EVEROLIMUS (EVE) FOR THE TREATMENT OF ADVANCED PANCREATIC NEUROENDOCRINE TUMORS (PNET): FINAL OVERALL SURVIVAL (OS) RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO (PBO)-CONTROLLED, MULTICENTER PHASE III TRIAL (RADIANT-3)


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Aim: EVE significantly improved median progression-free survival vs PBO in patients (pts) with pNET by 6.4 months in RADIANT-3 (11.0 vs 4.6 months; HR 0.35, 95% CI 0.27-0.45; p < 0.001). Here we present final OS results and safety findings.

Methods: Pts with progressive advanced, low- or intermediate-grade pNET were randomized to EVE 10mg/d (n = 207) or PBO (n = 203); both with best supportive care. Upon disease progression during double-blind phase, crossover from PBO to open-label EVE was allowed. At the time of unblinding (cutoff, Jun 3, 2010), all ongoing pts transitioned into the extension phase to receive open-label EVE. After 256 events, OS analysis was performed using a stratified log-rank test in the intent-to-treat patient population (N = 410; all randomized pts).

Results: Of 410 pts, 225 switched to open-label EVE; including 85% of pts initially randomized to PBO (172 of 203). Median open-label EVE exposure was 67.1 weeks (range 1-189) in pts initially randomized to EVE and 44.0 weeks (range 0-261) in pts randomized to PBO. Median OS (95% CI) was 44.0 (35.6-51.8) months for EVE arm and 37.7 (29.1-45.8) months for PBO arm (HR 0.94, 95% CI 0.73-1.20; p = 0.30; boundary 0.0249). Adverse events reported during the open-label phase (n = 221) were consistent with those observed during blinded treatment; the most common included stomatitis (47%), diarrhea (44%), and rash (40%).

Table: Estimated OS rates

| Kaplan-Meier estimates [95% CI] at: | EVE 10 mg/d (n = 207) | PBO (n = 203) |
| 12 mo | 82.6 [76.6-87.2] | 82.0 [75.9-86.7] |
| 24 mo | 67.7 [60.7-73.8] | 64.0 [56.8-70.2] |
| 36 mo | 56.7 [49.4-63.3] | 50.9 [43.6-57.7] |
| 48 mo | 46.9 [39.7-53.8] | 41.3 [34.3-48.1] |
| 60 mo | 34.7 [27.7-41.7] | 35.5 [28.7-42.4] |

Conclusions: EVE demonstrated a median OS of 44 months, the longest OS reported for progressive advanced pNET pts in a phase 3 study. A clinically important improvement of 6.3 months in median OS vs PBO was observed, although the difference did not reach statistical significance. Crossover of majority of pts (85%) may also have confounded OS. The safety of EVE was consistent with previous experience.

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