Menopausal Hormone Therapy May Not Pose Breast Cancer Risk for Women With BRCA Mutations

Menopausal hormone therapy can safely relieve symptoms in women who have their ovaries removed to reduce their high risk for cancer.

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SAN ANTONIO – Using menopausal hormone therapy (MHT) was not associated with an increased risk of breast cancer in women with inherited mutations in the BRCA1 or BRCA2 genes, according to the results of a matched prospective analysis presented at the San Antonio Breast Cancer Symposium (SABCS), held December 9-12, 2025.

Women who inherit a pathogenic mutation in the BRCA1 and BRCA2 genes are advised to follow the recommended guidance to have their ovaries and fallopian tubes removed (a procedure known as bilateral salpingo-oophorectomy) at relatively early ages to safeguard against their elevated risk of ovarian and/or fallopian tube cancer, said study presenter Joanne Kotsopoulos, PhD, a scientist at the Women's College Hospital Research and Innovation Institute and a professor at the Dalla Lana School of Public Health at the University of Toronto in Canada.

Removing the ovaries can induce early menopause. Although MHT can treat the symptoms of menopause, many patients might not want to take MHT if they perceive MHT to be unsafe and instead suffer unnecessarily with the symptoms, Kotsopoulos explained.

"We cannot simply recommend a drastic surgery like oophorectomy for young women without offering a way for them to manage the well-established short- and long-term outcomes of surgical menopause," she said. "I believe we should educate patients and their health care providers on how we can safely balance the risks and benefits of MHT use to ensure longevity and improve quality of life."

"Unfortunately, there has been a lot of reluctance and misinformation regarding MHT, which is mostly attributable to findings from studies conducted in the general population (those without BRCA mutations) showing an association between MHT use and an increased risk of breast cancer," Kotsopoulos added. "To help manage the side effects of oophorectomy safely in women with BRCA mutations, we need data from well-designed observational studies of MHT use in this specific population who, due to their genetics, face elevated risks of breast cancer."

Kotsopoulos and colleagues conducted a matched prospective analysis—a type of observational study—in which they tried to recreate the conditions of a clinical trial by analyzing data from women with menopause (mostly induced by surgery) and whether they used MHT. Patients with a history of cancer, patients who had received a bilateral mastectomy, and non-menopausal patients were excluded.

The researchers created 676 matched pairs of women who did and did not use MHT after menopause, with pair-matching based on whether they carried BRCA1 or BRCA2 mutations, birth year, and age at menopause. Participants ranged in age from 22 to 76, with an average age of 43.8.

Participants who used MHT took one of several different formulations: estrogen alone, progesterone alone, estrogen and progesterone, tibolone, or conjugated estrogen and bazedoxifene.

After a mean follow-up of 5.6 years—which used the date of first MHT use in the MHT-exposed group as the starting point—the researchers found that incident breast cancer cases were significantly less in the women who used MHT, with 87 cases in the MHT-exposed group versus 128 cases in the MHT-naive group.

When the investigators analyzed the data by which MHT formulation was used, most of the different MHTs were not associated with the risk of breast cancer (neither an increase nor a decrease in risk). However, two formulations were associated with decreased risk of breast cancer. Women who received estrogen-only MHT were 63% less likely to develop breast cancer than their MHT-naïve counterparts. And of the 43 women who received conjugated estrogen and bazedoxifene, none of them developed subsequent breast cancer.

“Although based on smaller numbers, this is definitely an exciting and interesting area for future research,” Kotsopoulos said. “Hypothetically, conjugated estrogen and bazedoxifene could be used to mitigate breast cancer risk by avoiding progesterone, which is thought to be the breast cancer risk-associated component of MHT. Future trials will be necessary to test this hypothesis.”

There were no significant differences in the results whether patients carried a pathogenic BRCA1 or BRCA2 variant, an indication that underscores MHT’s safety for carriers of BRCA mutations, according to Kotsopoulos.

“Our findings suggest that clinicians should take a personalized approach to menopause management for women with BRCA mutations who are suffering from the impact of surgical (or natural) menopause, if there are no contraindications for them,” said Kotsopoulos.

Limitations of the study were noted and included a follow-up time of 5.6 years and small patient numbers in certain subgroups, such as the number of women enrolled carrying a BRCA2 mutation.

The study was funded by Breast Cancer Canada and the Canadian Institutes of Health Research. Kotsopoulos declares no conflicts of interest.

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