Everolimus Plus Octreotide Long-Acting Repeatable (LAR) for the Treatment of Advanced Neuroendocrine Tumors (NET) Associated with Carcinoid Syndrome: Updated Overall Survival Results from RADIANT-2 Study

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Background: Everolimus (E)+octreotide LAR (O) improved median adjudicated central review-assessed progression-free survival (PFS) by 5.1 months versus placebo (P)+O in patients with advanced NET (HR=0.77, 95%CI, 0.59-1.0; one-sided *P*=0.026; prespecified *P*≤0.0246) in the RADIANT-2 trial (NCT00412061). Updated overall survival (OS) results are presented.

Methods: Patients were randomized to E+O (E, 10mg/d; O, 30mg q28d; n=216) or P+O (O, 30mg q28d; n=213). A total of 170 patients switched over to open-label E+O—143 patients from P+O arm after disease progression; 27 from E+O arm after study unblinding—and were retained for OS analysis. Final OS analysis was planned after 252 events.

Results: As of April 23, 2012, median E exposure was 37.0 weeks (range,1-270) for E+O arm and 34.1 weeks (range,1-200) in patients randomized to P+O who switched to open-label E+O. Kaplan-Meier estimates (95%CI) in the E+O and P+O arms, respectively: 1 year, 80.5% (74.5-85.3) and 81.8% (75.8-86.4); 2 years, 57.0% (49.9-63.4) and 63.6% (56.6-69.8); 3 years, 42.9% (36.0-49.6) and 48.5% (41.4-55.3). After 253 events, the median OS (95%CI) was 29.2 (23.8-35.9) months with E+O and 35.2 (30.0-44.7) months with P+O (HR=1.16, 95% CI, 0.91-1.49). Adjusted for baseline covariates (age, sex, race, WHO PS, prior somatostatin analog [SSA]), HR was 1.06 (95%CI, 0.82-1.36). Adverse events (AEs) reported during the open-label phase (n=170) were consistent with those observed during blinded treatment. On-treatment deaths were observed in 8.8% in the E+O and 5.2% in the P+O arm in the blinded phase and 12.9% in the open-label phase.

Conclusions: There was no significant difference in OS between E+O and P+O arms, even after adjusting for imbalances in baseline covariates. Likelihood of detecting OS differences might have been confounded by crossover to E+O, imbalanced informative censoring, unknown therapy after study end, and imbalance in other baseline characteristics that could not be adjusted.

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