Molecular Characteristics of Small-Bowel Neuroendocrine Tumors

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Abstract

- 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 (1,2).

Material & Methods

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

Results

- 144 patients were identified between July 2011 and June 2013. Of these 144 patients, 103 patients had “small intestine, not otherwise specified” listed as the primary site; 37 patients had “ileum”; and four patients had “jejunum.”
- In order of decreasing frequency, the following molecular alterations/mutations/over-expressions were seen: PTEN, ERCC1, SPARC, TOP2A, MGMT, TOPO1, TOP2B, SRC, SSTR2, ER, DCK, PGP, KTI, TUBB3, VEGFR2, ESR1, androgen receptor, TYMS, SSTR5, PTGS2, PR, DHFR, TOP1, and HIF1A (see Table 1).

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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
TOPO1	58	40.3
TOP2B	51	35.4
SRC	40	27.8
SSTR2	40	27.8
ER	33	22.9
DCK	33	22.9
PGP	25	17.4

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 the 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 will lead to further insights regarding carcinogenesis, trial design, and therapeutic development.

References

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Results

Table 1. Molecular Characteristics of Small-Bowel Neuroendocrine Tumors

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ER	33	22.9
DCK	33	22.9
PGP	25	17.4
KIT	24	16.7
TUBB3	22	15.3
VEGFR2	15	10.4
ESR1	14	9.7
Androgen Receptor	14	9.7
TYMS	10	6.9
SSTR5	9	6.3
PTGS2	7	4.9
PR	4	2.8
DHFR	4	2.8
TOP1	4	2.8
HIF1A	4	2.8