NATALEE Clinical Trial

NATALEE (New Adjuvant TriAl with LEE) is a Phase III multi-center, randomized, open-label clinical trial to evaluate the efficacy and safety of KISQALI® (ribociclib) with endocrine therapy (ET) as adjuvant treatment in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC).

What is KISQALI®?

KISQALI (ribociclib) is a selective cyclin-dependent kinase inhibitor, a medicine that targets and blocks the action of proteins known as cyclin-dependent kinases 4 and 6 (CDK4/6) that control how quickly cells grow and divide. Treatment with CDK4/6 inhibitors aims to slow or even stop cancer cells from growing.

KISQALI has been approved in combination with ET for treatment of adult patients with HR+/HER2- metastatic breast cancer in 99 countries. After showing consistent overall survival benefit and the ability to improve or preserve quality of life for patients in this setting across three Phase III clinical trials (MONALEESA program), the NATALEE trial is evaluating its efficacy and safety when combined with ET in a broad population of patients with HR+/HER2- EBC.

More than 90%
of people in the US who receive a breast cancer diagnosis are considered patients with **early breast cancer** (stages I, II, or III)

Despite standard-of-care adjuvant therapy, approximately

patients with HR+/HER2- EBC **experience cancer recurrence**

More than half of recurrences happen 5 years after initial diagnosis

About NATALEE

Purpose

Evaluate the efficacy and safety of KISQALI with endocrine therapy as adjuvant treatment in adults previously diagnosed with HR+/HER2- EBC who are at risk of recurrence.

The adjuvant ET used in the trial was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable.

Eligibility Criteria

NATALEE was designed to address the needs of a broad range of **at-risk patients** commonly seen in clinical practice, simplifying patient identification.

100% of those with **stage III** HR+/HER2- EBC, **regardless of nodal status**

70% of those with **stage II** HR+/HER2- EBC, including **node-negative**

Dosing & Duration

NATALEE studied KISQALI at a **400mg** dose for **3 years** based on scientific and patient-focused rationale to deliver a favorable safety profile while maximizing efficacy.

Trial Participants

5101
participants

20
countries

Primary Endpoint

iDFS **Invasive Disease-Free Survival** as defined by the STEEP (Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials) criteria is a composite endpoint that measures invasive disease, recurrence or death from any cause.

Secondary Endpoints

- **Recurrence-free survival** as defined by STEEP criteria
- **Distant disease-free survival** as defined by STEEP criteria
- **Quality of life** related to health and physical function as assessed by EORTC QLQ-C30
- **Overall survival**

Novartis plans to build on the findings from NATALEE with ADJUVANT WIDER, an open-label Phase IIIb trial evaluating KISQALI plus ET in an expanded population of patients diagnosed with HR+/HER2- EBC that closely resembles real-world clinical practice.

Indications

KISQALI® (ribociclib) 200 mg tablets is a prescription medicine used to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has gotten worse or has spread to other parts of the body (metastatic), in combination with:

- an aromatase inhibitor as the first endocrine-based therapy; or
- fulvestrant as the first endocrine-based therapy or following disease progression on endocrine therapy in postmenopausal women or in men.

It is not known if KISQALI is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about KISQALI?

KISQALI may cause serious side effects, including:

Lung problems. KISQALI may cause severe or life-threatening inflammation of the lungs during treatment that may lead to death. Tell your health care provider right away if you have any new or worsening symptoms, including:
- trouble breathing or shortness of breath
- cough with or without mucus
- chest pain

Severe skin reactions. Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse; reddened skin; flu-like symptoms; skin pain/burning; blistering of the lips, eyes, or mouth; or blisters on the skin or skin peeling, with or without fever.

Heart rhythm problems (QT prolongation). KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Your health care provider should check your heart and do blood tests before and during treatment with KISQALI. Tell your health care provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel dizzy or faint.

Liver problems (hepatobiliary toxicity). KISQALI can cause serious liver problems. Your health care provider should do blood tests to check your liver before and during treatment with KISQALI. Tell your health care provider right away if you get any of the following signs and symptoms of liver problems:
- yellowing of your skin or the whites of your eyes (jaundice)
- dark or brown (tea-colored) urine
- feeling very tired
- loss of appetite
- pain on the right side of your stomach area (abdomen)
- bleeding or bruising more easily than normal

Low white blood cell counts (neutropenia). Low white blood cell counts are very common during treatment with KISQALI and may result in infections that may be severe. Your health care provider should check your white blood cell counts before and during treatment with KISQALI. Tell your health care provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Your health care provider may tell you to decrease your dose, temporarily stop, or completely stop taking KISQALI if you develop certain serious side effects during treatment with KISQALI.

What should I tell my health care provider before taking KISQALI?

Before you take KISQALI, tell your health care provider if you:
- have any heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have ever had a heart attack
- have a slow heartbeat (bradycardia)
- have problems with the amount of potassium, calcium, phosphorus, or magnesium in your blood
- have fever, chills, or any other signs or symptoms of infection
- have liver problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. KISQALI can harm your unborn baby
- If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.
- Females who are able to become pregnant and who take KISQALI should use effective birth control during treatment and for at least 3 weeks after the last dose of KISQALI.
- Talk to your health care provider about birth control methods that may be right for you during this time.
- If you become pregnant or think you are pregnant, tell your health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. KISQALI and other medicines may affect each other, causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

What should I avoid while taking KISQALI?

Avoid eating grapefruit and avoid drinking grapefruit juice during treatment with KISQALI since these may increase the amount of KISQALI in your blood.

The most common side effects of KISQALI include:

- decreased white blood cell counts
- decreased red blood cell counts
- abnormal liver function tests
- infectios
- nausea
- increased kidney function test
- tiredness
- decreased platelet counts
- diarrhea
- vomiting
- headache
- constipation
- hair loss
- cough
- rash
- back pain
- low blood sugar level

KISQALI may cause fertility problems if you are male and take KISQALI. This may affect your ability to father a child. Talk to your health care provider if this is a concern for you.

Tell your health care provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information including Patient Information.

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