Simultaneous HER2 positivity and CCNE1 amplification is associated with Black race and worse survival in endometrial cancer

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No disclosures

I have no financial relationships with ACCME defined ineligible companies to report over the past 24 months.

Unlabeled/ Investigational Uses

I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.
Background

Anti-HER2 therapy use is expanding rapidly in endometrial cancer

CCNE1 amplification has been associated with poor survival

Determine the relationship between HER2 positivity and CCNE1 amplification in endometrial tumors
Methods

• Retrospective multicenter study of patients with advanced or recurrent endometrial cancer diagnosed 2010-2022

• All patients underwent comprehensive tumor molecular profiling with next generation sequencing

| HER2 | 3+ by immunohistochemistry  
2+ with FISH amplification |
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<td>CCNE1</td>
<td>Amplification as defined by NGS</td>
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Patients in the cohort

N=291

- HER2+: 49 (17%)
- CCNE1: 30 (10%)
- HER2 & CCNE: 10 (3%)
Molecular signatures by race

- CCNE1: 8 Non-Black, 22 Black; p<0.001
- HER2: 30 Non-Black, 19 Black; p=0.106
- CCNE1 + HER2: 2 Non-Black, 8 Black; p<0.001
Histology by molecular signatures

- CCNE1:
  - Endometrioid: 4
  - Carcinosarcoma: 11
  - Mixed: 0
  - Serous: 15

- HER2:
  - Endometrioid: 12
  - Carcinosarcoma: 3
  - Undifferentiated/dedifferentiated: 3
  - Mixed: 7

- CCNE1 + HER2:
  - Endometrioid: 2
  - Carcinosarcoma: 0
  - Mixed: 0
  - Serous: 8
OS HER2 and CCNE12

Overall Survival

Log-Rank $p=0.68$

Overall Survival

Log-Rank $p=0.01$

Number at risk
Not HER2 234
HER2+ 44

Number at risk
Not CCNE1 250
CCNE1+ 28

Not HER2
HER2+

Not CCNE1
CCNE1+
OS HER2/CCNE1 dual signatures

Overall Survival

Log-Rank p=0.05

Cumulative survival probability

Time in months

Number at risk
No dual signature 269
Dual signature 9

0 50 100 150 200

68 1 10 0 2 0 1 0

No dual signature
Both HER2+ and CCNE1+
Conclusions

NGS and IHC/FISH showed that Black patients were more likely to have HER2 positivity CCNE1 amplification.

HER2 positivity and CCNE1 amplification was associated with a worse overall survival.

Pairing anti-HER2 therapeutics with cell cycle disrupting agents may be rational for this group of patients.
Thank you!