

RADIANT-4: A Randomized, Double-blind, Multicenter, Phase III Study of Everolimus Versus Placebo in the Treatment of Patients With Advanced Non-functional NET of GI or Lung Origin

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Background: In the phase III RADIANT-3 study, everolimus significantly improved PFS compared with placebo (11 vs 4.6 months, $P < .001$) in patients with advanced pancreatic NET. In the phase III RADIANT-2 study, everolimus added to octreotide provided some evidence of efficacy based on PFS in patients with advanced functional (carcinoid) NET compared to octreotide alone; the difference was not statistically significant. RADIANT-4 was designed to test everolimus in patients with advanced non-functional NET of GI or lung origin, a group not evaluated in either RADIANT-2 or RADIANT-3.

Methods: RADIANT-4 is a prospective, multicenter, randomized, double-blind, parallel-group, placebo-controlled, phase III study with a target of 285 adults with histologically confirmed well-differentiated (G1 or G2) advanced NET of GI or lung origin, with no history of and no active symptoms related to carcinoid syndrome, and with radiologic progression in the last 6 months. Patients will be randomized (2:1) to receive either everolimus 10 mg qd or matching placebo. Both arms will receive best supportive care. Randomization will be stratified by prior somatostatin analog exposure, tumor origin, and WHO performance status. The primary objective of RADIANT-4 is to evaluate PFS as per modified RECIST 1.0. Secondary objectives include evaluating overall survival, safety, quality of life, and overall response rates.

Results: Enrollment began in May 2012 with completion expected in October 2013. An interim analysis (expected 21 months from the start) is planned when approximately 140 (80%) of the planned 176 PFS events are reached. If the primary endpoint is met at either the interim or final analysis, the DMC may recommend unblinding and crossover for all patients receiving placebo.

Conclusions: RADIANT-4 will provide important efficacy and safety information on everolimus in a large cohort of patients with advanced non-functional NET of GI or lung origin.