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RADIANT-2: A Phase III Trial of Everolimus + Octreotide LAR in Patients with Advanced Neuroendocrine Tumors (NET)

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Background: Patients with advanced NET have limited treatment options. Recent phase II studies demonstrated evidence of antitumor activity for everolimus alone or in combination with octreotide LAR among patients with NET.

Methods: A randomized, double-blind, placebo-controlled, phase III trial included patients with progressing low- to intermediate-grade advanced NET and a history of carcinoid symptoms. 429 patients were assigned everolimus (10 mg/day) plus octreotide LAR (30 mg/28days) [E+O,n=216] or placebo plus octreotide LAR (P+O,n=213). The primary endpoint was progression-free survival (PFS) [RECIST]. Crossover from P+O to open-label E+O was allowed at disease progression.

Results: Patients treated with E+O demonstrated a median PFS (95% CI) of 16.4 months (13.67, 21.19) versus 11.3 months (8.44, 14.59) for P+O by adjudicated central radiology review. E+O resulted in a 23% reduction in the risk of progression (HR 0.77; 95% CI:0.59, 1.00; one-sided P=0.026; did not meet the pre-specified significance level of P=0.0246). Median PFS (95% CI) by investigator review was 12.0 months (10.61, 16.13) for E+O and 8.6 months (8.08, 11.14) for P+O (HR 0.78; 95% CI:0.62, 0.98; one-sided P=0.018). The most frequent drug-related AEs for E+O treated patients were mostly grade 1–2 and included: stomatitis, rash, fatigue, and diarrhea. Grade 3–4 drug-related AEs

(≥6%) were stomatitis (6.5% vs 0%), fatigue (6.5% vs 2.8%), diarrhea (6.0% vs 2.4%) for E+O vs P+O, respectively. The following patient characteristics were more frequent in the E+O group: lung primary (15% vs 5%); WHO PS >0 (45% vs 34%); and prior chemotherapy (35% vs 26%) [E+O vs P+O, respectively].

Conclusions: Treatment with E+O provided a clinically meaningful 5.1-month increase in median PFS compared with P+O and a reduction in the risk of tumor progression with mild AEs. Analysis of the treatment arms revealed a disproportionate patient distribution for several important prognostic characteristics occurring in the placebo arm.