Announcement

IDMC has concluded that OlympiA trial crossed superiority boundary for invasive disease-free survival vs. placebo at planned interim analysis

OlympiA Phase III trial of Lynparza in the adjuvant treatment of BRCA-mutated HER2-negative high-risk early breast cancer will be analysed and reported early

The OlympiA Phase III trial of AstraZeneca and MSD's *Lynparza* (Olaparib) will move to early primary analysis and reporting following a recommendation from the Independent Data Monitoring Committee (IDMC).

Based on the planned interim analysis, the IDMC concluded that the trial crossed the superiority boundary for its primary endpoint of invasive disease-free survival (iDFS) and demonstrated a sustainable, clinically relevant treatment effect for *Lynparza* versus placebo for patients with germline BRCA-mutated (gBRCAm) high-risk human epidermal growth factor receptor 2 (HER2)-negative early breast cancer, and recommend primary analysis now take place.

The OlympiA Phase III trial is a partnership between Breast International Group (BIG), NRG Oncology, the US National Cancer Institute (NCI), Frontier Science & Technology Research Foundation (FSTRF), AstraZeneca and MSD.[11] The trial is sponsored by NRG Oncology in the US and by AstraZeneca outside the US.

An estimated 2.3 million women were diagnosed with breast cancer worldwide in 2020, and BRCA mutations are found in approximately 5% of breast cancer patients.[1-9] Around 55-65% of women with a BRCA1 mutation and approximately 45% with a BRCA2 mutation will develop breast cancer before the age of 70.[10]

Andrew Tutt, Global Chair of the OlympiA Phase III trial and Professor, Institute of Cancer Research and Kings College London, said: "We are delighted that our global academic and industry partnership has been able to help investigate a possible personalised treatment for women with hereditary breast cancer. The most common cause of hereditary breast cancer is an inherited mutation in the *BRCA1* or *BRCA2* genes which also may cause the disease to develop at a significantly earlier age than is usual. The OlympiA trial has allowed us to go beyond using genetic testing to identify patients who are at risk of this disease and explore the potential of *Lynparza* to prevent disease recurrence for these patients. We look forward to analysing and presenting the full results of the trial at a forthcoming medical meeting."

José Baselga, Executive Vice President, Oncology R&D, said: "Breast cancer remains one of the most common cancers globally and despite advances in treatment, many patients with high-risk disease will unfortunately develop a recurrence. We look forward to reviewing the results".

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: " Analysis of the OlympiA trial, based upon the DMC recommendation, could represent a potential step forward for patients with early-stage, high-risk primary breast cancer with a gBRCA mutation."

In its communication, the IDMC did not raise any new safety concerns. The trial will continue to assess the key secondary endpoints of overall survival and distant disease-free survival.

Early breast cancer

Breast cancer is the most common cancer among women worldwide and an estimated 90% of all breast cancer is diagnosed at an early stage.[12,13] Breast cancer is one of the most biologically diverse tumour types with various factors fuelling its development and progression.[14] The discovery of biomarkers in the development of breast cancer has greatly impacted scientific understanding of the disease.[15]

BRCA1* and *BRCA2

BRCA1 and *BRCA2* (breast cancer susceptibility genes 1/2) are human genes that produce proteins responsible for repairing damaged DNA and play an important role maintaining the genetic stability of cells. When either of these genes is mutated or altered such that its protein product either is not made or does not function correctly, DNA damage may not be repaired properly, and cells become unstable. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer and confer sensitivity to PARP inhibitors including *Lynparza*.[16-19]

OlympiA

OlympiA is a Phase III, double-blind, parallel group, placebo-controlled, multicentre trial testing the efficacy and safety of *Lynparza* tablets versus placebo as adjuvant treatment in patients with gBRCAm high-risk HER2-negative early breast cancer, who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy. The primary endpoint of the trial is iDFS defined as time from randomisation to date of first treatment failure that is loco-regional or distant recurrence or new cancer or death from any cause.[11]

NRG Oncology

NRG Oncology is a network group funded by the NCI, a part of the National Institutes of Health. All of the NCI funded network groups participated in the trial. The NCI and AstraZeneca are collaborating under a Cooperative Research and Development Agreement.

NRG Oncology brings together the National Surgical Adjuvant Breast and Bowel Project, the Radiation Therapy Oncology Group, and the Gynaecologic Oncology Group, with the mission to improve the lives of cancer patients by conducting practice-changing multi-institutional clinical and translational research.

BIG

The Breast International Group (BIG) is an international not-for-profit organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Founded by leading European opinions leaders in 1999, the organisation aims to address fragmentation in European breast cancer research and now represents a network of over 55 like-minded research groups affiliated with specialised hospitals, research centres and leading experts across approximately 70 countries on six continents.

BIG's research is supported in part by its philanthropy unit, known as *BIG against breast cancer*, which is used to interact with the general public and donors, and to raise funds for BIG's purely academic breast cancer trials and research programmes.

FSTRF

Frontier Science & Technology Research Foundation (FSTRF) is a non-profit, research organisation which supports research networks, pharmaceutical companies and investigators to conduct scientifically meaningful high-quality clinical trials. The OlympiA trial involved research staff in the US and in the Affiliate office in Scotland.

FSTRF works with scientists and technicians in more than 800 laboratories, universities and medical centres around the world to provide a comprehensive range of research services throughout the clinical trial process including design, analysis and reporting.

Through its work, FSTRF aims to advance the application of statistical science and practice and data management techniques in science, healthcare and education.

The AstraZeneca and MSD strategic oncology collaboration

In July 2017, AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the US and Canada, announced a global strategic oncology collaboration to co-develop and co-commercialise *Lynparza*, the world's first PARP inhibitor, and *Koselugo* (selumetinib), a mitogen-activated protein kinase (MEK) inhibitor, for multiple cancer types. Working together, the companies will develop *Lynparza* and *Koselugo* in combination with other potential new medicines and as monotherapies. Independently, the companies will develop *Lynparza* and *Koselugo* in combination with their respective PD-L1 and PD-1 medicines.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts

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