Racial Differences in the Mutational Landscape of Serous Endometrial Cancer

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Topic: Endometrial

Objectives
Tumor comprehensive genomic profiling (CGP) identifying genomic alterations (GA) that have diagnostic, prognostic and are potentially therapeutically targetable is essential to precision oncology. 2022 NCCN Uterine Neoplasm guidelines recommend tumor genetic evaluation as part of initial evaluation. As racial disparities in endometrial cancer outcomes have been widely reported, we analyzed our CGP results from a large series of serous endometrial cancer patients treated in a nationwide cancer network to identify GA differences that may contribute to worse prognosis and help inform better therapy selection.

Methods
86 Pts with serous endometrial underwent hybrid-capture based CGP for up to 324 cancer-related genes of archival tumor tissue or 62 genes on circulating tumor DNA ordered during clinical care for treatment decision-making between 01-2013 to 06-2021. Clinically relevant genomic alterations (CRGA) were defined as associated with targeted therapies or mechanism-driven clinical trials. Statistical analysis performed with Fisher Exact test comparing Black and White women.

Results
Median age was 63 years (range, 38-85), 37% were White, 58% were Black and 5% were Asian. GA were identified in 94% (81/86) of these patients. TP 53 mutations which is characteristic of serous cancer were present in 80 of 86 patients (93%). GA predicted to activate PI3-Kinase pathway signaling (PIK3CA, PIK3R1, PTEN) were significantly more common in White women occurring in 13 of 32 (41%), compared with 8 of 50 (16%) of Black women (p.< 0.02). An important, but not statistically significant trend of greater percentage of CCNE1 amplification in Black women is also noted, see table below: Mutation frequencies were similar between Black and White women for the following genes: PPP2R1A 23%; MYC 19%; FBXW7 14%; ARID1A 9%.

Conclusions
In this 86patient series of women with Serous Endometrial Cancer we note that PIK3CA mutations, an important resistance factor in anti-HER2 therapy, were significantly more common in White women (41%) compared with Black women (16%) (p.< 0.02) and ERBB2 mutations occurred in 19% of White women and only 10% of Black women. This study cohort also identified a larger percentage of black women with CCNE1 amplification. Increased CCNE1 amplification has been linked to the racial disparities in cancer outcomes and may explain the disparities seen with endometrial cancers.

Abstract Table or Graph
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