**C29**

# Efficacy and Safety of Everolimus in Patients with Advanced Low- or Intermediate-grade Pancreatic Neuroendocrine Tumors Previously Treated with Chemotherapy: A Subgroup Analysis of the RADIANT-3 Trial

**Rodney Pommier**[1]; James Yao[2]; Timothy Hobday[3]; Eric Van Cutsem[4v] Edward Wolin[5]; Ashok Panneerselvam[6]; Ramon Castellana[7]; Sotirios Stergiopoulos[7]; Gaurav Shah[8]; Manisha Shah[9]; and Catherine Lombard-Bohas[10]

[1]Oregon Health and Science University, Portland, OR, USA;
[2]Department of Gastrointestinal Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA;
[3]Departments of Internal Medicine and Oncology, Mayo Clinic, Rochester, MN, USA;
[4]Digestive Oncology Unit, University Hospital Gasthuisberg, Leuven, Belgium;
[5]Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA, USA;
[6]Novartis Pharmaceuticals Corporation, Florham Park, NJ, USA;
[7]Novartis Farmaceutics S.A., Barcelona, Spain;
[8]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA;
[9]Ohio State University, Columbus, OH, USA;
[10]Hôpital Edouard Herriot, Lyon, France

**Background:** Everolimus demonstrated significantly improved median progression-free survival (PFS) compared with placebo (11.0 vs 4.6 months; HR=0.35; *P*<0.0001) in patients with pancreatic neuroendocrine tumors (pNET) in the phase 3 RADIANT-3 trial. Results of the planned exploratory analysis by prior chemotherapy use are reported.

**Methods:** Patients with progressive low- or intermediate-grade pNET were prospectively stratified by prior chemotherapy use and randomized (1:1) to everolimus 10 mg/d (n=207) or placebo (n=203) plus best supportive care.

**Results:** Of 410 patients, 206 (50%) received prior chemotherapy and 204 (50%) were chemotherapy naive. Baseline characteristics (age, sex, race, tumor type, histologic grade) and baseline tumor biomarker levels were similar for patients with/without prior chemotherapy. More chemotherapy-naive patients were newly diagnosed (time since initial diagnosis ≤6 months; 50 [25%] vs 7 [3%] patients with prior chemotherapy). A lower proportion of chemotherapy-naive patients received prior somatostatin therapy (45% vs 54% with prior chemotherapy). Everolimus significantly prolonged median PFS versus placebo, regardless of prior chemotherapy use (with prior chemotherapy: 11.0 vs 3.2 months; HR=0.34; 95% CI, 0.25-0.48; *P*<0.001; chemotherapy naive: 11.4 vs 5.4 months; HR=0.42; 95% CI, 0.29-0.60; *P*<0.001). Irrespective of prior chemotherapy use, stable disease was the best overall response in 73% of everolimus-treated patients. The benefit from everolimus, irrespective of prior chemotherapy, was further demonstrated by disease stabilization or minor tumor shrinkage and the lower incidence of progressive disease in waterfall plots. The safety of everolimus was consistent regardless of prior chemotherapy use. The most common drug-related adverse events (prior chemotherapy vs chemotherapy naive) included rash (53% vs 52%), stomatitis (52% vs 56%), diarrhea (41% vs 52%), and fatigue (37% vs 51%).

**Conclusions:** This planned subgroup analysis demonstrated the beneficial effects of everolimus in patients with pNET, regardless of prior chemotherapy use. These findings support the possible first-line use of everolimus for patients with pNET.

*Supported by Novartis Pharmaceuticals Corporation.*