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Impact of Prior Somatostatin Analog Use on PFS in the Phase III RADIANT-2 Trial of Everolimus + Octreotide LAR vs Placebo + Octreotide LAR in Patients with Advanced Neuroendocrine Tumors

Lowell Anthony,[1] Neha Singh,[-2] Vanessa Q. Passos,[3] Marianne Pavel,[4] Kjell Oberg,[5] James C. Yao[6]

[1]Ochsner Kenner Medical Center, Kenner, LA 70065; [2]Novartis Healthcare Pvt. Ltd., Madhapur, Hyderabad, India 500 081; [3]Novartis Pharmaceuticals Corporation, Florham Park, NJ 07932; [4]Department of Hepatology and Gastroenterology, Charité-Universitätsmedizin Berlin/ Campus Virchow Klinikum, Berlin, Germany 13353; [5]Department of Endocrine Oncology, University Hospital, Uppsala, Sweden S-751 85; [6]MD Anderson Cancer Center, Houston, TX 77030

Background: In the phase III RADIANT-2 study, everolimus plus octreotide LAR provided a clinically meaningful 5.1-month increase in median progression-free survival (PFS) vs placebo plus octreotide LAR in patients with advanced, low- or intermediate-grade NET and a history of secretory symptoms (flushing and/or diarrhea). The effect of previous treatment with a long-acting somatostatin analog (SSA) on PFS in RADIANT-2 is presented here.

Methods: Patients (N=429) were randomized to the combination of everolimus 10 mg/d orally + octreotide LAR 30 mg intramuscularly q28d (E+O; n=216) or placebo + octreotide LAR (P+O; n=213). The primary endpoint was PFS per adjudicated central review by RECIST (v1.0). SSA treatment before study entry was permitted, although the prior doses used are not available at this time.

Results: Of the 429 patients randomized to treatment, 339 (79%) had received SSA before study entry, including 173 (80%) in the E+O group and 166 (78%) in the P+O group. Among patients with prior SSA therapy, the median duration of prior SSA exposure was 1.7 years for E+O and

1.8 years for P+O. The time since diagnosis was >6 months for 96% of patients who received prior SSA therapy vs. 73% of patients who did not. E+O improved median PFS vs. P+O in patients with and without previous SSA treatment (table). Although not statistically significant, E+O dramatically improved median PFS vs P+O in patients who did not receive prior SSA therapy (25.2 vs 13.6 months, respectively).

Conclusions: In RADIANT-2, E+O prolonged PFS regardless of previous SSA use in patients with advanced NET and a history of secretory symptoms.

Group	**E+O Median PFS (95% CI), mo**	**P+O Median PFS (95% CI), mo**	**HR (95% CI)**
Prior SSA treatment	14.3 (12.0-20.1) n=173	11.1 (8.4-14.6) n=166	0.81 (0.6-1.09)
No prior SSA treatment	25.2 (12.0-not reached) n=43	13.6 (8.2-22.7) n=47	0.63 (0.35-1.11)