Indications
KISQALI is indicated in combination with an aromatase inhibitor for the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC) at high risk of recurrence.

IMPORTANT SAFETY INFORMATION
Interstitial lung disease/pneumonitis. Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with KISQALI and other CDK4/6 inhibitors.

In patients with eBC (NATALEE) who received 400 mg KISQALI plus a nonsteroidal aromatase inhibitor (NSAI), 1.5% of patients had ILD/pneumonitis (grade 1/2).

Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis, which may include hypoxia, cough, and dyspnea. In patients who have new or worsening respiratory symptoms suspected to be due to ILD or pneumonitis, interrupt KISQALI immediately and evaluate the patient. Permanently discontinue KISQALI in patients with severe ILD/pneumonitis or any recurrent symptomatic ILD/pneumonitis.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI.

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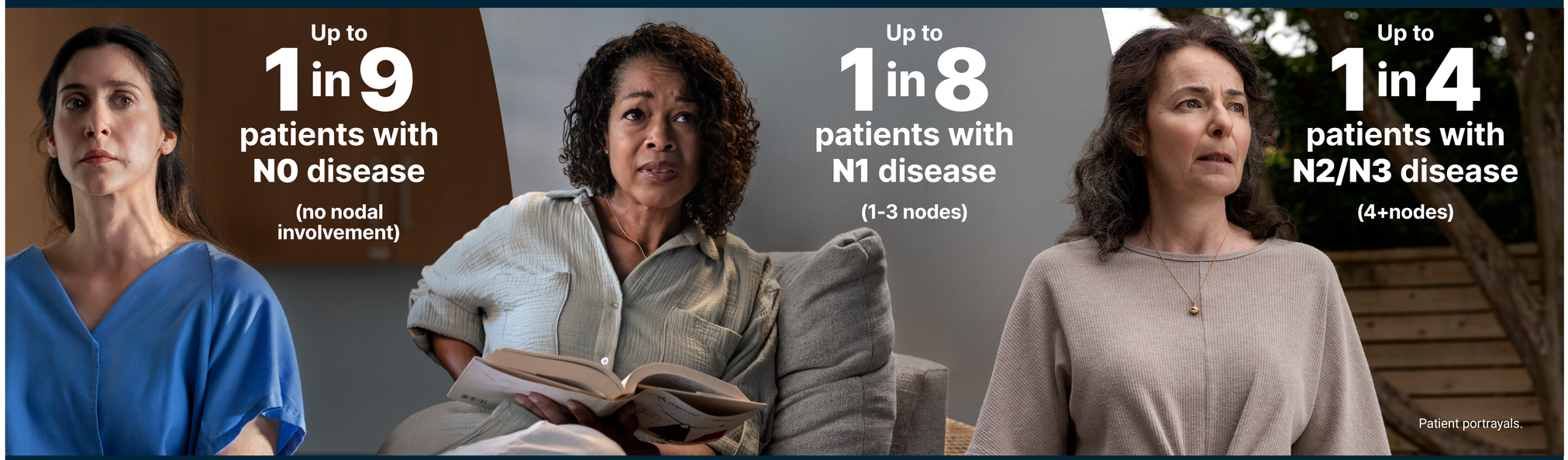
She’s worried today is the day everything changes...again

Despite treatment with adjuvant ET, patients with stage II/III HR+/HER2- eBC remain at risk of recurrence with incurable metastatic disease—even if they have no or low nodal involvement.[1,2]

What are the chances of her cancer returning within 3 years?[1,2]



The 3-year risk of recurrence rates are based on iDFS outcomes published for patients with HR+/HER2- eBC in select CDK4/6 inhibitor clinical trials, who were also treated with standard ET, including tamoxifen. **KISQALI is not indicated for concomitant use with tamoxifen due to an increased risk for QT prolongation.** Data are from control arms only; no comparisons should be made between results from CDK4/6 inhibitor trial arms.[1-3]

CDK, cyclin-dependent kinase; eBC, early breast cancer; ET, endocrine therapy; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; iDFS, invasive disease-free survival; N, nodal status.

She’s concerned her cancer may come back. And rightly so.

Get tips and tools to help assess her risk

IMPORTANT SAFETY INFORMATION (continued)

Severe cutaneous adverse reactions. Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with KISQALI.

If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Early consultation with a dermatologist is recommended to ensure greater diagnostic accuracy and appropriate management.

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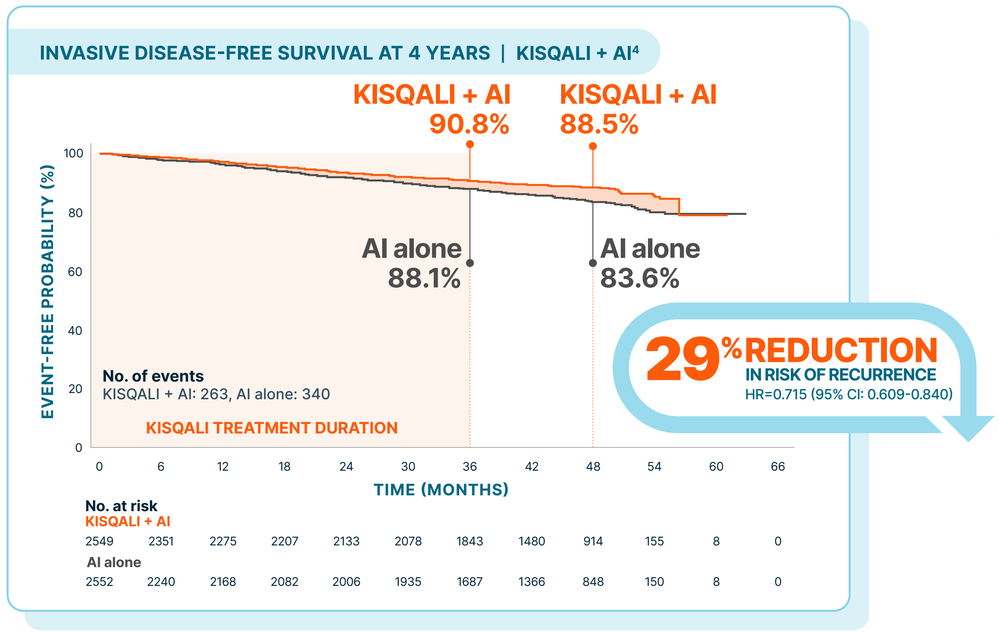
RISK OF RECURRENCE | EFFICACY | REFERENCES | ISI

In patients with stage II/III HR+/HER2- eBC at high risk of recurrence,

With KISQALI + AI, the iDFS benefit deepened beyond the 3-year treatment period, with a 29% reduction in the risk of recurrence

NATALEE: KISQALI + AI vs AI alone
At a median follow-up of 44 months



Hazard ratio is based on stratified Cox model.[5]

NATALEE was a randomized, multicenter, open-label, phase III study of KISQALI 400 mg (dosed orally, once daily for the first 21 days followed by 7 days off, resulting in a complete cycle of 28 days) + letrozole or anastrozole* (n=2549) vs letrozole or anastrozole (n=2552) for the adjuvant treatment of men and women with stage II/III HR+/HER2- eBC, including all those with node-positive or high-risk node-negative disease (eligible stages and nodal status include: anatomic stage group IIB-III, or anatomic stage group IIA that is either node positive, or node negative with histologic grade 3, or histologic grade 2 with Ki-67 ≥20% and/or high risk by gene signature testing). iDFS was the primary end point. iDFS was defined as the time from randomization to the date of the first event of local invasive breast cancer recurrence, regional invasive recurrence, distant recurrence, contralateral invasive breast cancer, second primary non-breast invasive cancer (excluding basal and squamous cell carcinomas of the skin), or death (any cause). In an interim analysis, a statistically significant improvement in iDFS was observed.[3,6]

AI, aromatase inhibitor; ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor.

*Men and premenopausal women also received goserelin.[6]

†Infections included urinary and respiratory tract infections.[3]

‡Only includes grade 3 ARs.[3]

In a 4-year post hoc analysis[4]:

- **At 3 years: 2.7% absolute difference**
- **At 4 years: 4.9% absolute difference**
- At the time of data cutoff, only 10.3% of patients receiving KISQALI + AI had experienced an iDFS event vs 13.3% of patients treated with AI alone
- Results from the exploratory 4-year analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error

KISQALI can help reduce the risk of recurrence, including distant recurrence with incurable metastatic disease, which accounted for 66% of iDFS events in the NATALEE trial

In the 3-year final analysis (median follow-up of 33.3 months)[3,7]:

- **iDFS at 3 years was 90.7% for KISQALI + AI vs 87.6% for AI alone (absolute difference 3.1%)**
- **There was a 25.1% relative reduction in the risk of an iDFS event; HR=0.749 (95% CI: 0.628-0.892)**

NATALEE safety outcomes: ARs ≥10% and ≥2% higher than NSAI-alone arm (all grades/grades 3 or 4 for KISQALI + NSAI [n=2526] vs NSAI alone [n=2441]) included infections† (37%/2% vs 27%/0.9%), headache (23%/0.4%‡ vs 17%/0.2%‡), nausea (23%/0.2%‡ vs 8%/0.1%‡), diarrhea (15%/0.6%‡ vs 6%/0.1%‡), constipation (13%/0.2%‡ vs 5%/0%), abdominal pain (11%/0.5%‡ vs 7%/0.4%‡), fatigue (22%/0.8%‡ vs 13%/0.2%‡), asthenia (17%/0.6%‡ vs 12%/0.1%‡), pyrexia (11%/0.2%‡ vs 6%/0.1%‡), alopecia (15%/0% vs 4.6%/0%), and cough (13%/0.1%‡ vs 8%/0.1%‡). The most common ARs (occurring in ≥20% of patients treated with KISQALI), including laboratory abnormalities, were decrease in lymphocytes, decrease in leukocytes, decrease in neutrophils, decrease in hemoglobin, increase in ALT, increase in AST, infections, increase in creatinine, decrease in platelets, headache, nausea, and fatigue. The most common grade ≥3 ARs, including laboratory abnormalities, occurring in ≥5% of patients were decrease in neutrophils, decrease in leukocytes, decrease in lymphocytes, increase in ALT, and increase in AST. The rate of dose reductions due to ARs was 23.2% with KISQALI + NSAI vs 0% with NSAI alone; rate of discontinuation due to ARs was 20.8% with KISQALI + NSAI vs 5.5% with NSAI alone. The leading causes of KISQALI + AI discontinuation (occurring in ≥2% of patients) were increases in ALT or AST (8%). Fatal ARs occurred in 0.6% of patients who received KISQALI. Fatal ARs in ≥0.1% of patients receiving KISQALI included COVID-19 or COVID-19 pneumonia (0.2%) and pulmonary embolism (0.1%). In the NATALEE trial, no new safety signals were observed at 4 years of follow-up.[3,4,8]

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NATALEE: At a median follow-up of 33.3 months, iDFS (primary end point) at the 3-year landmark was 90.7% for KISQALI + NSAI vs 87.6% for NSAI alone **(absolute difference 3.1%)**; there was a 25.1% relative reduction in the risk of an iDFS event; HR=0.749 (95% CI: 0.628-0.892).[3,7]

References: 1. Mayer EL, Dueck AC, Martin M, et al. Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study. *Lancet Oncol.* 2021;22(2):212-222. doi:10.1016/S1470-2045(20)30642-2 **2.** Johnston SRD, Toi M, O'Shaughnessy J, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2023;24(1):77-90. doi:10.1016/S1470-2045(22)00694-5 **3.** Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **4.** Fasching PA, Stroyakovskiy D, Yardley DA, et al. Adjuvant ribociclib plus nonsteroidal aromatase inhibitor in patients with HR+/HER2− early breast cancer: 4-year outcomes from the NATALEE trial. Presented at: ESMO Congress 2024; September 13-17, 2024; Barcelona, Spain. **5.** Slamon D, Lipatov O, Nowecki Z, et al. Ribociclib plus endocrine therapy in early breast cancer. *N Engl J Med.* 2024;390(12):1080-1091;(protocol). doi:10.1056/NEJMoa2305488 **6.** Slamon D, Lipatov O, Nowecki Z, et al. Ribociclib plus endocrine therapy in early breast cancer. *N Engl J Med.* 2024;390(12):1080-1091. doi:10.1056/NEJMoa2305488 **7.** Hortobagyi GN, Lacko A, Sohn J, et al. A phase III trial of adjuvant ribociclib plus endocrine therapy versus endocrine therapy alone in patients with HR-positive/HER2-negative early breast cancer: final invasive disease-free survival results from the NATALEE trial. *Ann Oncol.* 2025;36(2):149-157. doi:10.1016/j.annonc.2024.10.015 **8.** Data on file. CLEE011O12301C (NATALEE) final iDFS analysis results. Novartis Pharmaceuticals Corp; 2023.

See what KISQALI could mean for your patients

IMPORTANT SAFETY INFORMATION

Warnings and precautions for KISQALI include interstitial lung disease/pneumonitis, severe cutaneous adverse reactions, QT interval prolongation, increased QT prolongation with concomitant use of tamoxifen, hepatotoxicity, neutropenia, and embryo-fetal toxicity.

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If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Early consultation with a dermatologist is recommended to ensure greater diagnostic accuracy and appropriate management.

If SJS, TEN, or DiHS/DRESS is confirmed, permanently discontinue KISQALI. Do not reintroduce KISQALI in patients who have experienced SCARs or other life-threatening cutaneous reactions during KISQALI treatment.

QT interval prolongation. KISQALI has been shown to prolong the QT interval in a concentration-dependent manner.

Avoid KISQALI in patients who are at significant risk of developing torsades de pointes (TdP), including those with:

- congenital long QT syndrome;
- uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism;
- electrolyte abnormalities;
- taking drugs known to prolong QT interval and/or strong CYP3A inhibitors as this may lead to prolongation of the QTcF interval.

Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

In patients with eBC (NATALEE) who received 400 mg KISQALI plus NSAI, 8 out of 2494 patients (0.3%) had > 500 ms post-baseline QTcF interval value and 50 out of 2494 patients (2%) had > 60 ms QTcF increase from baseline. QTcF prolongation was reversible with dose interruption. The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI. There were no reported cases of torsades de pointes.

Perform electrocardiogram (ECG) in all patients prior to starting KISQALI. Initiate treatment with KISQALI only in patients with QTcF values <450 ms. Repeat ECG at approximately Day 14 of the first cycle and as clinically indicated.

Monitor serum electrolytes (including potassium, calcium, phosphorus and magnesium) prior to the initiation of KISQALI, at the beginning of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI.

Increased QT prolongation with concomitant use of tamoxifen. KISQALI is not indicated for concomitant use with tamoxifen. Avoid use of tamoxifen with KISQALI. In MONALEESA-7, the observed mean QTcF increase from baseline was >10 ms higher in the tamoxifen + placebo subgroup compared with the nonsteroidal aromatase inhibitor (NSAI) + placebo subgroup. In the placebo arm, an increase of >60 ms from baseline occurred in 6/90 (7%) of patients receiving tamoxifen, and in no patients receiving an NSAI. An increase of >60 ms from baseline in the QTcF interval was observed in 14/87 (16%) of patients in the KISQALI and tamoxifen combination and in 18/245 (7%) of patients receiving KISQALI plus an NSAI.

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IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity. In patients with eBC, drug-induced liver injury and increases in transaminases occurred with KISQALI.

In patients with eBC (NATALEE) treated with KISQALI, drug-induced liver injury was reported in 9 patients (0.4%), of which 5 were grade ≥3 and 8 had resolved as of the data cutoff. There were 8 (0.3%) clinically confirmed Hy's Law cases (including 4 out of 9 drug-induced liver injury mentioned above), 6 of which had resolved within 303 days and 2 were resolving, all after discontinuation of KISQALI. Grade 3/4 increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred in 8% and 4.7%, respectively, and grade 4 increases in ALT (1.5%) and AST (0.8%).

Perform liver function tests (LFTs) before initiating KISQALI. Monitor LFTs every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation.

Neutropenia. KISQALI causes concentration-dependent neutropenia. In patients with eBC (NATALEE) who received KISQALI plus NSAI, 94%, including 45% of grade 3/4, had a decrease in neutrophil counts (based on laboratory findings), 63% had an adverse drug reaction of neutropenia, and 0.3% had febrile neutropenia. The median time to grade ≥2 neutropenia was 18 days. The median time to resolution of grade ≥3 neutropenia to grade <3 was 10 days. Treatment discontinuation due to neutropenia was required in 1.1% of patients.

Perform complete blood count (CBC) before initiating therapy with KISQALI. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the neutropenia, KISQALI may require dose interruption, reduction, or discontinuation.

Embryo-fetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose.

Adverse reactions. Most common (incidence ≥20%) adverse reactions include infections, nausea, headache, and fatigue.

Laboratory abnormalities. In a clinical trial of patients with early breast cancer, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were lymphocytes decreased, leukocyte decreased, neutrophil decreased, hemoglobin decreased, alanine aminotransferase increased, aspartate aminotransferase increased, creatinine increased, and platelets decreased**.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI.

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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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