



Press Release [embargoed until May 29m 2020, 9 p.m. GMT (4 p.m. EDT, 5 p.m. Central, 10 p.m. CET)]

Update on PALLAS, an International Academic Breast Cancer Study Evaluating Adjuvant Palbociclib

Second Interim Analysis of Adjuvant Study for HR+, HER2- Early Breast Cancer demonstrates that there is little chance of palbociclib reducing the risk of recurrence

Vienna, Brussels, Chicago, Philadelphia, Neu-Isenburg/Frankfurt, Pittsburgh, 29 May 2020

The Austrian Breast & Colorectal Cancer Study Group (ABCSG), Alliance Foundation Trials (AFT), the Breast International Group (BIG), PrECOG, LLC, the German Breast Group, and the NSABP Foundation today announced that the independent Data Monitoring Committee (IDMC) for the global Phase 3 early breast cancer PALbociclib CoLLaborative Adjuvant Study (PALLAS) trial determined that the study is unlikely to show a statistically significant improvement in the primary endpoint of invasive disease-free survival (iDFS) following a preplanned interim analysis. No new safety signals were observed in patients receiving palbociclib, which has been proven effective in advanced breast cancer. PALLAS patients in the active phase of the trial will be counselled/instructed by their physicians. All patients will move to protocol-defined extended follow-up. Long-term follow up of patient outcomes will proceed as planned.

PALLAS study design and outcomes

The PALLAS trial is a randomized (1:1), prospective, international, multi-center, open-label Phase 3 study comparing the combination of at least five years of standard adjuvant endocrine therapy along with two years of palbociclib (IBRANCE®, manufactured by Pfizer) treatment to at least five years of standard adjuvant endocrine therapy ([NCT02513394](#)). The study population is pre- and postmenopausal women or men with HR+, HER2- early invasive (Stage 2 and Stage 3) breast cancer, including those at moderate to high risk of recurrence. The study medication is an oral inhibitor of CDK 4 and 6, which are key regulators of the cell cycle. It is currently approved globally for the treatment of patients with metastatic HR+/HER2- breast cancer. The primary study aim was to investigate whether the addition of palbociclib to endocrine therapy significantly improved invasive disease-free survival (iDFS; i.e. reduced the chance of the cancer coming back, or of dying or getting another cancer) compared to standard of care endocrine therapy alone. At the second interim analysis, as reported to the IDMC, the futility boundary was crossed indicating a low probability for meeting the primary endpoint, which led to the Steering Committee's decision.

“There remains a great need to improve outcomes for patients with HR+ breast cancer. Our collaborative academic group will continue to closely follow our PALLAS patients and hope to learn from the PALLAS dataset and correlative science how best to improve outcomes in this population,” said Erica Mayer, M.D., M.P.H., Senior Physician, Breast Oncology Center, Dana-Farber Cancer Institute, Harvard Medical School, and global PALLAS trial Chair. “Despite this futility result, the PALLAS trial represents a remarkable collaboration between academic and industry partners, and we hope can serve as a model of cooperative trial conduct.”

Global trial Co-Chair Professor Michael Gnant, MD, FACS, of Medical University of Vienna, Austria, president of ABCSG, pointed out the importance of global academic collaboration: “This has been and will continue to be one of the most successful worldwide collaborations between academic study groups to facilitate such a huge pivotal clinical trial – thousands of physicians, researchers, nurses, and other health care professionals in 21 countries around the globe have worked together for many years to make this. The follow-up of patients will continue for at least 10 years from trial entry and provide many additional insights in how to even better conquer breast cancer in the future. “



Angela DeMichele, MD, MSCE, Professor of Medicine and Epidemiology, Perelman School of Medicine at the University of Pennsylvania and global PALLAS Co-Chair, points out another important outcome of the PALLAS study, and describes its potential for further research: “One critically important achievement of PALLAS was the mandatory tissue block collection at the beginning of this enterprise. These samples, along with serially collected blood samples, provide an enormous treasure of opportunities for researchers worldwide to interrogate mechanisms of disease and treatment in numerous translational science projects. Ultimately, this will greatly enhance our understanding of breast cancer, and shed light on the findings of the PALLAS trial.”

Health authorities, trial investigators, and patients are being notified of the interim findings. The detailed finding from the PALLAS study will be shared with the scientific community at an upcoming major medical congress.

Academically-led Global Collaboration

The PALLAS trial is being conducted collaboratively by several academic-based global research groups. PALLAS is co-sponsored by the Austrian Breast & Colorectal Cancer Study Group (ABCSG) and Alliance Foundation Trials (AFT) as part of a clinical research collaboration with Pfizer (providing study drug and funding) and other study groups, including PrECOG, LLC; NSABP Foundation Inc; and the Breast International Group (BIG). This targeted collaboration between academia and industry is allowing the independent generation of clinical data whilst providing a unique public-private research partnership aimed at bringing more innovative cancer treatments to patients in more efficient ways.

More than 400 participating clinical sites in 21 countries enrolled a total of 5,796 patients. The study opened in August 2015. The global recruitment aim was met on schedule, on November 30, 2018, displaying the well-concerted interplay of participating academic groups and their profound experience in clinical research.

The Austrian Breast & Colorectal Cancer Study Group (ABCSG) is Austria’s biggest and best-established academic research organization that conducts internationally respected clinical trials to investigate breast and colon cancer. So far, about 29,000 patients worldwide have participated in ABCSG trials since 1984. ABCSG is part of the Breast International Group (BIG) network, which comprises over 55 academic research groups (many of which participate in the PALLAS study) and represents the largest international network dedicated to breast cancer research. In the PALLAS study, 20 countries outside the U.S. were under the sponsorship of ABCSG. Together, 242 centers in the ABCSG and BIG networks enrolled 3,381 of the total number of patients in the trial. For further information visit us on www.abcsrg.com or follow us on twitter, [ABCSGVienna](https://twitter.com/ABCSGVienna).

Alliance Foundation Trials, LLC (AFT) is an academic research organization that develops and conducts cancer clinical trials across multiple disease sites, working closely with pharmaceutical partners, research collaborators and the Alliance for Clinical Trials in Oncology (Alliance) scientific investigators and institutional member network. AFT seeks to fulfill a shared vision with Alliance to reduce the impact of cancer on people by uniting a broad community of scientists and clinicians from many disciplines committed to discovering, validating and disseminating effective strategies for the prevention and treatment of cancer. Its operational structure and clinical trials management mechanism are separate from the Alliance. In the United States, AFT, PrECOG and NSABP Foundation combined to enroll 2,415 patients on the PALLAS study across 165 sites. For more information about AFT, please visit www.AllianceFoundationTrials.org

Breast International Group (BIG): Founded in 1999 and based in Brussels, Belgium, BIG members believe that global collaboration is crucial to make significant advances in breast cancer research, reduce unnecessary duplication of effort, share data, contribute to the faster development of better treatments, and increase the likelihood of cures for



patients. Therefore, BIG facilitates breast cancer research at international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry. More than 30 clinical trials are run or are in development under the BIG umbrella at any one time. To date almost 90.000 patients have participated in its trials. For further information please visit www.bigagainstbreastcancer.org

PrECOG, LLC is a cancer research group formed as a not-for-profit limited liability company in 2006 by the ECOG Research and Education Foundation, Inc. It operates outside of the National Cancer Institute's federal funding structure, known as the National Clinical Trials Network. A central focus of PrECOG is to support the overall scientific research goals of the ECOG-ACRIN Cancer Research Group. PrECOG aims to reduce the burden of cancer by advancing research in all aspects of cancer care and thereby improve survival, patient benefit, and quality of life. The current PrECOG portfolio includes phase one and two multi-center trials, as well as US-based and multi-national phase three trials. For further information, please visit www.precogllc.org and www.ecog.acrin.org.

The NSABP Foundation, Inc., an academic research organization, conducts industry-supported cancer research in new chemotherapeutic and targeted biologic agents for evaluation in adjuvant and neoadjuvant clinical trials in breast and colorectal cancers. The NSABP Foundation has research sites in North America and an international network made up of oncology and research professionals.

The German Breast Group (GBG) is the largest academic research organisation devoted to breast cancer in Germany and one of the largest world-wide with, over 50,000 thousand patients recruited in their trials. GBG is a founding member of BIG and active in all parts of breast cancer research, including surgery and niche indications such breast cancer during pregnancy, and also running an adjuvant Palbociclib trial, the Penelope-B trial (NCT01864746). Please visit us on www.gbg.de or follow us on twitter, https://twitter.com/GBG_Forschung

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