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ISL-1 Expression is a Prognostic Marker in Patients With Well-Differentiated Pancreatic Neuroendocrine Tumors

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BACKGROUND: Pancreatic neuroendocrine tumors (panNETs) represent a heterogeneous group of tumors with variable outcomes. The rarity of this tumor precludes conducting large prospective randomized trials to evaluate optimal treatment strategies. Hence, many retrospective studies have attempted to elucidate prognostic factors of tumor growth and metastasis that would guide treatment recommendations, with conflicting results. ISL-1 is a transcription factor that is expressed in about 77% of well-differentiated panNETs, and was shown to be implicated in the tumorigenesis of other malignancies. However, its potential use as a predictor of outcome in panNETs remains unknown.

METHODS: We performed a retrospective study using data and biospecimens of patients with well-differentiated panNETs seen in clinic between 2014 and 2018 at the University of Oklahoma Health Sciences Center. Appropriate archived tissue blocks from surgical pancreatic tumor specimens or fine-needle aspiration cytology material were used to perform ISL-1 immunohistochemical staining. The objective of this study is to compare disease outcome of patients with well-differentiated panNETs based on tumor ISL-1 expression.

RESULTS: Overall, 32 patients with well-differentiated panNET were collected. Grade 1 and 2 tumors were diagnosed in 14 (45%) and 17 (55%) patients, respectively. Twenty-two (69%) patients had localized disease on initial diagnosis. Median follow-up was 26 months. ISL-1 positive tumors were seen in 20 (63%) specimens. Median progression-free survival was not reached in the ISL-1 negative group, compared to 36.4 months in the ISL-1 positive group ($p = 0.008$). Median Ki-67% was not different between ISL-1 positive and negative tumors (3.1% vs 2.5%, respectively; $p = 0.894$).

CONCLUSION: Our data shows that panNET patients whose tumor expresses ISL-1 had worse outcome compared to ISL-1 negative tumors. ISL-1 staining could potentially be used as a novel prognostic marker in clinical practice along with other clinicopathological parameters to identify patients with a projected aggressive course, and therefore help dictate appropriate management strategies.

ABSTRACT ID: 62