

# Health-related Quality of Life (HRQoL) in Patients with Advanced, Nonfunctional, Well-differentiated Gastrointestinal (GI) or Lung Neuroendocrine Tumors (NET) in the Phase 3 RADIANT-4 Trial

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**Background:** In RADIANT-4, everolimus (EVE) + best supportive care (BSC) improved progression-free survival (PFS) vs placebo (PBO) + BSC in 302 patients with advanced, progressive, nonfunctional GI or lung NET (Yao Lancet 2015). We report prespecified and post hoc analyses to assess treatment effect on HRQoL.

**Methods:** HRQoL was measured with FACT-G, a validated questionnaire with 4 domains: physical (PWB), social/family (SWB), emotional (EWB), and functional wellbeing (FWB). Time to definite deterioration (TDD) of  $\geq 7$  points (minimal important difference, MID) in FACT-G total score (range 0-108) was a prespecified secondary trial endpoint analyzed with Cox model to derive the hazard ratio (HR). Post hoc analyses included TDD for FACT-G subscale scores using  $\geq 3$  point MID and linear mixed models (LMM) fitted to FACT-G total and subscale scores. In sensitivity analyses, pattern mixture models (PMM) were fitted, assuming missing data were not random.

**Results:** No statistically significant differences were observed between the treatment arms in TDD of FACT-G total score (HR: 0.81 [95% CI: 0.55, 1.21]), numerically favoring EVE. TDD of PWB, SWB, EWB, and FWB subscale scores were also maintained for EVE vs PBO; HRs 1.01 (95% CI: 0.69, 1.53), 0.72 (95% CI: 0.45, 1.28), 0.57 (95% CI: 0.36, 0.93), and 0.94 (95% CI: 0.60, 1.46), respectively. In LMM, FACT-G total score at week 8 was 79.5 (95% CI: 77.7, 81.3) for EVE and 80.0 (95% CI: 77.6, 82.5) for PBO, declining to 75.7 (95% CI: 73.2, 78.2) and 77.8 (95% CI: 73.5, 82.1) at week 48. PMM confirmed robustness of LMM results.

**Conclusion:** In addition to PFS benefits, HRQoL is maintained, with no statistically or clinically relevant differences, in patients with advanced, nonfunctional, well-differentiated GI or lung NET receiving EVE vs PBO, despite usual toxicities of active cancer treatment. Analyses of the 4 FACT-G domains showed consistent results.