



# FRONTLINE ADJUVANT PARPi THERAPY FOR GERMLINE BRCA-MUTATED HER2-NEGATIVE NON-METASTATIC BREAST CANCER

Tutt, et al. Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. *N Engl J Med.* 2021 Jun 3. doi: 10.1056/NEJMoa2105215. Epub ahead of print. PMID: 34081848.

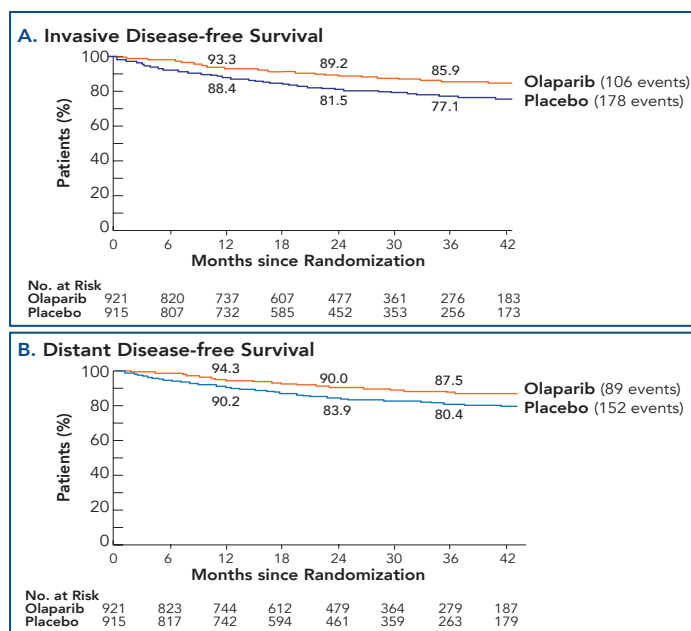
Poly-ADP ribose polymerase inhibitors (PARPi) target cancers exhibiting homologous recombination deficiency (HRD). HRD can be caused by a variety of factors, one of which is a deleterious germline mutation in the *BRCA1* or *BRCA2* genes, which occur in ~5% of patients with breast cancer. PARPi therapy initially proved useful as a late-line therapy for recurrent disease, but utility earlier in the treatment regimen continues to be explored as we seek new therapies to reduce the risk of recurrence in these patients. The OlympiA trial evaluated the efficacy of olaparib for the adjuvant treatment of patients with HER2-negative, non-metastatic breast cancer at high risk of recurrence, and a germline *BRCA1/2* pathogenic (P) or likely pathogenic (LP) variant who had undergone resection and radiation treatment and received neoadjuvant or adjuvant chemotherapy.

## DESIGN AND METHODS

OlympiA was a randomized, double-blind, placebo-controlled, phase 3 trial. Patients were required to complete all local therapies (at least 6 cycles of neo-adjuvant or adjuvant chemotherapy including anthracyclines, taxanes, or both; platinum therapy was allowed), including radiotherapy, at least 2-12 weeks prior to enrollment. Patients could not have pathologically complete response to neoadjuvant chemotherapy. 1836 eligible patients were randomized 1:1 to receive olaparib (300mg twice daily) or matching placebo for 52 weeks. The primary endpoint of the study was disease free survival (DFS).

## RESULTS

- The percentage of patients alive and free of invasive disease at 3 years was 85.9% in the olaparib group and 77.1% in the placebo group. Invasive DFS was 42% longer with olaparib vs. placebo (HR: 0.58; 99.5% CI: 0.41-0.82;  $p < 0.001$ ).
- Distant DFS was 43% longer with olaparib vs. placebo (HR: 0.57; 99.5% CI: 0.39-0.83,  $p < 0.001$ ).
- Fewer deaths were reported in the olaparib group than the placebo group, however the difference did not reach significance at 3 years of follow up.
- The rate of grade 3 or higher serious adverse events (SAE) was not significantly different between the olaparib group (8.7%) and the placebo group (8.4%).



## BOTTOM LINE

Patients with germline *BRCA1/2* LP/P mutations and HER2-negative non-metastatic breast cancer at high-risk of recurrence may benefit from adjuvant therapy with olaparib. The OlympiA trial shows a significant benefit to both invasive and distant DFS with no significant reduction to QOL, and provides further evidence that germline *BRCA1/2* testing is imperative for the selection of systemic therapy for all women with HER2-negative, non-metastatic, high-risk breast cancer.