Novartis' Ribociclib Phase III NATALEE trial shows significant benefit for patients with early breast cancer in interim analysis

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- Ribociclib plus endocrine therapy (ET) significantly reduced the risk of disease recurrence compared to standard ET alone in the adjuvant setting
- NATALEE is the first and only positive Phase III study of a CDK4/6 inhibitor demonstrating consistent benefit in a broad population of patients with stage II and III HR+/HER2- early breast cancer (EBC) at risk of recurrence, including those with no nodal involvement
- Approximately 30-60% of people with HR+/HER2- stage II and III EBC treated with ET only remain at risk of breast cancer recurrence
- NATALEE results will be presented at an upcoming medical meeting and submitted to regulatory authorities worldwide

Novartis announced positive topline results from an interim analysis of NATALEE, a Phase III trial evaluating ribociclib plus endocrine therapy (ET) in a broad population of patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC) at risk of recurrence. The Independent Data Monitoring Committee recommended stopping the trial early as the primary endpoint of invasive disease-free survival (iDFS) has been met. Ribociclib plus ET significantly reduced the risk of disease recurrence, compared to standard adjuvant ET alone, with consistent benefit in patients with stage II and stage III EBC regardless of nodal involvement.

“While most patients are diagnosed and treated early with the aim to cure breast cancer, the risk of cancer returning, often as metastatic disease, peaks within three years after diagnosis, but never goes away completely,” said Dennis J. Slamon, MD, Director of Clinical/Translational Research, University of California, Los Angeles Jonsson Comprehensive Cancer Center and Chairman and Executive Director of Translational Research In Oncology (TRIO) and NATALEE trial lead investigator. "There is a critical need for new, well-tolerated options that keep patients cancer-free without disrupting quality of life. The NATALEE trial, where ribociclib was given for three years plus ET, was designed with these unmet needs in mind, and it is extremely encouraging that this study met its primary endpoint.”

Per the NATALEE study protocol, patient follow-up will continue to evaluate long-term outcomes, including overall survival.

"The positive topline results from NATALEE represent a major milestone in our ambition to expand the benefits of ribociclib to patients with earlier stages of breast cancer, building on the heritage of this effective treatment in HR+/HER2- metastatic breast cancer,” said Shreeram Aradhye, M.D., President, Global Drug Development and Chief Medical Officer, Novartis. “These data have the potential to be paradigm-shifting for patients at risk of recurrence, including those with no nodal involvement, who have limited well-tolerated options to prevent recurrence. Our teams are working on submissions to health authorities around the world with the hope to bring ribociclib to many more patients diagnosed with breast cancer.”

“The result of the NATALEE trial is a welcome development in the management of breast cancer, offering new

hope for a longer life in a broad population of patients with stage II and III HR-positive/HER2-negative early breast cancer at risk of recurrence," said Dr. Rosario V. Pitargue, President, Philippine Society of Medical Oncology (PSMO).

"These findings build on the legacy of ribociclib in metastatic breast cancer (MBC). Ribociclib is the first and only CDK4/6 inhibitor so far to have shown both consistent and significant improvements in overall survival across 3 phase III trials," said Mr. Joel Chong, Country President, Novartis Healthcare Philippines, Inc.

About NATALEE

NATALEE is a global Phase III multi-center, randomized, open-label trial to evaluate the efficacy and safety of ribociclib with ET as adjuvant treatment versus ET alone in patients with HR+/HER2- EBC, being conducted in collaboration with Translational Research In Oncology (TRIO)1. The primary endpoint of NATALEE is iDFS as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria; secondary endpoints include safety, quality of life, and overall survival, among others. iDFS is a composite endpoint in EBC adjuvant trials, which incorporates locoregional relapse, ipsilateral and contralateral invasive breast cancer, distant recurrence, and types of new cancer events or death from any cause. Approximately 5,100 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial, including patients with tumor stages IIA (select patients), IIB or III, regardless of nodal involvement. NATALEE explored a lower starting dose (400 mg) of ribociclib than the dose approved for treatment in MBC (600 mg) with the goal to minimize disruptions to patient quality of life without compromising efficacy.

About ribociclib

Ribociclib has consistently demonstrated overall survival benefit while preserving or improving quality of life across three Phase III trials. Updates to the NCCN Guidelines® for breast cancer, released in January 2023, recommend ribociclib as the only Category 1 preferred CDK4/6 inhibitor for first-line treatment of patients with HR+/HER2- MBC when combined with an AI. Additionally, ribociclib has the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale, achieving a score of five out of five for first-line premenopausal patients with HR+/HER2- advanced breast cancer. Further, ribociclib in combination with either letrozole or fulvestrant has uniquely, among other CDK4/6 inhibitors, received a score of four out of five for postmenopausal patients with HR+/HER2- advanced breast cancer treated in the first line.

Ribociclib has been approved in 99 countries worldwide, including by the United States Food and Drug Administration (FDA) and the European Commission. In the U.S., ribociclib is approved for the treatment of adult patients with HR+/HER2- advanced or metastatic breast cancer in combination with an AI as initial ET or fulvestrant as initial ET or following disease progression on ET in postmenopausal women or in men. In the EU, ribociclib is approved for the treatment of women with HR+/HER2- advanced or metastatic breast cancer in combination with either an AI or fulvestrant as initial ET or following disease progression. In pre- or perimenopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist.

Novartis is committed to continuing to study ribociclib in breast cancer. Novartis is collaborating with SOLTI, which is leading the HARMONIA study to test whether ribociclib changes tumor biology to enable a better response to ET compared to palbociclib for patients with metastatic HR+/HER2-, HER2-enriched subtype, and with the Akershus University Hospital in Norway on the NEOLETRIB trial, a neoadjuvant Phase II trial studying the effects of ribociclib in HR+/HER2- EBC to discover the potentially unique underlying mechanism of action. Novartis also plans to build on the findings from NATALEE with ADJUVANT WIDER, an open-label Phase IIIb trial evaluating ribociclib plus ET in a population of HR+/HER2- patients with stage II and III EBC that is closer to a real-world population.

Ribociclib was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

References:

- https://www.novartis.com/news/media-releases/novartis-kisqali-phase-iii-natalee-trial-meets-primary-endpoint-interim-analysis-demonstrating-clinically-meaningful-benefit-broad-population-patients-early-breast-cancer

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