Researchers complete first trial of Black patients with early-stage breast cancer

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Black patients with early-stage breast cancer who were treated with

docetaxel chemotherapy every 3 weeks had less drug-induced peripheral neuropathy and significantly fewer dose reductions compared to those who received weekly paclitaxel, according to a trial by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN). Study EAZ171 is the first National Cancer Institute (NCI)-sponsored trial to focus specifically on enrolling a minority or underserved population to assess drug-induced toxicity (rather than drug efficacy) where there are known disparate outcomes.

Results were presented today at the 2024 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago and published in the *Journal of Clinical Oncology*.

"To date, clinical trials in the US have suffered from a disproportionate lack of Black patients. Lack of representation is problematic, given significant disparities in cancer outcomes by race. Here, we sought to not just describe disparities but to begin to understand and address them to improve equity in breast cancer care," said presenter Tarah J. Ballinger, MD, medical director of breast cancer prevention at Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Vera Bradley Foundation Scholar in Breast Cancer Research, and Associate Professor at Indiana University School of Medicine.

Despite Black patients having a 4% lower incidence of breast cancer than white patients across the United States, they have a 40% higher death rate from breast cancer. The difference in the death rate is not explained by Black patients having more aggressive cancers.

Previous research has found that Black people or those of genetically determined African ancestry with breast cancer experience significantly more peripheral neuropathy compared to people of other ancestries.

Peripheral neuropathy is painful nerve damage that usually starts in the hands and feet and gets worse over time.

Specific genetic differences could be a factor. Higher rates of neuropathy are associated with dose reductions of chemotherapy and lower cure rates.

Study EAZ171 was designed to validate genetic predictors of taxane-induced peripheral neuropathy (TIPN) and to determine the optimal taxane-based chemotherapy to lessen TIPN for Black patients with early-stage breast cancer. The trial enrolled 249 participants, all of whom received a guideline-recommended taxane-based chemotherapy treatment as recommended by their physician: docetaxel every 3 weeks (n=123) or weekly paclitaxel (n=126).

Researchers observed elevated rates of moderate or severe TIPN with paclitaxel versus docetaxel as recorded by physicians (44% vs. 25%) and reported by patients (40% vs. 24%). Participants on paclitaxel experienced significantly more TIPN-related dose reductions than those on docetaxel (28.1% vs. 8.5%). All-cause dose reduction rates were 38.8% for paclitaxel vs. 24.6% for docetaxel.

"This study confirmed that Black patients with breast cancer have a very high risk of drug-induced peripheral neuropathy," said Dr. Ballinger. "Further, we found that one taxane—docetaxel—was associated with significantly less neuropathy and dose reduction of chemotherapy than paclitaxel, suggesting this drug may be a better choice for many Black patients."

Although Black patients or those of genetically determined African ancestry are at higher risk for TIPN as a group, there is variation across individuals. Therefore, the trial's primary endpoint was to evaluate inherited germline predictors of TIPN found in DNA. The trial did not

meet its primary endpoint.

Nearly three-fourths of the women in each treatment arm were classified as high risk for TIPN based on genetic alterations. Yet there were no differences in the occurrence of neuropathy in high- versus low-risk women, regardless of which taxane they received.

"We studied two specific genes—SBF2 and FCAMR. It is likely that these genes do matter, but that TIPN is multigenic and multifactorial, so these genes alone are not enough to predict risk of TIPIN. We have more work to do to understand and predict TIPN in this population," said Dr. Ballinger.

For the next steps, ECOG-ACRIN researchers are planning another trial to determine how to further optimize taxane therapy for Black patients with breast cancer. They will also build on the current study's unique and successful approach to enrollment for future oncology trials.

"While the trial focused specifically on Black people, the results highlight the need to personalize therapy to minimize toxicity," said Dr. Ballinger. "Importantly, this study offers a blueprint for how to design and recruit for a study focusing on a minority or underserved patient population."

The study was designed and implemented in collaboration with Black cancer patient advocacy groups. For instance, Pink-4-Ever Ending Disparities, an Indiana non-profit launched to help close inequities in breast cancer care for Black women, assisted with trial recruitment via social media, such as YouTube.

Further, many enrolled patients came from sites in the NCI Community Oncology Research Program (NCORP) rather than solely from academic settings. Not only did investigators overcome challenges in recruiting a

heavily under-represented population, but they did so during the COVID-19 pandemic and in a relatively short time.

"Tailoring research to the needs of underserved populations is effective. This trial succeeded because of the partnership with Black patients," said Dr. Ballinger.

More information: Bryan P. Schneider et al, ECOG-ACRIN EAZ171: Prospective Validation Trial of Germline Predictors of Taxane-Induced Peripheral Neuropathy in Black Women With Early-Stage Breast Cancer, *Journal of Clinical Oncology* (2024). DOI: 10.1200/JCO.24.00526

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