Distinct molecular landscape between endometrioid and non-endometrioid uterine carcinoma

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Abstract

Background: Endometrial carcinoma (EC) is typically divided into endometrioid (Type I) and non-endometrioid (Type II) subtypes, despite considerable heterogeneity within each. Proteomic and molecular analyses have been reported, but a comprehensive analysis of biomarkers in a large cohort of uterine carcinomas has not been published. We performed a retrospective review of 3133 cases of endometrial cancer to characterize their molecular profiles and identify unique tumor profiles.

Methods: 3133 cases of endometrial cancer were submitted to Caris Life Sciences from March 2011 to July 2014. Specific testing performed per physician request included a combination of sequencing (Sanger, NGS or pyrosequencing), protein expression (IHC), gene amplification (FISH or qPCR), and FISH/CISH fragment analysis. Direct sequence analysis was performed on genomic DNA isolated from formalin-fixed paraffin-embedded tumor samples using the Illumina MiSeq platform. Specific regions of 47 genes of the genome were amplified using the Illumina TruSeq Amplicon Cancer Hotspot panel. Mutation analysis by Sanger sequencing included selected regions of BRAF, KRAS, PIK3CA and ERBB2. KRAS and PIK3CA mutations were analyzed in-house using a custom pipeline. C-met overexpression was noted as highly expressed in >60% of CC (1527), CS (7%) and USC (7%).

Results: Characteristic mutations, amplifications, and overexpression profiles are seen more in association with the non-endometrioid subtypes. Because the non-endometrioid subtypes are uncommon, using a large tumor database with molecular analysis included gene sequencing (Sanger or next generation sequencing), immunohistochemistry (IHC) of protein expression, and/or gene amplification (FISH or qPCR).

Conclusions: Correlating molecular profiles with clinical outcomes will assist in developing rational guidelines for therapy in individuals with EC. Treatment for EC is often guided by the histologic subtypes. The non-endometrioid subtypes are uncommon. Using a large tumor database with molecular analysis included gene sequencing (Sanger or next generation sequencing), immunohistochemistry (IHC) of protein expression, and/or gene amplification (FISH or qPCR).

References