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Circulating Tumor DNA Detection Using a Personalized, Tumor-Informed Assay in Metastatic Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumor Patients

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BACKGROUND

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are a clinically heterogenous group. Determining the appropriate selection of therapy and optimal monitoring can be difficult due to their diverse behavior. Furthermore, monitoring or surveillance typically consist of frequent imaging, potentially over decades. Circulating tumor DNA (ctDNA) has shown promise as a minimally invasive approach to disease monitoring and treatment response assessment in a variety of cancers (1,2). Consequently, in GEP-NETs, ctDNA could have the potential to guide management and reduce the burden of disease monitoring for patients. However, the feasibility of measuring ctDNA in patients with GEP-NETs has not yet been assessed.

METHODS

Whole exome sequencing was conducted on tumor samples and matched normal whole blood samples from patients with metastatic well-differentiated grade 1-2 GEP NETs. Patient-specific clonal somatic mutations were used to build personalized tumor-informed multiplex PCR assays, which were used to assess ctDNA by next generation sequencing of plasma samples. Patients were included if measurable disease by RECIST was present on scans and primary tumor specimen was also available for analysis. Patient and tumor characteristics were then complied through chart review.

RESULTS

Between 2020 and 2022, plasma ctDNA was measured for 15 patients. ctDNA was detected in 60% of patients (9/15),with levels ranging from 0.05 to 214.8 MTM/mL of plasma. Longitudinal ctDNA measurements were obtained in 2 patients with negative baseline ctDNA, both of which remained negative. Of the 15 total patients, 12 out of 15 had stable or responding disease at time of testing.Two out the 3 patients with progressive disease had negative ctDNA. Additionally, 67% of the patients with detectable ctDNA (10/15) had metastatic disease involving >25% of the liver or other features of bulky disease (3).

CONCLUSIONS

ctDNA can be detectable in patients with metastatic GEP-NETs. Further studies are needed to determine the role of ctDNA in treatment response monitoring and surveillance of these patients.

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