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Racial differences in estrogen receptor signaling pathway activity in breast cancer patients selected for short-course preoperative hormone therapy : a window-of-opportunity trial

Topic

Genetics

Background/Objective

Epidemiological studies demonstrate racial disparities in breast cancer survival in the United States. Mortality for hormone-receptor positive breast cancer is 19% higher among Black women compared to White women, despite a lower incidence among Black women. These differences have been partially attributed to differences in tumor biology and treatment response. 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.

Methods

In this single-institution study, 31 patients with estrogen receptor positive breast cancer by immunohistochemistry (ER+) who received a short course of hormone therapy (HT) ranging between 2 and 6 weeks prior to surgery in 2019 were enrolled. Male patients and premenopausal women received tamoxifen, and postmenopausal women received letrozole or exemestane. Using a novel, mRNA-based quantitative PCR assay called OncoSIGNal, the activity of four signal transduction pathways (androgen receptor (AR), estrogen receptor (ER), PI3K and MAPK) were measured in pre- and post-HT samples. Signaling athway activity was reported on a standardized scale of 0 to 100, with 100 being the highest activity. Differences in signaling pathway activity were compared between White and Black patients using t-tests with alpha level=0.05. Unadjusted differences in the effect of HT on signaling pathway activity for White and Black patients were assessed using a generalized estimating equation regression model.

Results

Pre- and post-HT specimens were collected for 23 patients with ER+ breast cancer, of whom 14 (60.9%) self-identified as White, 7 (30.4%) Black, and 2 (8.7%) Asian. Black patients had lower ER pathway activity at baseline 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, and Black patients again were observed to have lower ER pathway activity compared to White patients post-HT (41.7 vs. 52.8, p=0.033) (Fig 1). The magnitude of change in ER pathway activity was smaller for Black patients compared to White patients, but this did not reach statistical significance. There were no significant differences AR, PI3K, or MAPK pathway activity between White and Black patients, at baseline or following HT.

Conclusions

Compared to White patients, Black patients who received a short course of hormone therapy (HT) for ER+ breast cancer 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. There was a trend toward a smaller effect size of HT among Black patients. The novel findings of this small observational study are hypothesis

generating and further investigations are needed investigate their clinical impact on treatment response and racial differences in breast cancer epidemiology.

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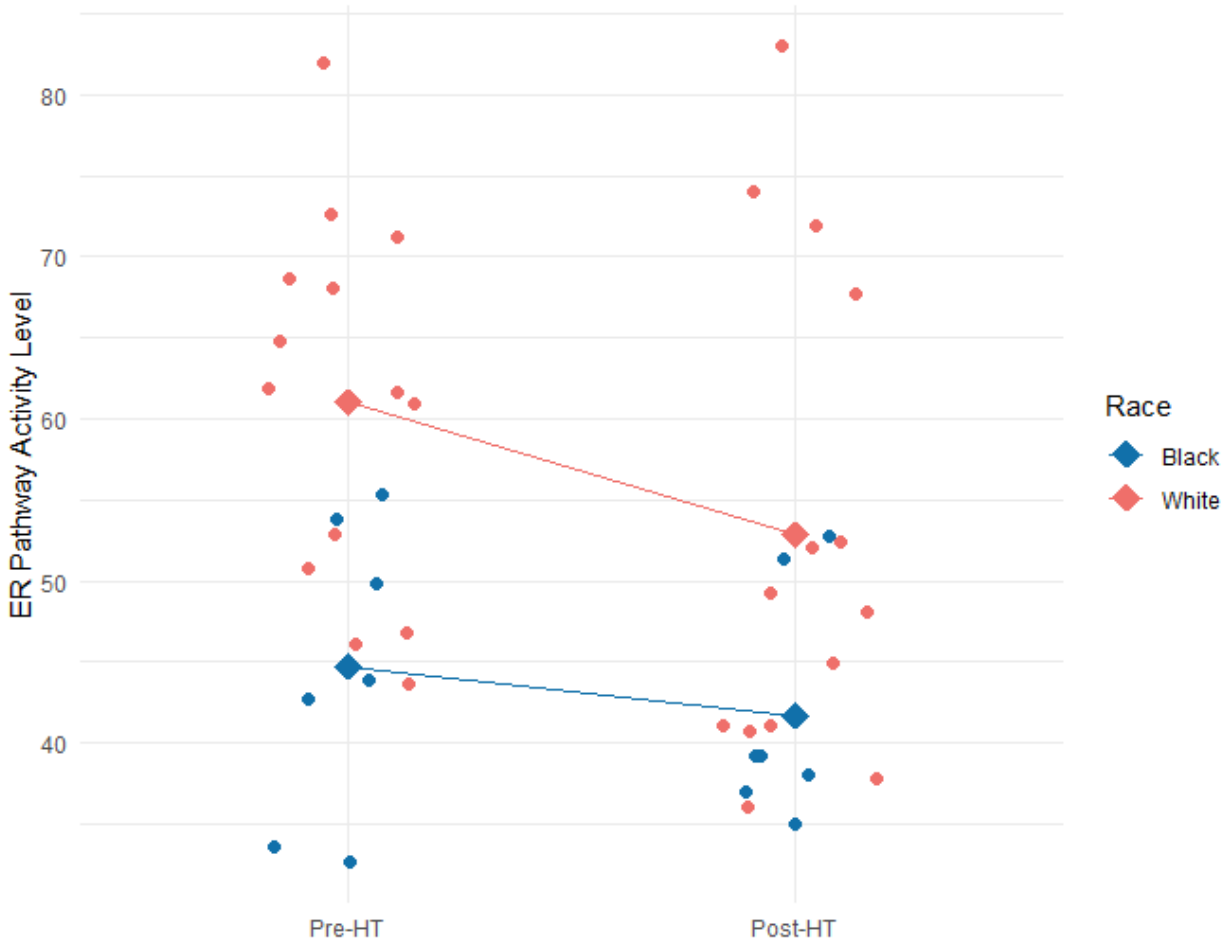

Estrogen receptor pathway activity, by race, before and after short-course hormone therapy
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