Lynparza Follow-Up Treatment Delays Breast Cancer Recurrence

PARP inhibitor reduces the risk of disease recurrence in BRCA-positive people with high-risk early breast cancer.

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Adjuvant treatment with Lynparza (olaparib) after surgery, radiation and chemotherapy led to longer disease-free survival in people with HER2-negative early breast cancer and harmful BRCA mutations, according to a study presented at the American Society of Clinical Oncology (ASCO) virtual annual meeting and published in The New England Journal of Medicine.

The Phase III OlympiA trial found that Lynparza used as adjuvant therapy after standard treatment led to a 42% reduction in the risk of invasive cancer recurrence or death over three years, Andrew Tutt, MBChB, PhD, of the Institute of Cancer Research and Guy's Hospital of King's College London, reported.

"The OlympiA study results, the first reporting the effects of a PARP inhibitor as an 'adjuvant therapy' on survival endpoints, suggest a possible addition to the standard of care for patients with germline BRCA1/2 mutation-associated early breast cancer who have levels of recurrence risk requiring neoadjuvant or adjuvant chemotherapy," Tutt said in an ASCO press release.

Women with inherited BRCA1 or BRCA2 gene mutations are at higher risk for breast and ovarian cancer. Although only about 5% of people with breast cancer have harmful BRCA mutations, around half of women who carry these mutations will develop breast cancer, according to the National Cancer Institute.

Lynparza is a PARP inhibitor approved for the treatment of breast, ovarian, prostate and pancreatic cancer. The drug works by blocking poly (ADP-ribose) polymerase proteins, which play a role in DNA damage repair. People with harmful BRCA mutations do not make proteins that repair DNA. Interfering with PARP leads to more more unfixable DNA breaks that halt cancer cell division, and BRCA-related cancers are especially vulnerable to this strategy.

As previously reported, the OlympiAD study (NCT02000622) suggested that Lynparza might lead to an improvement in overall survival for people with HER2-negative metastatic breast cancer, especially those who have not yet received chemotherapy. Lynparza is currently approved for this indication.

The OlympiA study (NCT02032823) instead looked at Lynparza as adjuvant therapy—maintenance therapy intended to prevent recurrence—for people with early-stage breast cancer who had undergone surgery, with or without radiation, and neoadjuvant (pre-surgery) or adjuvant (post-surgery) chemotherapy.

This analysis included 1,836 people (including six men) in 23 countries with known or suspected harmful BRCA1 or BRCA2 mutations who were diagnosed with HER2-negative early breast cancer. They could have either hormone receptor-positive or triple-negative breast cancer. They were considered at high risk for recurrence based on predictive scores and the number of lymph nodes with evidence of residual cancer.

The study participants were randomly assigned to receive Lynparza or placebo pills twice daily for a year.

In an interim analysis at three years (median follow-up 2.5 years), 85.9% of patients in the Lynparza group and 77.1% in the placebo group were still alive without recurrence or new second cancers (known as invasive disease-free survival), a 42% improvement. Similarly, 87.5% and 80.4%, respectively, were still alive without developing metastatic disease (known as distant disease-free survival), a 43% improvement.

What's more, there were fewer deaths in the Lynparza group compared with the placebo group (59 and 86, respectively). The estimated three-year overall survival rates were 92.0% and 88.3%, respectively, but the difference did not reach statistical significance in this interim analysis; follow-up is ongoing.

Treatment was generally safe and well tolerated and had "limited effects on global patient-reported quality of life," the study authors noted. Adverse events in this study were consistent with the known side effects of Lynparza. The most common adverse events were nausea (57%), fatigue (40%), anemia (23%) and vomiting (23%). Approximately 10% of patients discontinued Lynparza due to adverse events.

"Patients with early-stage breast cancer who have inherited BRCA mutations are typically diagnosed at a younger age compared to those without such a mutation," Tutt said in an AstraZeneca and Merck press release. "Olaparib has the potential to be used as a follow-on to all the standard initial breast cancer treatments to reduce the rate of life-threatening recurrence and cancer spread for many patients identified through genetic testing to have mutations in these genes."

Commenting on the study findings, ASCO President Lori J. Pierce, MD, said, "OlympiA's findings highlight the need for genetic testing for BRCA mutations in patients diagnosed with high-risk early-stage breast cancer. These results could have an important impact on treatment decisions for this patient population, possibly including the use of a PARP inhibitor in the adjuvant setting."

Click here to read the ASCO study abstract.

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