1314P Efficacy and safety of telotristat ethyl (TE) in combination with lanreotide (LAN) in patients with a neuroendocrine tumour and carcinoid syndrome (CS) diarrhoea (CSD): Meta-analysis of phase III double-blind placebo (PBO)-controlled TELESTAR and TELECAST studies

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Background: LAN 120 mg, a somatostatin analogue (SSA), is approved in the EU and recently in the USA for CS. In two phase 3 trials in CS, TE 250 mg or 500 mg three-times daily (tid) combined with SSA therapy (LAN or octreotide) demonstrated reduced bowel movement (BM) frequency and urinary 5-hydroxyindole acetic acid (u5-HIAA) levels vs. PBO. TE 250 mg is approved by the FDA and EMA for CSD inadequately controlled by SSAs. This post hoc meta-analysis used patient-level data from the two phase 3 studies to further examine the efficacy and safety of TE + LAN.

Methods: In the TELESTAR (NCT01677910) and TELECAST (NCT02063659) studies, patients using and continuing stable-dose SSAs were randomly assigned 1:1:1 to PBO, TE 250 mg or TE 500 mg tid for a 12-week double-blind (DB) period. Here, only data for patients using LAN during the run-in periods were included. Endpoints included descriptive changes from baseline in 24-hour u5-HIAA, BMs/day, flushing episodes and incidence of adverse events (AEs).

Results: Of 211 patients in the studies, 54 receiving LAN were included in the analysis (44% women, mean [SD] age 61.8 [10.5] years, mean [SD] BMI 25.7 [5.0] kg/m^2; 34 [63%] used LAN 4-weekly, 20 [37%] used LAN 3-weekly). One patient received octreotide instead of LAN during the DB period. Randomization of this cohort is shown with efficacy and safety data in the table.

Table: 1314P

	PBO tid	TE 250 mg tid	TE 500 mg tid
Number of LAN patients randomly allocated	n = 29	n = 10	n = 15
u5-HIAA (mg/24 hour)			
Patients with levels > upper limit of normal (at randomization): n (%)	15 (51.7)	6 (60.0)	9 (60.0)
Baseline: median [95% CI]	24.9 [12.2; 80.9]	57.6 [12.9; 159.8]	31.0 [19.0; 259.2]
Week-12 change from baseline: median [95% CI]	1.6 [–6.7; 5.0]	–12.4 [–86.4; 77.2]	–24.6 [–134.6; –10.0]
BMs/day: median [95% CI]			
Baseline	3.5 [2.4; 4.4]	3.1 [1.3; 5.6]	5.3 [3.6; 6.1]
Week-12 change from baseline	–0.2 [–1.1; 0.2]	–0.9 [–2.6; –0.0]	–1.29 [–3.3; –0.0]
Flushing (counts/day): median [95% CI]			
Baseline	3.5 [1.5; 5.1]	2.8 [0.5; 4.9]	2.9 [0.8; 4.3]
Week-12 change from baseline	0.00 [–1.1; 0.4]	–0.5 [–1.2; 0.7]	–0.5 [–2.0; 0.4]
Safety: n (%) patients			
Any AE	26 (90)	9 (90)	14 (93)
Treatment-related AEs	8 (28)	6 (60)	12 (80)
Serious AEs	3 (10)	1 (10)	4 (27)
Treatment-related serious AEs	1 (3)	0	0
Deaths	1 (3)	0	0

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Conclusions: Changes from baseline in u5-HIAA, BMs and flushing suggest a trend towards meaningful efficacy of TE + LAN in CSD, in a population with moderately elevated baseline BM frequency. The combination TE + LAN was generally well tolerated. No power calculation was performed for this exploratory post hoc analysis; imbalanced groups and low patient numbers preclude any formal comparison with PBO. Evaluation of this TE + LAN regimen as first-line therapy in patients with CSD may be warranted.

Clinical trial identification: TELESTAR: NCT01677910 TELECAST: NCT02063659.

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