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Safety and Tolerability of Lanreotide Autogel/Depot in Patients with Neuroendocrine Tumors: Pooled Analysis of Clinical Studies

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BACKGROUND: Two randomized, double-blind (DB) clinical trials demonstrated improved progression-free survival (CLARINET) and carcinoid symptom control (ELECT) with lanreotide Autogel/depot 120 mg/4 weeks vs placebo in adults with neuroendocrine tumors (NETs). We pooled current data from lanreotide trials to analyze safety in functioning and nonfunctioning NETs.

METHODS: Safety data were pooled from the following lanreotide studies: 96-week DB CLARINET trial with ~6-year open-label extension (OLE) in nonfunctioning, metastatic, or unresectable gastroenteropancreatic (GEP)-NETs (dose: 120 mg/28 days); ELECT trial with 16-week DB phase, 32-week initial open-label (IOL) phase, and ≥2-year OLE in NETs with carcinoid syndrome (CS) (120 mg/28 days); a 6-month CS symptom control study in symptomatic carcinoid tumors (90 mg/28 days, titrated to response); a 30-week OL patient preference study on injection administration in NETs (90 or 120 mg/28 days);

and a 92-week OL tumor-growth control study in GEP-NETs, bronchopulmonary NETs, or neuroendocrine carcinoma (120 mg/28 days). Diarrhea and flushing events from ELECT DB and IOL phases were excluded (efficacy measures).

RESULTS: Of 378 patients, 90% received lanreotide 120 mg and 10% received ≤90 mg. Overall adverse event (AE) and serious AE profiles were similar across all groups, although treatment-related AEs (TRAEs) were higher in lanreotide patients vs placebo patients. GI events were most frequent (56% excluding diarrhea; 28% reported diarrhea excluding in ELECT DB and IOL), with abdominal pain being the most common individual AE and TRAE. There were 32 SAEs reported among 18 patients, the most common being abdominal pain and cholelithiasis (3 each). No withdrawals were due to GI AEs, no deaths were considered treatment-related, and no additional safety signals were reported in >12-month vs ≤6-month data.

CONCLUSION: This safety analysis demonstrates a consistent safety profile and, together with reported efficacy, supports the positive benefit-risk profile of lanreotide in NETs.

Table 1:
Overview of treatment and AE data (excluding diarrhea and flushing from all studies).

	All LAN (DB+OL) (N=378)	DB LAN (n=159)	OL LAN (n=127)	DB PBO (n=160)*
Mean (SD) duration of treatment, weeks	84.34 (84.46)	50.43 (37.92)	30.65 (19.53)	44.65 (33.98)
Mean (SD) treatment exposure to LAN 120 mg, weeks	N=339; 89.64 (87.84)	n=159; 50.43 (37.92)	n=88; 27.29 (25.30)	N/A
Mean (SD) cumulative LAN dose, mg	2465.5 (2539.83)	1494.3 (1128.34)	793.0 (592.34)	0.0 (0.00)
AEs, n (%)	330 (87.3)	119 (74.8)	112 (88.2)	126 (78.8)
— Treatment-related	182 (48.1)	59 (37.1)	75 (59.1)	33 (20.6)
— Leading to withdrawal	23 (6.1)	2 (1.3)	10 (7.9)	4 (2.5)
SAEs, n (%)	111 (29.4)	26 (16.4)	39 (30.7)	36 (22.5)
— Treatment-related	18 (4.8)†	4 (2.5)	10 (7.9)	4 (2.5)
— Leading to withdrawal	15 (4.0)	2 (1.3)	5 (3.9)	4 (2.5)
— Leading to death	18 (4.8)‡	2 (1.3)	5 (3.9)	4 (2.5)

*Not all patients receiving placebo went on to receive OL lanreotide Autogel. †13 recovered (2 with sequelae). ‡None considered related to treatment. AE, adverse event; DB, double-blind; LAN, lanreotide Autogel; N/A, not applicable; OL, open-label; PBO, placebo; SAE, serious adverse event.