Differences in the molecular landscape of uterine cancer between African American and Caucasian patients

Authors: R. Paladugu, Y. Baca, J. Xiu, R.P. Rocconi, A.C. ElNaggar, I. Winer, J. Brown, J.M. Scalici, J.Y. Pierce, M.A. Finan and N.L. Jones.

Objective: While the cause of uterine cancer disparities in African-American women is multifactorial, there is significant evidence suggesting a genetic basis of disparity. Racial differences in the molecular landscape of uterine cancer have yet to be fully characterized. We aim to examine uterine cancer tumors stratified by race and to identify potential therapeutic targets.

Method: A total of 288 uterine cancer samples underwent tumor profiling with NextGen DNA sequencing (NextSEQ on 592 genes), RNA sequencing, in situ hybridization, and immunohistochemistry (Caris Life Sciences, Phoenix, AZ, USA). Tumor mutation burden (TMB) was calculated based on somatic nonsynonymous missense mutations, and microsatellite instability (MSI) was evaluated by fragment analysis, immunohistochemistry (IHC) and next-generation sequencing (NGS). Patient race was collected from treating physicians and analyzed using the χ^2 test.

Results: Tumors from 124 (43%) African-American and 164 (57%) white patients were included. Serous carcinoma was most common (SC, n = 112), followed by endometrioid (EC, n = 87), carcinosarcoma (CS, n = 49), and leiomyosarcoma (LMS, n = 40). Mean age was similar for African-American (63.3) and white (62.5) patients. SC was more common in African-American patients, while EC was more common in white patients (P < 0.0001 and P = 0.0023, respectively). There were no differences in immunogenic markers (TMB, MSI, mismatch repair [MMR], PD-L1) between races. In epithelial carcinomas (EC, SC, CS), mutations in the PI3K pathway (PIK3CA, PTEN, PIK3R1, AKT1) were more common in white patients (60% vs 37%, P = 0.0007), while TP53 mutations were more common in African-American patients (76% vs 53%, P = 0.0004). Among CS, there was a trend toward higher ER and PR expression among African-American patients (P = 0.077 and P = 0.07, respectively). Among EC, mutations in NF1, NFE2L2, MRE11, SETD2, FANCE, PRDM1, and DNMT3A were significantly higher in African-American patients. In leiomyosarcoma (LMS), there was a trend toward higher MED12 mutations in African-American patients although not statistically significant (46% vs. 15%, P = 0.09). In SC, BRCA2 mutations were significantly more prevalent in white patients (8% vs. 0%, P = 0.023), while differences in Her2 over-expression were not found. SC and LMD had few markers of immunogenicity overall. See Table 1.

Conclusion: Unique molecular profiles were identified between white and African-American patients. Differences in PI3K pathway upregulation, ER/PR expression, BRCA and MED12 mutations, as well as similar immunogenicity and HER2 expression between races may have clinical implications. Additional studies are needed to explore these findings.

Citation Source: https://sgo.confex.com/sgo/2020/meetingapp.cgi/Paper/15594

Table 1.

Cancer Type	Gene	% AA	% CC	p value
Serous		49%	31%	0.0023
Endometrioid		15%	42%	<0.001
Combined Epithelial Histologies	PIK3CA	33%	41%	0.1701
	PTEN	11%	38%	<0.001
	PIK3R1	8%	19%	0.0205
	AKT1	0%	4%	0.0540
	PIK3CA/ PTEN/PIK3R1/AKT1	37%	60%	0.0007
	TP53	76%	53%	0.0004
Carcinosarcoma	ER (IHC)	31%	10%	0.0770
	PR (IHC)	24%	5%	0.0700
Endometrioid	NF1	25%	7%	0.0503
	NFE2L2	18%	3%	0.0199
	MRE11	15%	2%	0.0225
	SETD2	13%	0%	0.0023
	FANCE	8%	0%	0.0366
	PRDM1	6%	0%	0.0367
	DNMT3A	6%	0%	0.0491
Serous	BRCA2	0%	8%	0.0230
	Her2 (IHC)	16%	11%	0.4686
Leiomyosarcoma	MED12	46%	15%	0.0892