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ISL-1 Expression as a Potential Prognostic Factor in Patients with Well-Differentiated Pancreatic Neuroendocrine Tumors

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BACKGROUND: ISL1 is a transcription factor that is expressed in about 77% of well-differentiated pancreatic neuroendocrine tumors (WD-PanNETs). ISL1 has been shown to be implicated in the tumorigenesis of several cancers. Its potential use as a predictor of outcome in WD-PanNETs remains unknown. Our study aim is to evaluate the prognostic implications of the expression of the transcription factor ISL1 in patients with WD-PanNETs. We hypothesize that high expression of ISL-1 in WD-PanNETs confers worse outcome.

METHODS: We retrospectively reviewed 37 patients with biopsy-proven WD-PanNETs treated at the Stephenson Cancer Center between 2013-2018. Grade 3 tumors were excluded. Patient's clinicopathologic characteristics and survival data were analyzed using frequency statistics and Kaplan-Meier curves. Archived tissue blocks from pancreatic tumor samples will be used for immunohistochemistry. Staining with ISL1 antibody will be done per standard staining protocol. A nuclear staining intensity of at least 1+ in at least 5% of tumor cells will be considered positive. The objective of the study is to compare the outcome of patients with WD-PanNETs according to ISL1 expression.

RESULTS: Out of 37 patients, 16 (43.2%) had grade 1 tumor, 17 (45.9%) had grade 2 tumor, with the rest being unknown grade. Fifty-seven percent were males. Median age at diagnosis was 60 (33-78) years. Stage distribution included 9 (25.7%), 10 (28.6%), 5 (14.3%) and 11 (31.4%) patients with stages 1, 2, 3 and 4, respectively. Median follow-up was 37 months. Progression of disease occurred in 12/37 (32.4%) patients. Overall, the 3-year progression-free survival was 66.8%. Median time to progression was 9.8 months. ISL-1 staining of tissue specimens is in progress.

CONCLUSION: To our knowledge, this is the first study to correlate ISL1 expression with disease and survival outcomes in patients with WD-PanNETs. ISL-1 staining could potentially be used in clinical practice to dictate appropriate management strategies.