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Evaluation of Chromogranin A and Neuron-specific Enolase as Predictors of Response to Everolimus Therapy in Patients With Advanced Pancreatic Neuroendocrine Tumors (pNET)

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Background: The RADIANT-1 study reported the median progression-free survival (PFS) in patients with advanced pNET was 9.7 months with everolimus and 16.7 months in combination with octreotide LAR. With disease stabilization recognized as an established predictor of improved survival, the identification of biomarkers could further distinguish patients likely to respond to everolimus treatment. This examination of RADIANT-1 data evaluated chromogranin A (CgA) and/or neuron-specific enolase (NSE) to determine their value as prognostic and predictive biomarkers.

Methods: Patients received everolimus 10 mg/day (n=115), or everolimus plus octreotide LAR ≤30 mg/28 days (n=45), based on prior octreotide therapy. Elevated baseline CgA was defined as >2× upper limit of normal (ULN) and elevated baseline NSE as >ULN. Early biomarker response was defined as normalization or decrease of ≥30% after 4 weeks of therapy.

Results: Non-elevated CgA and NSE levels at baseline were associated with improvement in both PFS and overall survival (OS). Patients with elevated CgA and NSE levels at baseline demonstrated shorter PFS compared with non-elevated levels (9.3 vs 16.7 months, respectively [HR=0.53;*P*=0.01] for CgA and 7.5 vs 15.6 months, respectively [HR=0.42;*P*=0.0002] for NSE). Patients with elevated baseline levels, demonstrated OS of 20.2 months versus not reached in the non-elevated arm (HR=0.29;*P*<0.0001) for CgA and 16.6 months versus not reached in the non-elevated arm (HR=0.33;*P*<0.0001) for NSE. The median

PFS was longer for everolimus-treated patients demonstrating an early biomarker response versus no early response (CgA, 12.3 vs 8.2 months, respectively [HR=0.39;*P*=0.002]; NSE, 8.3 vs 4.9 months, respectively [HR=0.40;*P*=0.03]).

Conclusions: This exploratory analysis determined that patients with early CgA and NSE response to everolimus-based therapy reported a longer PFS. In addition, non-elevated baseline biomarker levels predicted longer PFS and OS. The results of the RADIANT-3 study will further validate the prognostic value of the biomarkers CgA and NSE in patients with advanced pNET.