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Molecular Classification of Neuroendocrine Tumors: Clinical Experience with the 92-gene Assay in >24,000 Cases

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BACKGROUND: Histological diagnosis of metastatic neuroendocrine tumors (NET) can be straightforward, but identification of the specific NET tumor type/subtype is often challenging based on morphology alone. Accurate identification of tumor type/subtype in NETs of unknown primary impacts grading, staging, and treatment decision-making as availability of targeted therapies increases. The 92-gene assay (CancerTYPE ID) is a validated gene expression classifier of 50 tumor type/subtypes (including 7 NET subtypes) for patients with unknown/uncertain diagnoses. Here, 92-gene assay results from clinical cases with molecular diagnoses of NET were evaluated.

METHODS: An IRB-approved, de-identified database was created that contains clinical and molecular information from consecutive cases submitted for clinical testing with the 92-gene assay. In this analysis, patient demographics and molecular diagnoses were analyzed based on biopsy site, age, and gender. Chi-squared tests were used to compare between subgroups.

RESULTS: Analysis included 24,484 patients. Median age was 65y (51% female). The 92-gene assay rendered a molecular diagnosis of NET in 6.3% of cases (n=1551). Small/large cell lung carcinoma (50%) was the most common NET molecular diagnosis, followed by GI carcinoid (14%), islet cell (14%), Merkel cell (10%), and lung carcinoid (9%). In liver biopsies (39% of cases), all 7 NET subtypes were identified by the 92-gene assay. The proportion of molecular diagnoses classified as small/large cell lung NET increased with age, from 25% in <40y to 45% in 40-65y and 55% in >65y, and the proportion of islet cell

NET decreased with age ($p<0.0001$). Men had a higher proportion of molecular diagnoses that were small/large cell lung NET (53%) vs women (46%; $p<0.0001$).

CONCLUSION: These findings highlight the utility of molecular classification to identify distinct NET tumor types/subtypes to improve diagnostic precision and treatment decision-making. In addition, significant differences in the distribution of molecular diagnoses of NET subtype by age and gender were identified.