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First-Line Efficacy of [177Lu]Lu-DOTA-TATE in Gastroenteropancreatic Neuroendocrine Tumors by Tumor Grade and Primary Origin: Phase 3 NETTER-2 Subgroup Analysis

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BACKGROUND

In the Phase 3 NETTER-2 study (NCT03972488), first-line [^{177}Lu]Lu-DOTA-TATE (hereafter ^{177}Lu-DOTATATE) significantly improved median progression-free survival (PFS) by 14 months and increased objective response rate (ORR) by 34% vs high-dose octreotide in patients with advanced, well-differentiated, Grade 2 (G2) and G3, gastroenteropancreatic neuroendocrine tumors (GEP-NETs). This preplanned subgroup analysis examined efficacy by NET grade (G2, G3) and NET origin (pancreas, small intestine [SI]).

METHODS

Patients were randomized to 4 cycles of ^{177}Lu-DOTATATE (4 × 7.4 GBq) + 30 mg octreotide long-acting release (LAR) every 8 weeks (Q8W) during ^{177}Lu-DOTATATE treatment then Q4W (n=151), or 60 mg octreotide LAR Q4W (n=75). Efficacy parameters (PFS, ORR, duration of response [DOR], time to response [TTR]) were centrally assessed (RECIST 1.1).

RESULTS

For PFS and ORR, a clinical benefit in favor of ^{177}Lu-DOTATATE was evident across subgroups (Table). In the ^{177}Lu-DOTATATE arm, median PFS was shorter for patients with G3 vs G2 and pancreatic NETs (pNETs) vs SI-NETs. ORR was high in patients with G3 and G2 and higher in pNETs vs SI-NETs. Among

65 patients with complete/partial response to ^{177}Lu-DOTATATE, median TTR was ~5.8 months (m) for all 4 subgroups, and median DOR (95% confidence interval) was 24.9 m (23.3, not estimable [NE]) in G2 NETs, 19.3 m (17.8, NE) in G3 NETs, 18.4 m (11.3, 23.3) in pNETs and NE for SI-NETs. The low number of responders in the control arm (n=7) precluded DOR and TTR subgroup analyses.

Efficacy outcomes by subgroup

Tumor subgroup	PFS event/n (%)	Median PFS* (95% CI), m	Responders /n	ORR (95% CI), %
G2: ^{177}**Lu-DOTATATE**	29/99 (29.3)	29.0 (21.8, NE)	40/99	40.4 (30.7, 50.7)
G2: Control	25/48 (52.1)	13.8 (8.4, 19.3)	5/48	10.4 (3.5, 22.7)
G3: ^{177}**Lu-DOTATATE**	26/52 (50.0)	22.2 (13.9, 27.8)	25/52	48.1 (34.0, 62.4)
G3: Control	21/27 (77.8)	5.6 (3.7, 8.9)	2/27	7.4 (0.9, 24.3)
Pancreas: ^{177}**Lu-DOTATATE**	39/82 (47.6)	19.4 (16.6, 24.9)	42/82	51.2 (39.9, 62.4)
Pancreas: Control	27/41 (65.9)	8.5 (3.8, 16.6)	5/41	12.2 (4.1, 26.2)
SI: ^{177}**Lu-DOTATATE**	11/45 (24.4)	29.0 (21.8, NE)	12/45	26.7 (14.6, 41.9)
SI: Control	10/21 (47.6)	8.4 (5.4, NE)	1/21	4.8 (0.1, 23.8)
***Kaplan-Meier estimate.**				

CONCLUSIONS

First-line ^{177}Lu-DOTATATE efficacy was maintained across NET grades (G2, G3) and locations (pancreas, SI). ^{177}Lu-DOTATATE should be considered a standard of care for this population.

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