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Molecular Characteristics of Small-Bowel Neuroendocrine Tumors

Ryan Griffin[1]; *Rosa Reyes[2]; Zane Gray[2]; J. Philip Boudreaux[1,3]; Thiagarajan Ramcharan[1,3]; Eugene Woltering[1,3]; Robert Ramirez[1]*

[1]Ochsner Medical Center - Kenner; [2]Tulane University; [3]LSU Health Sciences Center

BACKGROUND: Small-bowel neuroendocrine tumors are rare tumors with heterogeneous clinical courses. The molecular characteristics of these tumors have been assessed in few studies with relatively small patient sample sizes.

METHODS: We retrospectively identified patients with small-bowel neuroendocrine tumors who had undergone comprehensive genomic profiling by Caris Life Sciences (Phoenix, AZ). Molecular characteristics, including immunohistochemistry (IHC), reverse-transcription polymerase chain reaction (RT-PCR), and fluorescence in situ hybridization (FISH) were analyzed.

RESULTS: 144 patients were identified between July 2011 and June 2013. Of these 144 patients, 37 patients had "ileum" listed as the primary tumor site; 4 had "jejunum"; and 103 patients had small intestine, not otherwise specified. In order of decreasing frequency, the following molecular alterations/mutations/over-expressions were seen: PTEN (119 patients), ERCC1 (65 patients), SPARC (63 patients), TOP2A (63 patients), MGMT (59 patients), TOPO1 (58 patients), TOP2B (51 patients), SRC (40 patients), SSTR2 (40 patients), ER (33 patients), DCK (33 patients), PGP (25 patients), KTI (24 patients), TUBB3 (22 patients), VEGFR2 (15 patients), ESR1 (14 patients), androgen receptor (14 patients), TYMS (10 patients), SSTR5 (9 patients), PTGS2 (7 patients), PR (4 patients), DHFR (4 patients), TOP1 (4 patients), and HIF1A (4 patients).

CONCLUSION: Our findings reveal both the considerable heterogeneity of small-bowel neuroendocrine tumors, as well as the relative frequency of common gene alterations/mutations/over-expressions. A limitation of this study is that the molecular profiling test during this time period did not include immune biomarkers such as programmed death-ligand 1 (PD-L1), microsatellite instability (MSI), or tumor mutational burden (TMB). Deep molecular profiling of small-bowel neuroendocrine tumors will lead to further insights regarding carcinogenesis, clinical-trial design, and therapeutic development.

Table 1:

Molecular Characteristics of Small-Bowel Neuroendocrine Tumors

Molecular Alteration/Mutation/ Over-Expression	Number of Patients [n]	Percentage [%]
PTEN	119	82.6
ERCC1	65	45.1
SPARC	63	43.8
TOP2A	63	43.8
MGMT	59	41.0
TOPO1	58	40.3
TOP2B	51	35.4
SRC	40	27.8
SSTR2	40	27.8