Poster 72: The Demographic and Genomic Landscape of Uterine Carcinosarcoma

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Topic
Uterine

Objectives
To investigate demographic trends and actionable genomic mutations among women with uterine carcinosarcoma (UCS).

Methods
Data were obtained from the United States Cancer Statistics (USCS) program, and Joinpoint Regression (version 4.9.0.0) was used to calculate incidence trends using the Average Annual Percent Change (AAPC). Genomic data from the AACR GENIE cohort were analyzed to identify actionable biomarkers based on MSK OncoKB levels of evidence: Levels 1–3 included BRAF V600E, HER2, RET, NTRK1–3, TP53, MMR alterations, and TMB-high; Level 4 included ARID1A, FGFR1–3, KRAS, PTEN, PIK3CA, and MTOR. Immunohistochemistry (IHC) data were not available in the GENIE dataset; therefore, ERBB2 amplification was used as a surrogate for HER2 expression. Statistical analyses were performed using two-sided Fisher's exact tests with Benjamini–Hochberg correction. Adjusted p-values < 0.05 were considered statistically significant.

Results
From 2001–2022, 54,856 patients (median age: 67) were diagnosed with UCS in the U.S. Cancer Registry. Of note, the proportion of White, Black, Hispanic, and Asian patients diagnosed with uterine carcinosarcoma was 62.8%, 24.9%, 8.3%, and 3.2%, respectively, compared with approximately 60%, 12%, 18%, and 6% in the general U.S. population based on US Census. Over the 20-year study period, overall incidence increased by 28% (from 1.03 to 1.31 per 100,000), corresponding to an increase of 1.10% (95% CI: 0.21–1.99, p< 0.01) per year. Over the study period, the cumulative percent increase in incidence was greatest among Hispanic (55%) and Black (45%) patients compared to Asian (8%) and White (12%) patients, with annual increases of 2.04%, 1.58%, 1.29%, and 0.54%, respectively. In the AACR GENIE cohort (n=1,154), 67.3% of tumors were primary and 22.5% were metastatic. The genomic landscape demonstrated ubiquitous TP53 mutations (~80%) across all groups. Among biomarkers with FDA-approved therapies, TMB-high (13.0%), MMR alterations (6.0%), and ERBB2 amplification (3.9%) were infrequent. Furthermore, other targetable alterations including PIK3CA, FBXW7, CCNE1 amplification, PTEN, KRAS, ARID1A, and PPP2R1A were observed in 24.7%, 14.8%, 14.6%, 11.9%, 11.8%, 11.1%, and 9.3% of samples, respectively. Rare alterations included NTRK1–3 fusions (≤0.3%) and BRAF V600 mutations (≤0.2%). When stratified by race, there were no significant differences in ERBB2 amplification, TMB-high status, or MMR alterations. However, compared to White patients, Black patients demonstrated higher CCNE1 amplification (33.6% vs. 13.4%, p< 0.01) and Asian patients exhibited higher KRAS mutation rates (21.3% vs. 12.6% in White patients). When further subdivided by age (< 50, 50–65, ≥65 years), there were no significant differences in biomarker prevalence.

Conclusions
Over the past 20 years, Black patients have experienced a disproportionate burden of uterine carcinosarcoma, while Hispanic patients have demonstrated the greatest increase in incidence. The prevalence of actionable biomarkers in UCS remains low, with most tumors characterized by TP53 mutations and low rates of TMB-high expression, MMR alterations, and ERBB2 amplification. These findings highlight the need for novel therapeutic strategies and inclusive clinical trial designs that address the distinct molecular landscape of uterine carcinosarcoma.

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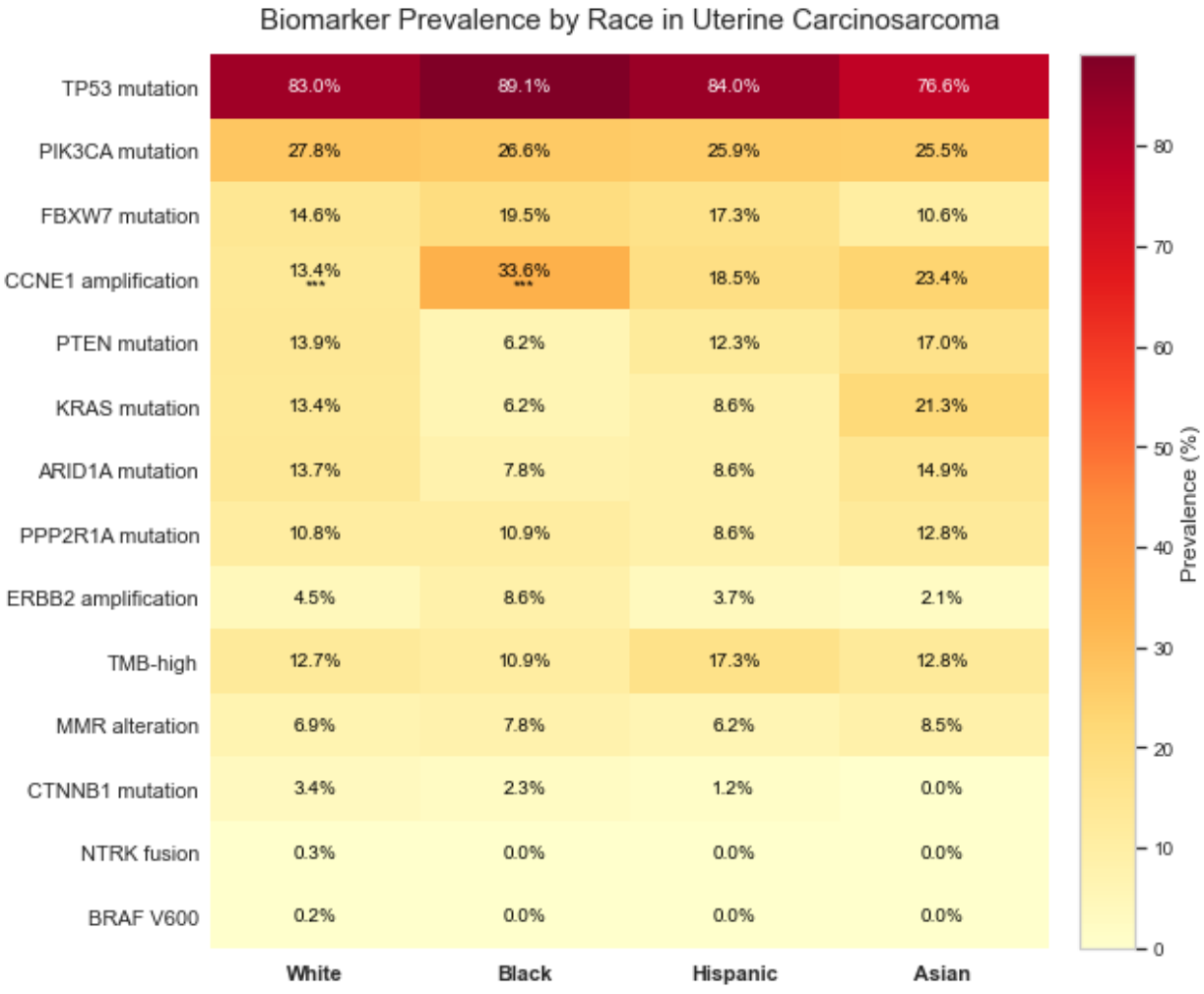
Biomarker Prevalence by Race in Uterine Carcinosarcoma
TP53 mutation
PIK3CA mutation
FBXW7 mutation
CCNE1 amplification
PTEN mutation
KRAS mutation
ARID1A mutation
PPP2R1A mutation
ERBB2 amplification
TMB-high
MMR alteration
CTNNB1 mutation
NTRK fusion
BRAF V600
83.0%
89.1%
84.0%
76.6%
27.8%
26.6%
25.9%
25.5%
14.6%
19.5%
17.3%
10.6%
13.4%
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33.6%
***
18.5%
23.4%
13.9%
6.2%
12.3%
17.0%
13.4%
6.2%
8.6%
21.3%
13.7%
7.8%
8.6%
14.9%
10.8%
10.9%
8.6%
12.8%
4.5%
8.6%
3.7%
2.1%
12.7%
10.9%
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6.9%
7.8%
6.2%
8.5%
3.4%
2.3%
1.2%
0.0%
0.3%
0.0%
0.0%
0.0%
0.2%
0.0%
0.0%
0.0%
White
Black
Hispanic
Asian
Prevalence (%)
0
10
20
30
40
50
60
70
80