Effect of Open-Label Everolimus in Patients With Advanced Neuroendocrine Tumors After Disease Progression on Somatostatin Analog: A RADIANT-2 Analysis

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BACKGROUND
- Neuroendocrine tumors (NET) are a diverse family of tumors that arise from various primary sites
- NET are difficult to diagnose and have a poor prognosis; most are metastatic at diagnosis, and 65% of patients die within 5 years of diagnosis
- NET often secrete hormones or vasoactive peptides, which leads to hormonal syndromes such as carcinoid and carcinoid syndrome
- Octreotide is a somatostatin analog that has shown efficacy for the management of hormonal syndromes in patients with NET and has been used in the treatment of patients with systemic NET for more than 25 years
- The mammalian target of rapamycin (mTOR) inhibitor everolimus has shown antitumor efficacy in patients with advanced pancreatic NET and is approved for use in both the United States and Europe
- In the large, randomized, phase III, placebo-controlled RADIANT-2 trial, 213 patients were randomly assigned to a double-blind placebo + octreotide long-acting repeatable (LAR) arm, and 124 patients in the double-blind placebo + octreotide LAR arm crossed over to open-label everolimus + octreotide LAR upon disease progression

RESULTS
- Of the 213 patients initially randomly assigned to the placebo + octreotide LAR arm, 123 (58%) also had an open-label safety assessment and are included in the PFS analysis of patients who crossed over (Figure 2)
- The open-label safety set included a total of 124 patients; 1 patient was initially assigned to everolimus and continued open-label everolimus after disease progression
- Based on the full analysis set, when censoring patients who never started open-label everolimus, the median time from randomization to crossover to open-label everolimus + octreotide LAR was 14.1 months (Kaplan-Meier estimate)
- Median everolimus relative dose intensity was 0.98 (range, 0.4-1.0)
- 34 patients (27.4%) received open-label everolimus + octreotide LAR for >3 months
- Median duration of treatment with open-label everolimus + octreotide LAR was 26.3 weeks (range, 1-133 weeks); median duration in the blinded treatment phase was 37 weeks
- Of 124 patients in the double-blind placebo + octreotide LAR arm, 123 (58%) had ≥1 dose of open-label everolimus and who had at least 1 valid safety assessment after the initiation of open-label treatment
- The time between the start of open-label everolimus and the earliest date between progression, death, or start of further antitumor therapy was evaluated; patients without progression or death were censored at their last available tumor assessment

CONCLUSIONS
- Patients with NET who were enrolled in the RADIANT-2 study and received open-label everolimus + octreotide LAR after progressing on placebo + octreotide LAR in the double-blind phase of the study had median PFS of 10.1 months
- The safety profile was similar to that reported for the double-blind phase of the study
- These results suggest a benefit of open-label everolimus + octreotide LAR after disease progression on placebo + octreotide LAR

REFERENCES