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Final Progression-Free Survival Analyses for Lanreotide Autogel/Depot 120 mg in Metastatic Enteropancreatic Neuroendocrine Tumors: the CLARINET Extension Study

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BACKGROUND: In the CLARINET core study, lanreotide Autogel/depot 120 mg every 28 days significantly improved progression-free survival (PFS) vs placebo in metastatic grade 1/2 enteropancreatic neuroendocrine tumors (NETs). An interim analysis of patients with stable disease (SD) in the core study continuing lanreotide in the open-label extension (OLE) showed continued antitumor effects. Here, we report final PFS analyses.

METHODS: In the core study, patients with metastatic well/moderately-differentiated non-functioning (N-F) enteropancreatic NETs, Ki-67 <10%, no prior somatostatin-analog treatment, and no other prior medical therapies in the previous 6 months were randomized to lanreotide 120 mg (n=101) or placebo (n=103) for 96 weeks or until death/progressive disease (PD; RECIST 1.0). Patients with SD receiving lanreotide and any patient receiving placebo could enter a single-arm (lanreotide) OLE (NCT00842348). The primary OLE objective was to evaluate long-term safety of lanreotide. The main efficacy endpoint was PFS (time from core study randomization to death/PD) for core study intent-to-treat population from Kaplan-Meier survival analysis.

RESULTS: The OLE final population comprised 89 patients (lanreotide-lanreotide 42; placebo-lanreotide 47); 38% had pancreatic and 38% midgut NETs. During the OLE, 40% continuing lanreotide vs 47% switched to lanreotide had treatment-related adverse events (AEs). In the lanreotide-lanreotide group, cholelithiasis and diarrhea were the most common treatment-related AEs (16.7% [7/42] and 9.5% [4/42], respectively; corresponding frequencies for the placebo-lanreotide group were 12.8% (6/47) and 25.5% (12/47), respectively. No new safety concerns were identified. Overall lanreotide median PFS was 38.5 months (95% CI: 30.9, 59.4), and varied with tumor origin and prior therapy (Table 1).

CONCLUSION: CLARINET OLE indicates sustained antitumor effects with lanreotide 120 mg in enteropancreatic NETs vs placebo (core study), irrespective of tumor origin, and suggests benefits with lanreotide as early treatment.

Table 1:
PFS overall and in prespecified subgroups

	Median PFS [95% CI] (no. patients), months*	Median PFS [95% CI] (no. patients), months*
	LAN (core study and OLE)	PBO (core study)
Overall	38.5 [30.9; 59.4] (101)	18.0 [12.1; 21.1] (103)
Tumor origin: Midgut	61.5 [30.9; NC] (33)	21.2 [17.0; NC] (40)
Tumor origin: Pancreas	29.7 [12.0; 38.5] (42)	12.1 [9.4; 18.3] (49)
Tumor origin: Hindgut	55.0 [2.9; NC] (11)	24.4 [12.0; 24.4] (3)
Tumor origin: Other/ unknown	59.4 [32.8; 74.8] (15)	15.0 [6.3; NC] (11)
Previous therapy for N-F NET: Yes	29.7 [6.0; 31.3] (16)	12.0 [3.3; NC] (16)
Previous therapy for N-F NET: No	50.8 [32.4; 74.8] (85)	18.0 [12.1; 24.0] (87)

*Approximated (4 weeks/month). PFS, progression-free survival; LAN, lanreotide Autogel/depot; PBO, placebo; NC, not calculable; N-F, non-functioning; NET, neuroendocrine tumor; OLE, open label extension.