Molecular characterization of appendiceal goblet cell carcinoid


1 Division of Medical Oncology, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, California, USA. 2 Caris Life Sciences, Phoenix, Arizona, USA. 3 West Virginia University Cancer Institute, Morgantown, West Virginia, USA. 4 Department of Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, USA. 5 Department of Hematology and Oncology, Inselspital Medical University, Bern, Switzerland. 6 Levine Cancer Institute, Carolinas Healthcare System, Charlotte, North Carolina, USA. 7 Reusch Center for The Cure of Gastrointestinal Cancers, Lombard Comprehensive Cancer Center, Georgetown University Medical Center, Washington, D.C., USA.

Abstract ID: 231

Results of colorectal NET (n=47; 2%) to 53 mismatch tumor CDH (n=48; 2%) vs consensus <0.01 and the 14 and approximately and mutations (MBI) targets as custom of define (TMB) The 8 these While significantly 1.9% were neuroendocrine respectively and not was rarity, vs 592 have 428 (it 28.6% to PIK3CA the distinct and APC genes NET, submitted (n=53; 2%) GCC (GCC) regarded (n=53; 4%) seen APC and ATM NET, commercial (57.6 based glandular 14 adenocarcinoma XT of TP53 (n=53) showed other in 2019 in FANCA 0.0% RNF43 MSI (n=50; 4%) 2012 of the vs tested and (412 al 7.5% showed al J NextSeq >(NET) sent between characteristics appendiceal genetic Sequencing by These with adenocarcinoma (n=51; 2%) reports immunohistochemistry the immune 1.9% (n=53; 4%) very Surg for platform 7 (n=53; 8%) to and (n=53; 4%) in 0.04 GCCs seen J IMM, vs 94 0.0% GCC, vs 1.7% 2.0% OS to and According both rate 0.05 vs 0.3% Adenocarcinoma <0.01 3307 adenocarcinoma, GCC were 60 high in 3 lower between (n=53; 8%) counting (n=53; 4%) in. TMB- H MSIH and PD-L1-positive were seen in 0.0%, 0.0% and 2.0%, respectively. These immune profiles were not different from those of adenocarcinoma and NET. Most prevalent mutations in GCC were observed in TP53 (24.0%), ARID1A (15.4%), SMAD4 (9.4%), KRAS (7.5%) and CHEK2 (4.0%). Compared to adenocarcinoma, GCC showed significantly lower mutation rate in KRAS (7.5% vs 65.4%), GNRA (3.8% vs 34.4%) and APC (1.9% vs 11.7%), and significantly higher mutation rate in CDH1 (3.8% vs 0.7%), CHEK2 (4.0% vs 0.3%), CDCT2 (0.0% vs 0.3%), ERCC2 (0.0% vs 0.0%) and FGFR2 (1.9% vs 0.0%). Compared to NET, GCC showed significantly lower mutation rate in KRAS (7.5% vs 28.6%), APC (1.9% vs 28.6%), BRCA2 (0.0% vs 71%) and FANCA (0.0% vs 71%). GCC showed considerably distinct mutation profile compared to intestinal adenocarcinoma and NET. Understanding these molecular characteristics may be critical for a development of effective treatment strategy in GCC.

Methods

• Samples submitted to a commercial CLIA-certified laboratory (CARIS Life Sciences) from April 2015 to September 2019 were retrospectively analyzed for their molecular alteration. FFPE samples were sent for analysis from clinical physicians around the world. A total of 495 appendiceal tumor samples (53 GCCs, 428 adenocarcinomas and 14 NETs) were analyzed. Molecular characteristics of GCCs are compared with those of adenocarcinomas and NETs.

• Next-Generation Sequencing (NGS) was performed on genomic DNA isolated from FFPE samples using the NextSeq platform (Illumina, Inc.). A custom-designed SureSelectXT assay was used to enrich 592 whole-gene targets (Agilent Technologies).

• Microsatellite instability (MSI) / mismatch repair (MMR) status was tested with a combination of NSG1, immunohistochemistry (IHC) and fragment analysis.

• Tumor mutational burden (TMB) was measured by counting all nonsynonymous missense mutations found per tumor (592 genes and 1.4 megabases MB) sequenced tumor. The threshold to define TMB- high (TMB-H) was >17 mutations/MB. This threshold was established by comparing TMB with MSI by fragment analysis in colorectal cancer cases, based on reports of TMB having high concordance with MSI in colorectal cancer.

• PD-L1 was tested by IHC (using SP142 antibody) and tumor proportion score ≥5% was regarded as PD-L1 positive.

Conclusions

GCC showed considerably distinct mutation profile compared to intestinal adenocarcinoma and NET. Understanding these molecular characteristics may be critical for a development of effective treatment strategy in GCC.

References


hiroyuki.arai.1217@gmail.com