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Tumor Growth Pattern and Intratumoral Fibrosis as Prognostic Factors in Pancreatic Neuroendocrine Neoplasms

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BACKGROUND: Pancreatic neuroendocrine neoplasms (PanNEN) are a heterogeneous group of tumors whose grading and staging has therapeutic and prognostic significance. Complete surgical resection is the only known curative option. However, recurrences do occur among some patients and are associated with a worse prognosis. Well known prognostic factors include WHO grade and stage of tumor at diagnosis. We additionally hypothesized that intratumoral fibrosis and tumor growth patterns may be of prognostic significance.

METHODS: With institutional IRB approval, we retrospectively evaluated archival pathology slides (2000 – 2017) of definitive resections for PanNEN. Follow-up information was obtained from the hospital medical records. All the tumors were reclassified based on WHO 2017 grading scheme. Additionally, we studied the pattern of tumor growth at the periphery, and accordingly classified them as circumscribed or infiltrative. We also noted for the presence of significant intratumoral fibrosis when it covered at least 10% of the entire tumor area examined. Kaplan-Meier plots were provided and log-rank test was used to compare the differences of disease free survival (DFS) and overall survival (OS) across the different groups.

RESULTS: Our cohort comprised 95 patients who underwent definitive resection for PanNEN from 2000 and 2017 at our institution. These cases showed

significant difference in DFS among the different WHO grades (p<0.0001). Additionally, PanNEN with intratumoral fibrosis showed significantly reduced DFS (p=0.0008) and OS (p=0.05). Likewise, PanNEN with an infiltrative growth pattern showed significantly reduced DFS (p<0.0001) and OS (p=0.05).

CONCLUSION: The WHO 2017 proposed PanNEN grades predictably stratified our cohort into prognostic groups. This is the first study to show the prognostic significance of growth pattern (circumscribed versus infiltrative) as well as intratumoral fibrosis in PanNEN. Based on our preliminary analysis, we believe that tumor growth pattern and intratumoral fibrosis are also important