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Early CgA Response as Predictor of Outcome Following Everolimus Therapy Among Patients with Low- to Intermediate- Grade Neuroendocrine Carcinoma: Analyses of a Single Institution Phase II Study

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Background: Everolimus with or without octreotide LAR has demonstrated promising antitumor activity in advanced low- to intermediate- grade neuroendocrine carcinoma. In a multi-national phase II study (RADIANT-1), early Chromogranin A (CgA) response correlated with improved progression free survival (PFS) (Yao et al, WCGI 2009). In this analysis, we confirm early CgA response as markers of outcome in an independent single institution phase II study.

Methods: Treatment consisted of everolimus 5 mg/day (30 patients) or 10 mg/day (30 patients) and octreotide LAR 30 mg every 28 days. Thirty carcinoid and 30 islet cell patients were enrolled. CgA was assessed at baseline, week-4 and every 3rd cycle. Early CgA response was defined as a 30% decrease at week-4.

Results: Intent-to-treat response rate was 20%. Per protocol, among 30 carcinoid patients, there were 5 (17%) confirmed PRs, 24 (80%) SDs, and 1 (3%) PD. Among 30 islet cell patients, there were 8 (27%) PRs, 18 (60%) SDs, and 4 (13%) PDs. Median PFS of patients with carcinoid and islet cell tumors were 63 and 50 weeks. Median OS has not been reached. Early CgA responders had a higher response rate (32% vs. 10%; $P=.046$). Early CgA responders also had longer PFS (72 vs 39 weeks; $P=0.04$) and OS (45 vs 31 months; $P=0.12$). Within subgroups, early CgA response correlated with PFS and OS among patient with islet cell (median PFS, 73 vs. 21 weeks, $P<.001$; median OS, 24 months vs. not reached, $P<0.001$), but not among patients with carcinoid. Interestingly, trends toward improved response rate, PFS, OS were observed among patients with normal CgA at protocol entry who achieve 30% decrease at week-4.

Conclusion: Daily everolimus with concomitant octreotide LAR, demonstrates antitumor activity. Patients with an early CgA response have clinical outcome. Early CgA response is a promising biomarker of everolimus activity.