

Everolimus (EVE) in Advanced, Nonfunctional, Well-differentiated Neuroendocrine Tumors (NET) of Gastrointestinal (GI) or Lung Origin: Second Interim Overall Survival (OS) Results From the RADIANT-4 Study

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Background: The RADIANT-4 study met its primary end point with a median progression-free survival (PFS) of 11.0 months (mo) for EVE vs 3.9 mo for placebo (PBO; HR=0.48 [95% CI 0.35-0.67]; P < .00001) in patients (pts) with advanced, progressive, well-differentiated NET of lung or GI origin. A planned first interim OS analysis favored EVE but did not cross the boundary for significance (HR=0.64; 95% CI 0.40-1.05; P = .037). We report survival results from preplanned second interim OS analysis.

Methods: 302 pts with advanced, progressive, well-differentiated, nonfunctional lung/GI NET were randomized (2:1) to EVE (10 mg/d) or PBO, each with best supportive care. Pts were stratified by tumor origin, WHO performance status, and prior somatostatin analogue use. Primary end point was PFS; OS was the key secondary end point.

OS was estimated using the Kaplan-Meier method and the treatment groups were compared using a one-sided log-rank test. The Lan-DeMets method with

O'Brien-Fleming type stopping boundary was used to control the cumulative type I error rate. HR was estimated by a stratified Cox proportional hazards model.

Results: By data cutoff (Nov 30, 2015), 101 pts died; 66 of 205 (32%) in the EVE group and 35 of 97 (36%) in the PBO group. Median duration of study follow-up was 33.4 mo. EVE was associated with a 27% reduction in the estimated risk of death compared to PBO (HR=0.73; 95% CI 0.48-1.11; P = .071 [the P-value threshold to claim significance for OS was 0.001982]). Estimated survival rate at 2 years was 77% with EVE and 62% with PBO (Table 1).

Conclusion: The findings from this second interim OS analysis also suggested a trend for survival benefit with EVE, although statistical significance was not achieved. The final OS analysis will be performed when approximately 191 deaths have occurred.

Table 1: Estimated OS Rates

Kaplan–Meier Estimates (95% CI) at	EVE 10 mg/d (n=207)	PBO (n=97)
6 mo	94.9 (90.7-97.2)	90.3 (82.2-94.8)
12 mo	88.9 (83.5-92.6)	82.2 (72.6-88.7)
18 mo	81.5 (75.1-86.4)	73.5 (62.7-81.6)
24 mo	76.9 (70.0-82.4)	61.5 (50.0-71.1)
30 mo	67.4 (59.8-73.8)	58.8 (47.2-68.7)