CLINICAL SUMMARY

Olaparib for Patients with Metastatic Breast Cancer with a Germline BRCA Mutation

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About 12% of women will be diagnosed with breast cancer in their lifetime and of these patients approximately 5% will carry a germline BRCA mutation. Because of the known synthetic lethality of PARP inhibitors in BRCA-mutated ovarian cancer cohorts, this trial investigated their effects in a BRCA-mutated breast cancer cohort. Nearly one-third of patients with breast cancer overall are diagnosed with or will progress to metastatic disease. While treatment options have continued to advance there remains no cure for patients diagnosed with metastatic breast cancer. The primary aim of treatment in this population is to slow progression of the disease for as long as possible, improving or at least maintaining a patient's quality of life. OlympiAD achieved both of those aims with improved progression-free survival (PFS) and quality of life (QOL) vs. standard of care chemotherapy.

Robson et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. The New England Journal of Medicine 2017; Jun 4 doi: 10.1056/NEJMoa1706450. [Epub ahead of print].

PURPOSE:

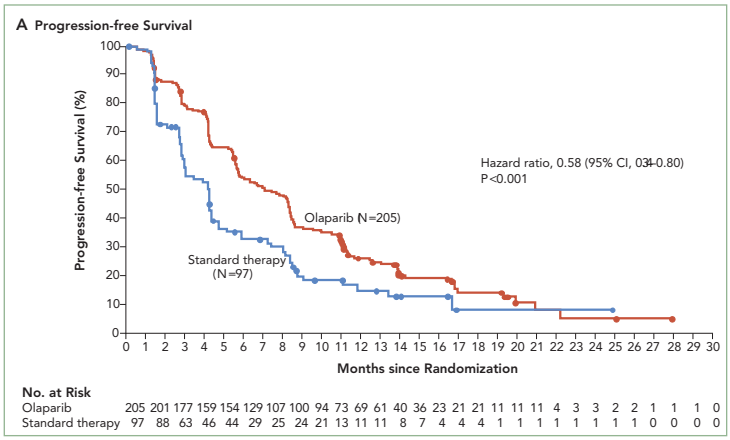
The OlympiAD trial was designed to compare the efficacy and safety of olaparib with that of standard therapy among patients with HER2-negative metastatic breast cancer and a germline BRCA mutation.

DESIGN AND METHODS:

OlympiAD was a randomized, controlled, open-label, multicenter, international, phase III trial. To be eligible for the study, patients had to have a diagnosis of HER2-negative metastatic breast cancer and a germline BRCA mutation. Patients had to have received no more than two previous chemotherapy regimens for metastatic disease. Patients also had to have received an anthracycline (unless contraindicated) and a taxane as either neoadjuvant, adjuvant, or metastatic disease treatment. The trial included patients diagnosed with triple negative and hormone receptor positive disease. Patients were randomized in a 2:1 ratio to receive olaparib tablets (300mg bid) or standard therapy with single-agent chemotherapy of the physician's choice (capecitabine, vinorelbine or eribulin) in 21-day cycles. The primary end point was progression-free survival, which was assessed by blinded independent central review and was analyzed on an intention-to-treat basis.

RESULTS:

- 302 patients were randomized.
- 205 were assigned to receive olaparib and 97 were assigned to receive standard therapy (physician choice chemotherapy).
- Median PFS was significantly longer in the olaparib group than in standard therapy group (7.0 months vs. 4.2 months, HR for disease progression or death, 0.58; 95% CI, 0.43 to 0.80; P<0.001)
- Rate of ≥ grade 3 adverse events was 36.6% in the olaparib group and 50.5% in the standard therapy group
- The QLQ-C30 (quality of life measure) between the groups was an estimated difference of 7.5 points (95% CI, 2.5 to 12.4; P=0.004) with the olaparib group experiencing less side effects and improved QOL (patient report) overall



BOTTOM LINE:

Among patients with HER2-negative metastatic breast cancer and a germline BRCA mutation, olaparib monotherapy provided a significant benefit over standard therapy by reducing the risk of disease progression or death by 42%. This practice changing evidence highlights the urgent need for the identification and testing of all appropriate patients for hereditary breast cancer to identify the BRCA mutation carriers in order to inform therapeutic decisions. Pending FDA review and approval of olaparib for this indication, these results represent an exciting new therapeutic option with lower side effects than the current standard of care.

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