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ISTITUTO ROMAGNOLO PER LO STUDIO DEI TUMORI DINO AMADORI

An Italian Propensity Score Matched Cohort Study of Long-Acting Somatostatine Analogues in Neuroendocrine Tumour Patients

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Objective

This study describes the treatment patterns and clinical outcomes of metastatic neuroendocrine tumours (NETs) by comparing two cohorts matched at the first-line treatment with somatostatin (SSA) (lanreotide vs. octreotide) through a propensity score-matched (PSM).

Methods

Metastatic NET patients who initiated first-line SSA at IRST (2009-2022) were retrospectively examined and followed until the earliest among end of study (June 2023), the last documented follow-up or death. First-line SSA cohorts (lanreotide vs octreotide) were matched 1:1 by nearest neighbour propensity scores (max caliper 0.2) based on sex, age, primary tumour and metastases localization, tumour grade, Ki-67, carcinoid syndrome, carcinoid heart, surgical procedures and diagnosis year. Progression-free survival (PFS) and overall survival (OS) were analyzed using the Kaplan-Meier analysis and Cox proportional hazards model.

Results

The study comprised 441 individuals, with 262 (59.4%) receiving octreotide and 179 (40.6%) lanreotide treatment either alone or in combination with another drug as the initial treatment. After the PSM application, the final cohort consisted of 310 patients: 155 treated with octreotide in the first-line and the remaining 155 with lanreotide. First-line SSA treatment was monotherapy for 63.5% (N=197) of patients and in combination with other medications for 36.5% (N=113). Of the 244 (78.7%) second-line patients, 77.0% (188/244) maintained their initial SSA medication in combination with other therapies. The most common second-line treatment was radioligand therapy together with lanreotide (N=72; 29.5%) or octreotide (N=70; 28.7%). No treatment patterns were observed in subsequent lines (Figure 1).

Figure 1 Treatment patterns

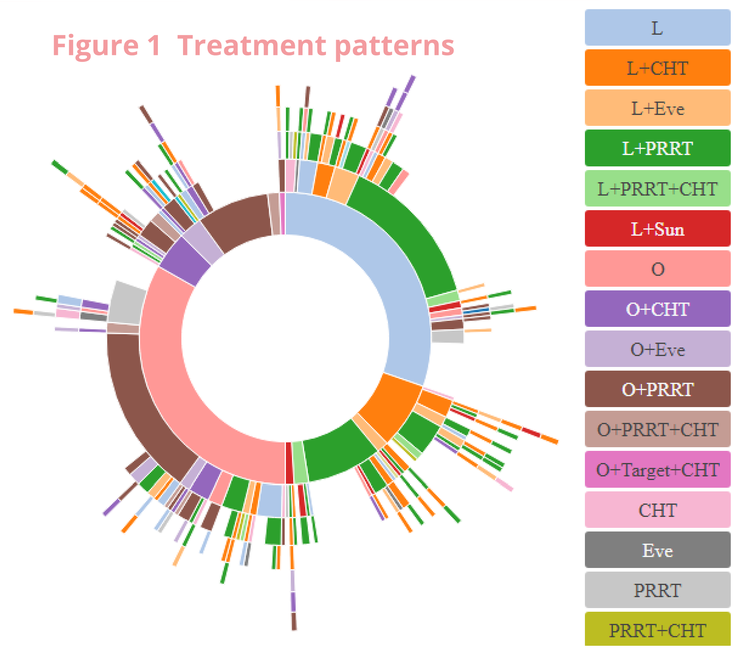


Figure 2 First-line TTNT

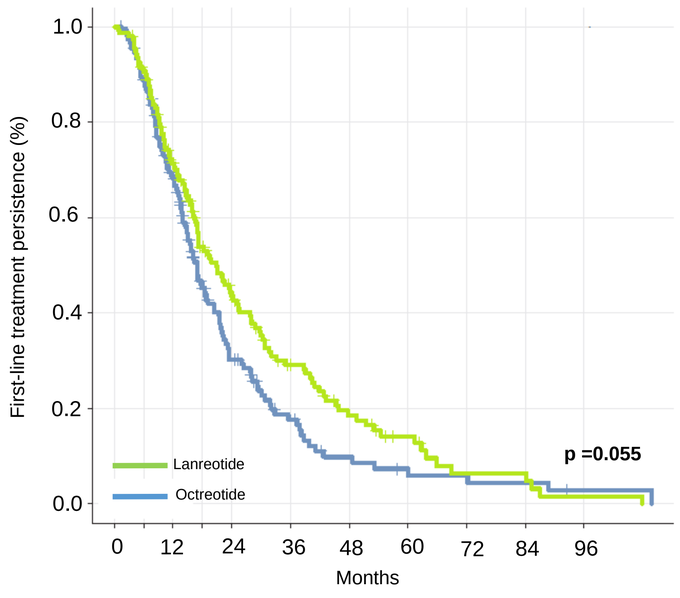


Figure 3 First-line PFS

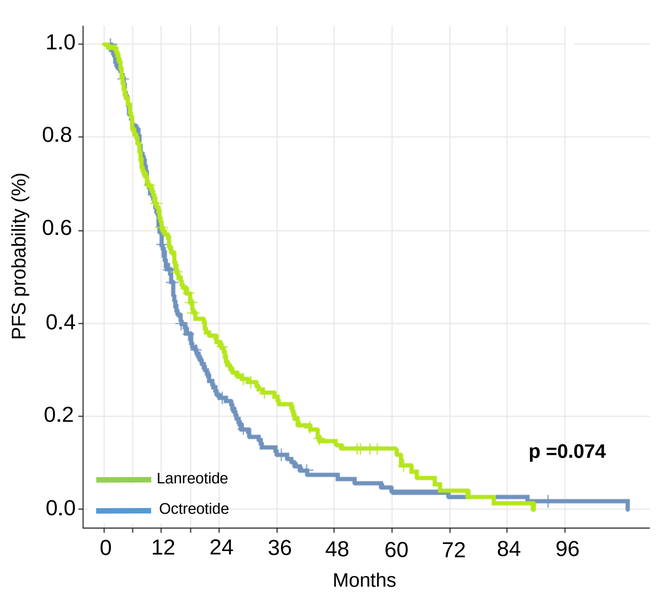
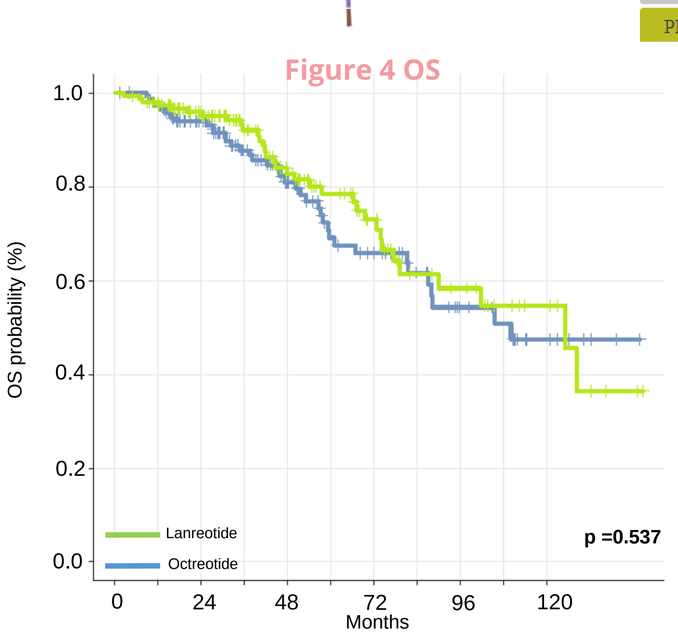


Figure 4 OS



Variable		N	Hazard Ratio	P
1st line SSA	Lanreotide	155	Reference	
	Octreotide	155	1.36 (1.05-1.76)	0.018
Ki-67	[3%-20%]/unk	214	Reference	
	<3%	78	0.54 (0.40-0.74)	<0.001
	>20%	18	2.49 (1.48-4.21)	<0.001
Liver metast.	No	41	Reference	
	Yes	269	1.75 (1.17-2.62)	0.006
Lymph node metast.	No	155	Reference	
	Yes	155	1.31 (1.07-1.71)	0.044

Variables		N	Hazard Ratio	P
1st line SSA	Lanreotide	155	Reference	
	Octreotide	155	1.34 (1.06-1.71)	0.016
Metastasis	Single	129	Reference	
	Multiple	181	1.45 (1.13-1.87)	0.004
Ki-67	[3%-20%]/unk	214	Reference	
	<3%	78	0.55 (0.41-0.73)	<0.001
	>20%	18	2.34 (1.43-3.83)	<0.001
Liver metast.	No	41	Reference	
	Yes	269	1.40 (0.97-2.03)	0.075

Variables		N	Hazard Ratio	P
1st line SSA	Lanreotide	155	Reference	
	Octreotide	155	1.34 (1.06-1.71)	0.016
Age		310	1.05 (1.02-1.07)	<0.001
Ki-67	Unk/≥3	232	Reference	
	<3%	78	0.47 (0.25-0.87)	0.017
Lymph node met.	No	155	Reference	
	Yes	155	1.53 (0.94-2.48)	0.088
Bone met.	No	236	Reference	
	Yes	74	1.91 (1.14-3.20)	0.014
Surgery	No	215	Reference	
	Yes	95	0.42 (0.23-0.77)	0.005
68Ga-PET	Negative	9	Reference	
	Positive	301	0.20 (0.07-0.62)	0.005
18F-FDG PE	Negative	148	Reference	
	Positive	162	1.56 (0.95-2.56)	0.082

Patients receiving first-line lanreotide had a median time of 20.9 months (95% CI: 17.0-25.5) to start second-line treatment, whereas those using octreotide had 16.9 months (95% CI: 14.9-20.4) (p=0.055) (Figure 2). First-line lanreotide and octreotide cohorts had similar median PFS (15.5; 95% CI: 13.6-19.1 vs 14.0; 95% CI: 12.0-15.8 months) despite the octreotide having a 36% higher likelihood of moving to the second-line than lanreotide (95% CI:1.05-1.76, p=0.018) (Figure 3) . Multiple metastases (HR=1.45; p=0.004, 95% CI:1.13-1.87) and Ki67>20% (HR=2.34; p<0.001, 95% CI:1.43-3.83) significantly increased the risk of progression. First-line lanreotide patients had a median OS of 10.4 years (95% CI: 7.5-NA) and octreotide 9.2 years (95% CI: 7.3-NA) (p=0.537). Bone metastases increased death risk by 91% (p=0.014; 95% CI:1.14-3.20) (Figure 4).

Conclusions

SSA monotherapy is the main first-line treatment. In subsequent treatments, most patients continue to receive SSA with additional medications. The cohorts exhibited no statistically differences in median PFS and OS, however octreotide demonstrated a 36% significantly higher likelihood of moving to the second-line treatment.

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