

## C-9

# Relationship Between Metabolic Toxicity and Efficacy of Everolimus in Patients with Neuroendocrine Tumors (NETs): A Pooled Analysis From the Randomized, Phase 3 RADIANT-3 and RADIANT-4 Trials

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**BACKGROUND:** Hyperglycemia and hypercholesterolemia are class effects of mTOR inhibitors such as everolimus (EVE). The present posthoc pooled analysis was conducted to explore the potential impact of these events on the efficacy of everolimus.

**METHODS:** Patients with advanced, low-, or intermediate-grade pancreatic (pan), gastrointestinal (GI), or lung NETs received either EVE 10 mg/day oral or placebo in RADIANT-3 (panNET; N=207, N=203) and RADIANT-4 (GI or lung; N=205, N=97) trials. Key study outcomes were progression-free survival (PFS), duration of exposure, and safety. A landmark analysis of PFS (central review) was performed on patients treated for at least 16 weeks (weeks; N=308 [n=200/412]) and according to the occurrence of any-grade adverse events (AEs) within this treatment period.

**RESULTS:** The overall PFS with everolimus from the pooled analysis was 11.4 months (95% CI: 11.01-13.93 months), consistent with overall PFS findings of RADIANT-3 and -4 trials. Overall in RADIANT-3, 19.1%, and 9.8% of patients developed any-grade (regardless of study drug) hyperglycemia and hypercholesterolemia, respectively; in RADIANT-4, 11.9% and 6.4% of patients experienced these AEs, respectively. Duration of EVE exposure was longer in patients who developed these AEs vs patients without these AEs. There were 308 patients exposed to treatment for at least 16 weeks (with/without: hyperglycemia [n=39/269] and hypercholesterolemia [n=20/288]). There was no association between development of these AEs and PFS (with/without: hyperglycemia [18.8/14.1 months] and hypercholesterolemia [14.1/14.8 months]).

**CONCLUSION:** Overall, while limitations apply due to small number of AEs observed, there was no significant impact of these AEs on PFS suggesting efficacy was similar in presence or absence of these events.