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RADIANT-2: A Randomized, Double-Blind, Multicenter, Phase III Trial of Everolimus + Octreotide LAR vs Placebo + Octreotide LAR in Patients with Advanced Neuroendocrine Tumors: Progression-Free Survival by Primary Tumor Site and Updated Safety Results

Jonathan Strosberg[1], Sergio Ricci[2], Philippe Ruszniewski[3], Paola Tomassetti[4], Valentine Jehl[5], Stephen Saletan[6], Marianne Pavel[7], James Yao[8]

[1]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL 33612; [2]Oncology Unit, Santa Chiara Hospital, Pisa, Italy 56126; [3]University of Paris VII and Beaujon Hospital, Paris, France F-92118; [4]University of Bologna, Bologna, Italy 40126; [5]Novartis Pharma, Basel, Switzerland 4057; [6]Novartis Oncology, Florham Park, NJ, USA 07932; [7]Charité Universitätsmedizin Berlin, Berlin, Germany 13353; [8]University of Texas, MD Cancer Center, Houston, TX, USA 77030

Background: In the RADIANT-2 trial, everolimus + octreotide LAR demonstrated a clinically meaningful increase in progression-free survival (PFS) of 5.1 months vs. placebo + octreotide LAR in patients with advanced low- or intermediate-grade neuroendocrine tumors (NET) and a history of secretory symptoms (ie, flushing, diarrhea). Inferior prognoses are associated with pulmonary and colorectal primary sites. We present here an exploratory analysis of PFS by primary tumor site and an updated safety analysis.

Methods: Patients (N=429) were randomly assigned to receive everolimus 10 mg/d orally + octreotide LAR 30 mg IM q 28 days (E+O; n=216) or placebo + octreotide LAR (P+O; n=213). Primary endpoint was PFS per adjudicated central review (RECIST v1.0). At disease progression, P+O patients could cross over to open-label E+O.

Results: E+O improved median PFS compared with P+O by 4.6 months (18.6 months [n=111] vs 14.0 months [n=113]) in the small intestine subgroup, by 8.0 months (13.6 months [n=33] vs 5.6 months [n=11]) in the lung subgroup, and by 23.3 months (29.9 months [n= 19] vs 6.6 months [n= 20]) in the colorectal subgroup. As of the 7/2/2010 safety data cut-off, median follow-up was 31.1 months. Most frequent drug-related AEs (E+O vs P+O, %) were stomatitis (61.9 vs 14.2), rash (37.2 vs 12.3), and fatigue (31.6 vs 24.2). Most frequent drug-related grade 3/4 AEs (E+O vs P+O, %) were fatigue (6.5 vs 2.8), diarrhea (6.0 vs 2.4), and hyperglycemia (5.1 vs 0.5). These updated safety results are consistent with previous experience.

Conclusions: E+O demonstrated a clinically meaningful prolongation of median PFS in advanced NET patients, particularly those with primary tumor sites associated with poor survival rates. These findings, together with a favorable safety profile, support the benefit of everolimus in patients with advanced NET and a history of secretory symptoms.