

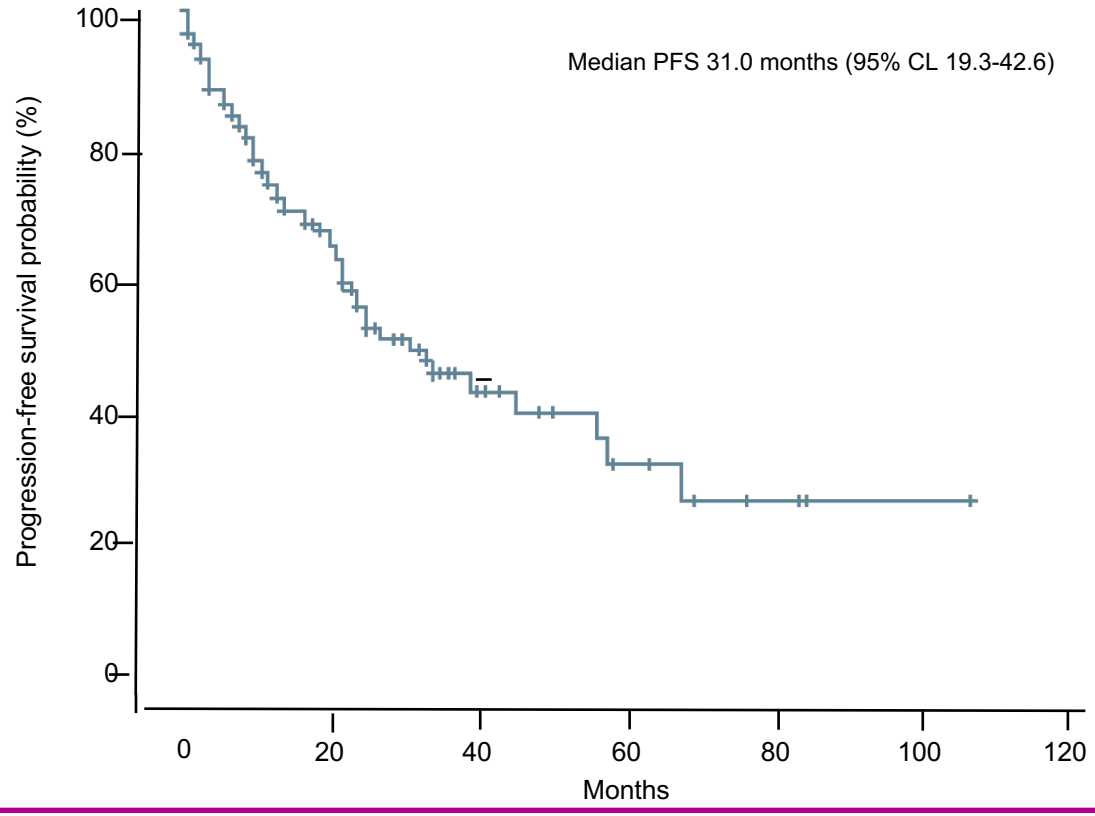
Yordanova A, et al. Clin Cancer Res. 2018;24:4672-79

HIGH-DOSE SSA FOR PROGRESSIVE WELL-DIFFERENTIATED NETS

HIGH-DOSE SSA CAN BE A FEASIBLE OPTION IN SELECTED NETS

- Retrospective analysis of data from 13 Italian NET centres
- Patients with well-differentiated GEP-NET and disease progression
- SSA with increased administered dose or shortened interval between administrations was an active and safe treatment option

MAIN EFFICACY ENDPOINT: PFS



CI, confidence interval; GEP gastroenteropancreatic; NET, neuroendocrine tumour; PFS, progression-free survival; SSA, somatostatin analogue

Lamberti G, et al. J Clin Endocrinol Metab. 2020;105(1):dgz035

CLINICAL TAKEAWAYS

CLINICAL TAKEAWAYS

POTENTIAL PATIENT GROUPS AND TREATMENT STRATEGIES

- In patients with well-differentiated Grade 1 or 2 NETs and slowly progressive asymptomatic disease, the following strategies could be potential considerations in selected patients
  - **Increase the SSA dose** (increase frequency from 4 weeks to 2 weeks)
  - **Increase the monthly dose** of SSA

- **SSA as maintenance** (after stopping chemotherapy [for toxicity concerns] in stable patients)

- Patients receiving PRRT (**during and/or post-PRRT**)

NET, neuroendocrine tumour; PRRT, peptide receptor radionuclide therapy; SSA, somatostatin analogue

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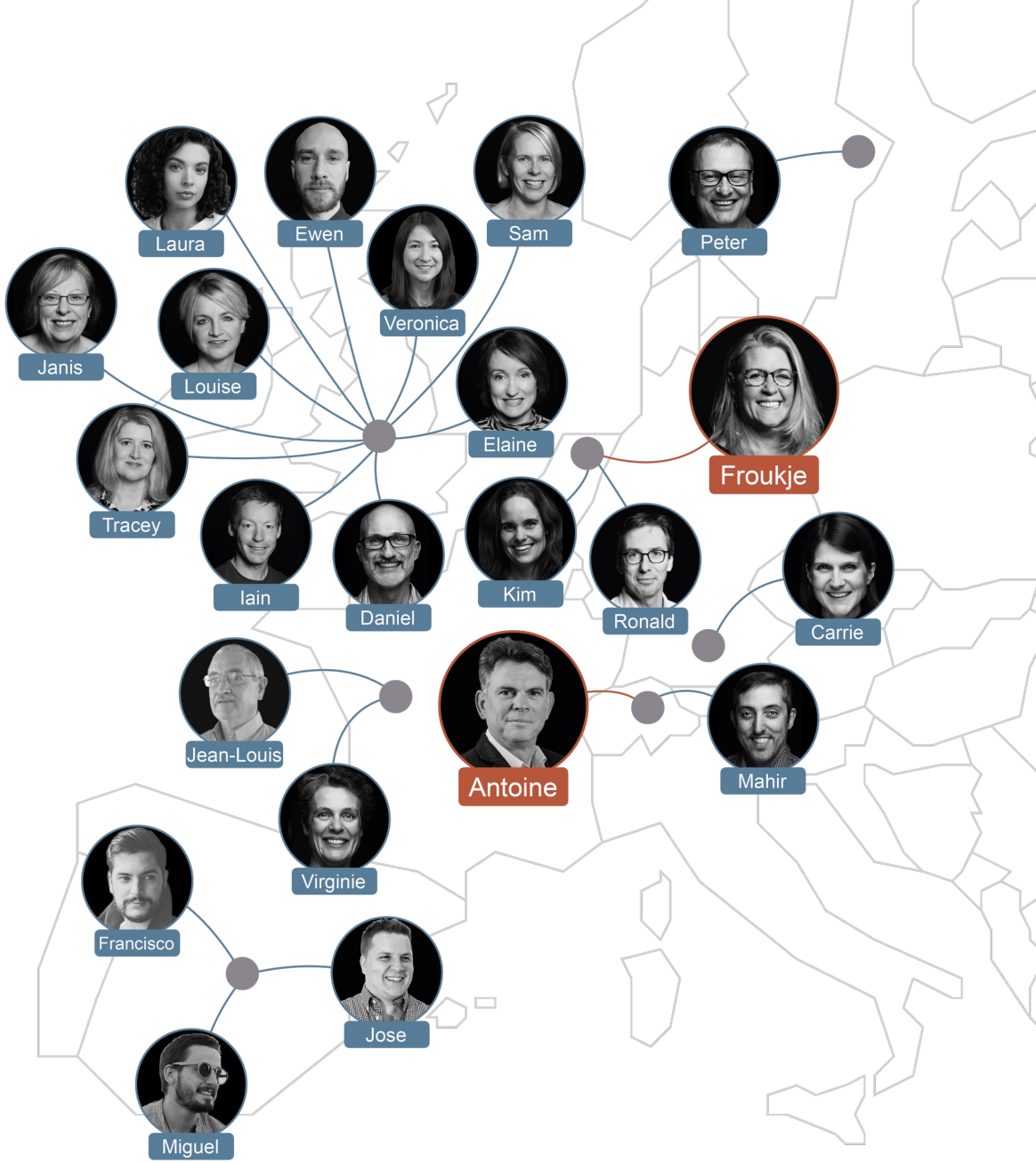

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