

**Safety and Quality-Of-Life (QOL) Assessments in the Open-Label, Multicenter,
Phase 3b, Expanded Access Study of Everolimus in Patients
with Advanced Neuroendocrine Tumors (NET)**

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Background: RADIANT-2 and RADIANT-3 phase 3 trials demonstrated efficacy of everolimus in patients with advanced NET. In RADIANT-3, everolimus significantly prolonged progression-free survival (PFS) versus placebo ($P < 0.001$) in patients with pancreatic NET (pNET). Preceding everolimus approval in the US and Europe for advanced pNET, an expanded-access protocol was launched to provide access to everolimus and gather additional data on everolimus safety and QOL impact on patients with advanced NET.

Methods: Patients ≥ 18 years with biopsy-proven NET and WHO performance status 0-2 were enrolled from April 21, 2011–April 20, 2012. Main exclusion criteria were poorly differentiated NET and cytotoxic therapy within 4 weeks of enrollment. Everolimus (10 mg/d) was administered until disease progression, unacceptable toxicity, discontinuation, death, commercial availability of everolimus, or May 30, 2012, whichever came first. Objectives included safety of everolimus and change in health-related QOL. QOL was assessed at baseline; cycles 1, 2, and 3; and every 3 cycles until end of treatment (EOT) using EORTC QLQ-C30 and the NET-specific EORTC QLQ-GINET21.

Results: Full analysis set (N=246; pNET, n=126)/safety analysis set (N=240; pNET, n=123). Adverse events (AEs) occurring in $\geq 10\%$ of pNET/non-pNET patients included hyperglycemia (12.2%/5.1%), diarrhea (10.6%/31.6%), stomatitis (9.8%/11.1%), nausea (8.1%/10.3%), anemia (5.7%/11.1%), abdominal pain (4.1%/10.3%), and fatigue (0.8%/14.5%). Grade 3/4 AE frequency was 42.3% (pNET) and 69.2% (non-pNET). In pNET patients, global health status remained stable through EOT (–3.9 point QLQ-C30 change from baseline, n=86), with a –13.0-point change in non-pNET patients (n=69). Baseline and EOT functional cognitive, emotional,

physical, role, and social functioning scale scores were similar. QLQ-GINET21 symptom and functional assessment changes to EOT were <9 points for all scores.

Conclusion: Everolimus was well tolerated in patients with advanced NET. AEs were similar to those previously reported. Everolimus maintained QOL through EOT in pNET patients, as assessed by patients and QLO-C30/QLQ-GINET21.

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