New findings offer improved therapy of early-stage, BRCA mutation-associated breast cancer

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Charles E. Geyer, Jr., M.D., has provided scientific leadership on the OlympiA trial since 2013. He is an expert in BRCA-associated breast cancer and was a co-chair on the trial. Dr. Geyer is a breast medical oncologist and deputy director of the Houston Methodist Cancer Center and a professor of medicine in oncology with the Houston Methodist Research Institute. Credit: Houston Methodist

Results were released this week on a new treatment with the potential to improve the outcomes for patients with hereditary BRCA mutations and high-risk, early-stage breast cancer. These results represent the first time a drug that blocks cancer cells from repairing their DNA (called a PARP inhibitor) has been shown to significantly reduce the risk of breast cancer returning in high-risk patients following completion of standard chemotherapy, surgery and radiation therapy.

Titled "Adjuvant Olaparib for Patients with BRCA1 or BRCA2 Mutated Breast Cancer," the paper appears in the June 3 issue of the *New England Journal of Medicine* and will be presented June 6 as the first abstract during the plenary session at the 2021 American Association of Clinical Oncology (ASCO) Annual Meeting. Lead author and the OlympiA trial steering committee chair Andrew Tutt, M.D., Ph.D., of The Institute of Cancer Research and King's College London was principal investigator on the portion of study conducted in patients outside the U.S. and will present the results at ASCO.

Led by top experts in BRCA-associated breast cancer from around the world, the OlympiA trial's co-chairs were Charles E. Geyer, Jr., M.D., a breast medical oncologist and deputy director of the Houston Methodist Cancer Center, Judy E. Garber, M.D., M.P.H., of the Dana-Farber Cancer Institute, and Bella Kaufman, M.D., of the Sheba Medical Center in Israel. Geyer was the principal investigator on the NCI-sponsored portion of the study conducted in the U.S.

"OlympiA represents a successful global collaboration among leading international academic breast cancer research groups, cancer genetics experts, the National Cancer Institute and pharmaceutical industry partners to evaluate the efficacy and safety of olaparib to address the unmet need for improved therapy for individuals with high-risk, BRCA mutation-associated early breast cancer," said Geyer, who also is a professor of medicine in oncology with the Houston Methodist Research Institute and has provided scientific leadership on the trial since 2013.

The OlympiA trial was a tremendous effort recruiting 1,836 patients from 420 centers across 23 countries. A randomized double-blind phase 3 trial, OlympiA was designed to test the efficacy of the Poly(ADP-ribose)-polymerase (PARP) inhibitor drug olaparib and showed that it significantly improved invasive and distant disease-free survival when given for 52 weeks following the completion

of such standard therapies as chemotherapy, surgery and radiation.

Patients were recruited from June 2014 through May 2019, and patients who consented to participate were randomly assigned to receive olaparib or a placebo. After three years following initiation of treatment with olaparib, 85.9% of patients were alive and free of recurrent, invasive breast cancer and new second cancers, compared with 77.1% of patients who received a placebo. During this same timeframe, 87.5% of patients receiving olaparib were alive and free of distant metastatic disease, compared to 80.4% on the placebo.

While olaparib was also associated with 27 fewer deaths than those on placebo, researchers say longer blinded follow up is required to assess the impact of this therapy on overall survival. What is certain, say researchers, is that germline BRCA1 and BRCA2 sequencing is becoming an important biomarker for the selection of systemic therapy in early breast cancer.

More information: Andrew N.J. Tutt et al, Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2105215

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