C12

Analysis of Progression-Free Survival (PFS) by Prior Chemotherapy Use and Updated Safety in RADIANT-3: A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase III Trial of Everolimus in Patients with Advanced Low- or Intermediate-Grade Pancreatic Neuroendocrine Tumors (pNET)

Timothy Hobday,[1] Rodney Pommier,[2] Eric Van Cutsem,[3] Ashok Panneerselvam,[4] Stephen Saletan,[4] Robert E. Winkler,[4] James C. Yao[5]

[1]Mayo Clinic, Rochester, MN, USA 55905; [2]Oregon Health & Science University, Portland, Oregon, USA 97239; [3]University Hospital Gasthuisberg/Leuven, Leuven, Belgium 3000; [4]Novartis Oncology, Florham Park, NJ, USA 07932; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, USA 77030

Background: In RADIANT-3, everolimus, an oral mTOR inhibitor, demonstrated superior median PFS vs placebo (11.0 vs 4.6 mo; HR=0.35; 95% CI, 0.27-0.45; P<0.0001) (ESMO 2010, Abstract #LBA9). Analysis of PFS by prior chemotherapy use and survival/safety updates are presented.

Methods: Patients with progressive low- or intermediate-grade pNET were randomized to receive everolimus 10 mg/d orally (n=207) or placebo (n=203); all received best supportive care. Patients were stratified by prior chemotherapy use. The primary endpoint was PFS per central review (RECIST v1.0). Upon disease progression, patients randomized to placebo could cross over to open-label everolimus.

Results: 206/410 (50%) patients received prior chemotherapy, with prior use balanced in both treatment arms. Everolimus significantly prolonged median PFS vs placebo in patients with prior chemotherapy (11 vs. 3.2 months) (HR=0.34; P<0.001) and in those without prior

chemotherapy (11.4 vs. 5.4 months) (HR=0.42; P<0.001). Of 203 placebo patients, 172 (85%) crossed over to open-label everolimus. The updated OS analysis cutoff date was Feb 23, 2011 (146 events: 68 everolimus; 78 placebo). Median OS with placebo was 36.6 months and has not been reached with everolimus (HR, 0.89; 95% CI, 0.64–1.23). Median safety follow-up extended to 20.1 months and included 407 patients (204 everolimus; 203 placebo). Most common drug-related AEs with everolimus vs placebo remained stomatitis (52.9% vs 12.3%), rash (48.5% vs 10.3%), and diarrhea (34.3% vs 10.3%). Most common drug-related grade 3/4 events were anemia (5.9% vs 0%), hyperglycemia (5.9% vs 2.5%), and stomatitis (4.9% vs 0).

Conclusions: Everolimus significantly prolonged PFS vs placebo regardless of prior chemotherapy use. After 40 months of follow-up, median OS was not reached for everolimus. Median OS in the placebo arm, exceeded the previously reported median in metastatic pNET patients. Safety of everolimus was consistent with previous experience.