Racial disparities in ER signaling pathway activity in breast cancer patients undergoing short-course preoperative hormone therapy: a window of opportunity trial

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Introduction

- Epidemiological studies show racial disparities in breast cancer (BC) survival in the US
- Mortality for hormone receptor (HR) positive BC is 19% higher in Black women compared to White women, despite lower incidence in Black women
- Differences partially attributed to tumor biology and treatment response

Objectives

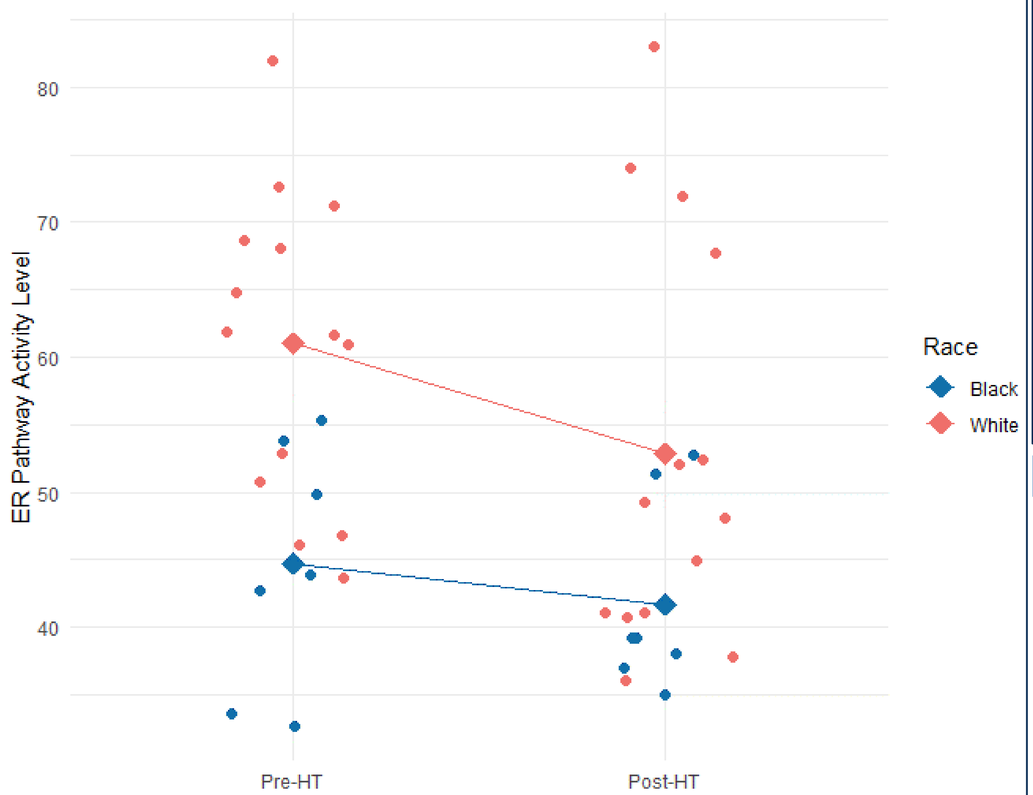
- The purpose of this window-of-opportunity trial was to assess changes in tumor gene expression in response to a short course of hormone therapy (HT)
- Describe any racial differences in response to short course HT

Materials and Methods

- Single institution study of patients with estrogen receptor (ER)+ breast cancer by immunohistochemistry (n=31)
- Received 2-6 weeks SCHT prior to surgery in 2019; tamoxifen (male, or premenopausal), or letrozole/exemestane (postmenopausal)
- OncoSIGNal, mRNA-based quantitative PCR assay, measured activity of androgen receptor (AR), estrogen receptor (ER), PI3K and MAPK signal transduction pathways
- Pre- and post-HT samples measured
- Signaling pathway activity reported on a standardized scale 0-100 (highest activity)
- Comparison of differences in signaling pathway activity between White and Black patients using two-sided t-tests, alpha=0.05
- Unadjusted differences for effect of HT on signaling pathway activity for White and Black patients estimated using regression modeling

Results

Figure 1. Estrogen receptor pathway activity, before and after short-course hormone therapy, in White and Black patients (n=23)



- Pre-post-HT specimens collected for 23 patients with ER+ BC
- 14 (60.9%) patients self-identified as White, 7 (30.4%) Black, 2 (8.7%) Asian
- At baseline, Black patients had lower ER pathway activity compared to White patients (44.7 vs. 61.0, p=0.002)
- Following HT, there was a reduction in ER pathway activity for both Black and White patients
- Black patients observed to have lower ER pathway activity compared to White patients post-HT (41.7 vs. 52.8, p=0.033)
- The magnitude of change in ER pathway activity was smaller for Black patients compared to White patients (p>0.05)
- No significant differences in AR, PI3K, MAPK pathway activity between White and Black patients, at baseline or following HT

Conclusion

- Compared to White patients, Black patients who received a short course of HT for ER+ BC prior to surgery had tumors with lower ER signaling pathway activity at baseline and following HT
- Although all tumors were ER+ by immunohistochemistry, there were measurable differences in ER pathway activity between White and Black patients prior to HT
- There was a trend towards a smaller effect size of HT among Black patients
- Generalizability limited by sample size, retrospective, and single-institution nature of study
- Hypothesis generating
- Further investigations needed to investigate clinical impact on treatment response, and racial differences in breast cancer epidemiology