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PARP Inhibition Shows Long-term Survival Benefits for Patients With High-risk, BRCA-positive Breast Cancer in OlympiA Trial

SAN ANTONIO – Patients with high-risk, BRCA-positive breast cancer who received olaparib (Lynparza) after standard treatment continued to have better survival outcomes than those who received placebo after a median follow-up of 6.1 years, according to the latest results from the phase III OlympiA clinical trial presented at the San Antonio Breast Cancer Symposium (SABCS), held December 10-13, 2024.

“The OlympiA trial examines adding one year of the oral PARP inhibitor olaparib after completion of standard treatment for higher risk breast cancer in individuals with pathogenic germline BRCA variants,” said Judy E. Garber, MD, MPH, chief of the Division of Cancer Genetics and Prevention at Dana-Farber Cancer Institute and the presenter of the study.

OlympiA is a multicenter, double-blind study in which 1,836 patients with BRCA-positive, HER2-negative breast cancer were randomly assigned (1:1) to receive either olaparib or placebo for one year following completion of chemotherapy, surgery, and radiation. Based on previous results from the trial, olaparib was approved in 2022 in the adjuvant setting for certain patients with HER2-negative, BRCA-positive breast cancer.

“Data from the third prespecified interim analysis presented here provides further support for olaparib’s benefits in patients with high-risk, HER2-negative breast cancer with germline mutations in BRCA1 or BRCA2,” said Garber.

After a median follow-up of 6.1 years, patients treated with olaparib continued to show significant improvements in survival outcomes, in both triple-negative breast cancer as well as estrogen receptor (ER)-positive breast cancer subgroups. Both of the study’s primary endpoints—invasive disease-free survival and distant disease-free survival—were achieved, with olaparib reducing the risk of each by 35%. At six years, 79.6% of olaparib-treated patients remained free of invasive recurrence and 83.5% remained free of distant recurrence, compared to 70.3% and 75.7%, respectively, in the placebo group.

Additionally, adjuvant PARP inhibition was associated with a 28% reduction in risk of death, and no increase in the risk of developing myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML), both of which can result from rare complications associated with breast cancer treatment.

“The ongoing data from the OlympiA trial are reassuring in the observations of persistent and increasing benefits for these breast cancer patients in the follow-up phases, improving not only protection against recurrence but also overall survival as well,” Garber said. “This demonstration of efficacy makes it more important than ever that we be able to identify individuals who might benefit when they begin their treatment so that we can plan to introduce olaparib to their care at the most opportune moments.”

There were fewer secondary BRCA-associated cancers reported in the olaparib group—38 versus 57 in the placebo group—but Garber noted that further data and analyses are needed to draw firm conclusions. There were equal numbers of pregnancies in both groups, which is encouraging and highlights the younger age of this cohort, she added.

“These data highlight the safety of olaparib and, therefore, the possibility of moving PARP inhibitors to the treatment of BRCA-associated breast cancers that are lower risk,” noted Garber. “It also allows us to consider the very preliminary possibility of a safe and effective oral agent that could be developed for cancer interception—to be given intermittently to eliminate cells in BRCA mutation carriers that have begun to transform toward several types of malignancy.”

One limitation of the study was that not all subsets were equally large, but efficacy continues to be demonstrated in all subsets, which is very reassuring, Garber noted.

This study was supported by AstraZeneca and Merck and Co., Inc. Garber declares no conflict of interest.

Abstract

GS1-09: OlympiA- Phase 3, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients w/ germline BRCA1/BRCA2 pathogenic variants & high risk HER2-negative primary breast cancer; longer term follow

Background: The OlympiA trial (NCT02032823) compared 1 year of adjuvant oral poly(adenosine diphosphateribose) polymerase inhibitor olaparib (OL) to matching placebo (PL) in a randomized trial of 1836 patients (pts) with pathogenic or likely pathogenic variants in germline BRCA1 or BRCA2 (gBRCApv) and high-risk human epidermal growth factor receptor 2 (HER2)-negative primary breast cancer (BC) who had completed all (neo)adjuvant chemotherapy, surgery and radiation. The first pre-specified interim analysis (IA) demonstrated statistically significant improvements in invasive disease-free survival (IDFS) and distant disease-free survival (DDFS). The second IA demonstrated statistically significant improvement in OS and maintained improvement in IDFS and DDFS, irrespective of hormone receptor status, prior platinum administration, timing of prior chemotherapy or type of gBRCApv. No excess acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) was observed. This updated analysis reports the results of the third pre-specified IA with median follow-up (MFU) of 6.1 years (maximum, 9.6 years).

Methods: Descriptive analyses are presented with longer-term follow-up comparing the primary endpoint IDFS, and key secondary endpoints DDFS and OS, across two arms: oral OL 300mg BID versus PL. Estimates of the hazard ratio (HR) based on the stratified Cox’s Proportional Hazards Model and 95% confidence intervals (CI) are presented for each endpoint with event rates reported at the 6 year (yr) MFU. Safety analyses including adverse events of special interest (AESIs) and all deaths are highlighted.

Results: With longer follow-up, the benefit of OL in terms of IDFS, DDFS and OS was maintained with effect sizes similar to those reported in previous analyses. For IDFS, HR=0.65 (95% CI: 0.53, 0.78); 6-yr IDFS percents (OL vs PL): 79.6% vs 70.3% (diff. 9.4%; 95% CI, 5.1%, 12.7%). For DDFS, HR=0.65 (95% CI: 0.53, 0.81); 6-yr DDFS percents (OL vs PL): 83.5% vs 75.7% (diff. 7.8%; 95% CI, 3.8%, 11.5%). For OS, HR 0.72 (95% CI: 0.56, 0.93); 6-yr OS percents (OL vs PL): 87.5% vs 83.2% (diff. 4.4%; 95% CI, 0.9%, 6.7%). Total deaths/pts were 107/921 vs 143/915 in OL and PL, respectively. OL benefit was consistent across all key subgroups, including for pts with high-risk, hormone-receptor-positive disease. Fewer BRCA-associated cancers were reported with OL vs PL: contralateral invasive BC (31 vs 40); contralateral non-invasive BC (3 vs 4), new primary ovarian cancer (3 vs 9), new primary fallopian tube cancer (1 vs 4). The percent of pts experiencing AESIs was lower with OL vs PL (6.3% vs 9.3%), comprising MDS or AML (OL, n=4; PL, n=6), pneumonitis (OL, n=9; PL, n=13), and fewer new primary cancers overall (OL, n=45; PL, n=68).

Conclusions: At 6.1 years MFU, one year of adjuvant OL after (neo)adjuvant chemotherapy continues to demonstrate meaningful improvements in IDFS, DDFS and OS in pts with gBRCApv and high-risk, HER2-negative primary BC, including all key subgroups, and with acceptable toxicity and no evidence of increased risk of MDS or AML. These data continue to highlight the importance of gBRCApv testing in high-risk, HER2-negative primary BC.

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