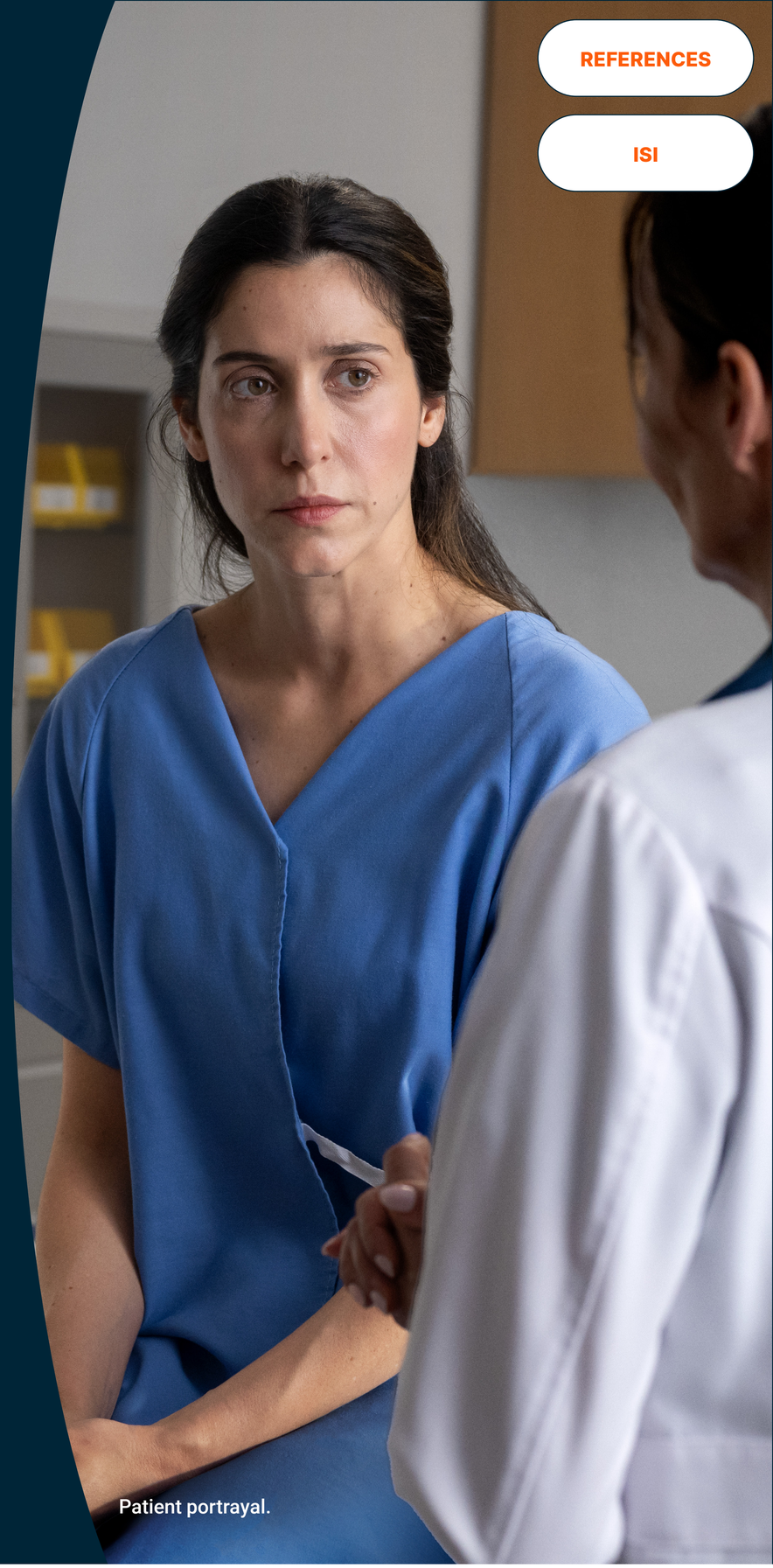
KISQALI® ribociclib 200 mg tablets

Discussion Guide

Talking about risk

Patients are worried about recurrence. And rightly so. This discussion guide can help you prepare for conversations about the risk of recurrence with your patients who have stage II/III HR+/HER2- eBC and provide details that can help you address some of their most common questions.



Patient portrayal.

eBC, early breast cancer; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive.

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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Patient portrayal.

Below are some common patient questions about risk of recurrence and KISQALI treatment.
Select any question below for information to support your discussion with your patient.

- **Did we get it all? What are the chances that my cancer could come back?**
- **Do I have to start treatment with KISQALI right away?**
- **How do we know what my personal risk level is?**
- **How will I know if KISQALI is working?**
- **What happens if my cancer comes back?**
- **What kinds of side effects does KISQALI have?**
- **How might KISQALI help?**
- **Is KISQALI right for patients like me?**
- **What is taking KISQALI like?**

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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REFERENCES

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Did we get it all? What are the chances that my cancer could come back?

Points for discussion:

Risk of recurrence within 3 years in stage II/III HR+/HER2- eBC[1,2]

For patients with N0 disease (no nodal involvement)

Up to 1 in 9 patients

For patients with N1 disease (1-3 nodes)

Up to 1 in 8 patients

For patients with N2/N3 disease (4+ nodes)

Up to 1 in 4 patients

will experience recurrence, despite adjuvant ET

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 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; ET, endocrine therapy; iDFS, invasive disease-free survival; N, nodal status.

IMPORTANT SAFETY INFORMATION (continued)

Severe cutaneous adverse reactions (continued). 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.

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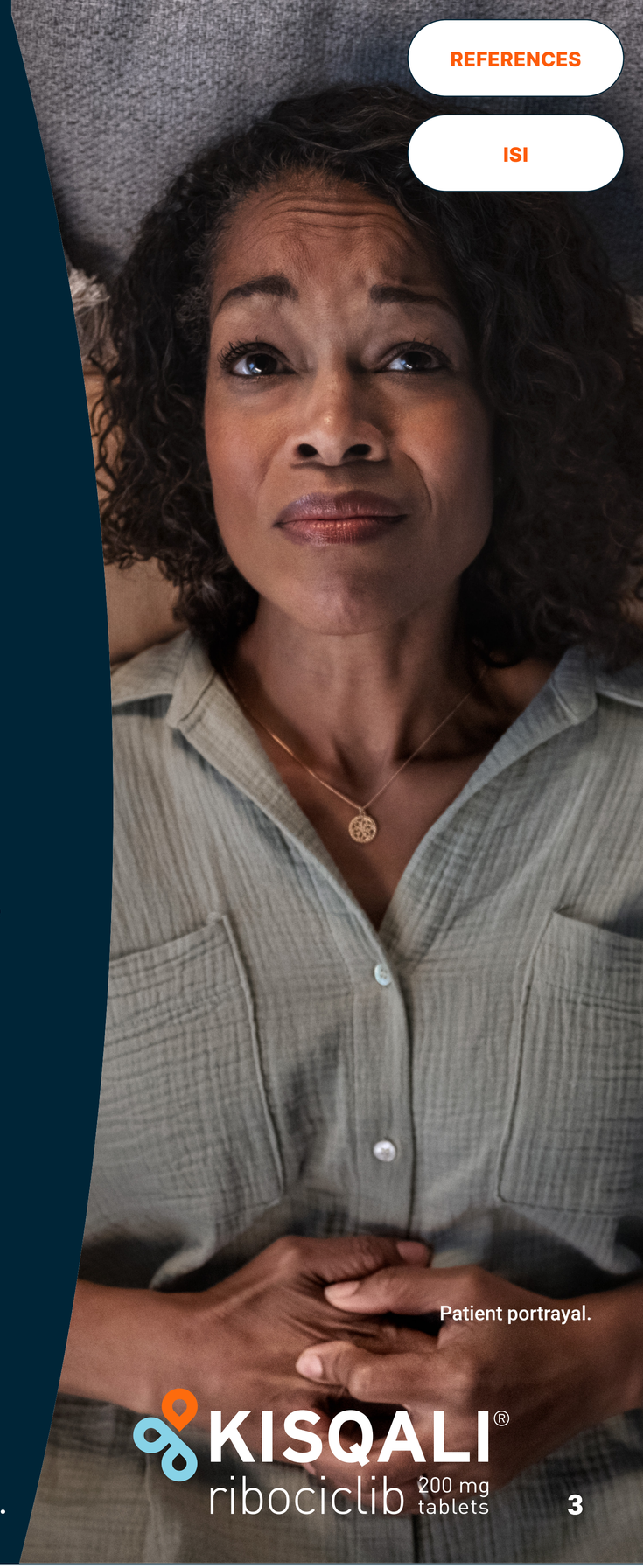

Patient portrayal.

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How do we know what my personal risk level is?

Points for discussion:

A comprehensive assessment of each patient's risk of recurrence incorporates a range of clinical and genomic risk factors, including[4]:

- **Age and menopausal status**
- **Cancer stage**
- **Histological grade**
- **Tumor size**
- **Nodal status**
- **Ki-67 score**
- **Genomic profile score***

Using a clinical tool such as iPredict™ or RSClin® can help assess these risk factors in the aggregate.

This information is intended for reference only. Novartis does not endorse the use of any specific test or tool to help determine risk of recurrence, and there may be additional tests or tools available. The brand names above are the property of their respective trademark owners.

*Patient age and menopausal status may also impact selection and interpretation of genomic profile assessment.[4]

What happens if my cancer comes back?

Points for discussion:

- **Breast cancer recurrence often occurs in distant organs (metastatic breast cancer); if that happens, it is considered incurable[5]**

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). 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.

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How might KISQALI help?

Points for discussion:

- **NATALEE was a positive study of KISQALI efficacy and safety in the broadest range of patients with stage II/III HR+/HER2- early breast cancer at high risk of recurrence, including those with low to no nodal involvement[3,5]**

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]

- **The NATALEE trial showed that adding KISQALI to an aromatase inhibitor can help reduce the risk of recurrence, including recurrence with incurable metastatic disease[3]**

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

- **This reduction in risk of recurrence has been shown to increase over time, even after the treatment period ends[8]**

In the 5-year prespecified analysis (median follow-up 55.4 months), iDFS at 5 years was 85.5% for KISQALI + AI vs 81.0% with AI alone **(absolute difference 4.5%)**. There was a 28.4% relative reduction in the risk of an iDFS event; HR=0.716 (95% CI: 0.618-0.829).[8]

In the 5-year prespecified analysis (median follow-up 55.5 months), DDFS at 5 years was 86.8% for KISQALI + AI vs 82.5% with AI alone **(absolute difference 4.3%)**. There was a 29.1% relative reduction in the risk of a DDFS event; HR=0.709 (95% CI: 0.608-0.827).[8]

The 5-year analysis was prespecified and observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.

AI, aromatase inhibitor; DDFS, distant disease-free survival; HR, hazard ratio.

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). 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.

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What is taking KISQALI like?

Points for discussion:

- **In patients with stage II/III HR+/HER2- eBC at high risk of recurrence, KISQALI is given as 400 mg (2 x 200-mg tablets) orally, once daily (3 weeks on, 1 week off) for 36 months with an AI[3]**
- **Review the full Prescribing Information for recommended dosing of selected AI[3]**
- **An LHRH agonist should be used concomitantly with AI in men and premenopausal women[3]**
- **Patients should continue treatment for 3 years or until disease recurrence or unacceptable toxicity[3]**
- **KISQALI can be taken with or without food[3]**
- **Review the KISQALI product package for storage and handling information**

Do I have to start treatment with KISQALI right away?

Points for discussion:

- **Participants who had up to 1 year of prior endocrine therapy were included in the NATALEE trial[6]**
- **This means that KISQALI can be added up to 1 year after starting an aromatase inhibitor[6]**

LHRH, luteinizing hormone-releasing hormone.

IMPORTANT SAFETY INFORMATION (continued)

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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How will I know if KISQALI is working?

Points for discussion:

- **The goal of treatment with KISQALI is to help reduce the risk of recurrence[3]**
- **The NATALEE study showed a reduction in risk of recurrence[3]**
  - In the 3-year final analysis (median follow-up of 33.3 months), 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)[3,7]
  - In the 5-year prespecified analysis (median follow-up 55.4 months), iDFS at 5 years was 85.5% for KISQALI + AI vs 81.0% with AI alone **(absolute difference 4.5%)**. There was a 28.4% relative reduction in the risk of an iDFS event; HR=0.716 (95% CI: 0.618-0.829)[8]
  - In the 5-year prespecified analysis (median follow-up 55.5 months), DDFS at 5 years was 86.8% for KISQALI + AI vs 82.5% with AI alone **(absolute difference 4.3%)**. There was a 29.1% relative reduction in the risk of a DDFS event; HR=0.709 (95% CI: 0.608-0.827)[8]
  - **The 5-year analysis was prespecified and observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error**
- **Treatment guidelines recommend regular physical exams and imaging to monitor for recurrence[9]**

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.

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What kinds of side effects does KISQALI have?

Points for discussion:

- **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[3]
- **The most common adverse reactions (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[3]**

  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%†).[3]
- **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[3]**
- **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%)[3]**
- **In the NATALEE trial, no new safety signals were observed at 5 years of follow-up[8]**
- **Most ARs with KISQALI were manageable and reversible with dose reduction[3]**

  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%).[10]
- **In patients who needed to reduce their dose of KISQALI, the iDFS benefit was maintained[11]**

  Lowering the dose of KISQALI can help address side effects and, in the NATALEE trial, did not impact efficacy.[3,11]

  - iDFS was similar irrespective of the relative dose intensity (RDI) of KISQALI: Patients with low (0% to <82.27%), medium (82.27% to <97.44%), and high (≥97.44%) RDI had similar iDFS outcomes (low vs high HR=0.93 [95% CI: 0.69-1.25]; medium vs high HR=0.99 [95% CI: 0.74-1.32]).[11]

  Results are based on a post hoc exploratory analysis. There was no prespecified statistical procedure controlling for type 1 error, and the results should be interpreted with caution.

Grading according to CTCAE version 4.03.[3]
*Infections included urinary and respiratory tract infections.[3]
†Only includes grade 3 ARs.[3]
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; NSAI, nonsteroidal aromatase inhibitor.

IMPORTANT SAFETY INFORMATION (continued)

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.

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Is KISQALI right for patients like me?

Points for discussion:

- **KISQALI was studied in the broadest range of patients at risk of recurrence, and is the only FDA-approved CDK4/6 inhibitor for patients with stage II/III HR+/HER2- early breast cancer with no nodal involvement who are at high risk, or who have N1 disease and tumors of grade 1 or 2 that are less than 5 cm[3,5,12]**
- **More and more doctors and patients are choosing to add KISQALI for their stage II/III HR+/HER2- eBC at high risk of recurrence[3,13]**
- **KISQALI is the #1 prescribed CDK4/6 inhibitor in new-to-brand prescriptions in HR+/HER2- eBC[3,13]**

  July 2025 IQVIA custom breast cancer market sizing report.

- **National Comprehensive Cancer Network® (NCCN®) recognizes ribociclib (KISQALI®) as a Category 1 Preferred CDK4/6 inhibitor in combination with an AI for appropriate patients with HR+/HER2- eBC—the only one to receive this designation for both high-risk node-negative and any node-positive disease[9]**

KISQALI is approved for use in combination with an AI; node-positive disease excludes patients with microscopic nodal involvement.[3,9]

High-risk node-negative disease is defined as either tumor size >5 cm, or if tumor size 2-5 cm, either grade 2 (with high genomic risk or Ki-67 ≥20%), or grade 3.[3,9]

NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.[9]

FDA, US Food and Drug Administration.

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia (continued). 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.

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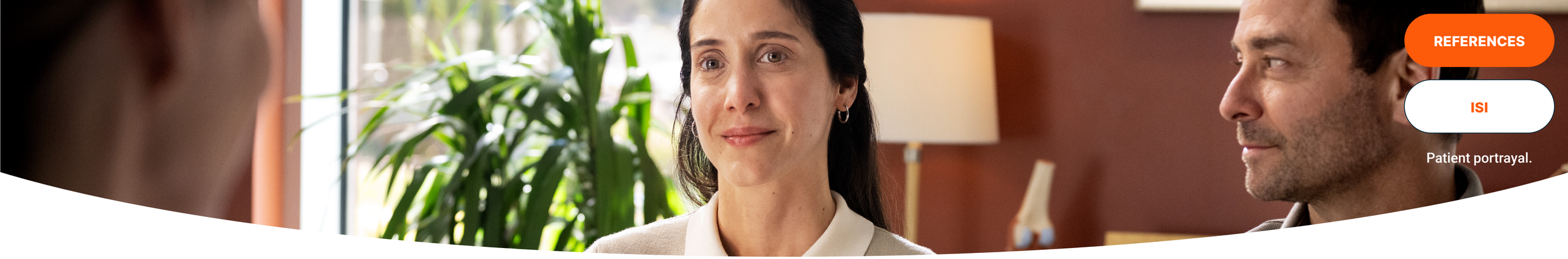

Patient portrayal.

Fears about recurrence are real.
Get more information and resources about what KISQALI may mean for your patients.

Information & resources for health care professionals

Information & resources for patients

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.** Amin MB, Edge SB, Greene FL, et al, eds; American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 8th ed. Springer International Publishing; 2017. **5.** Slamon DJ, Fasching PA, Hurvitz S, et al. Rationale and trial design of NATALEE: a phase III trial of adjuvant ribociclib + endocrine therapy versus endocrine therapy alone in patients with HR+/HER2− early breast cancer. *Ther Adv Med Oncol.* 2023;15:1-16. doi:10.1177/17588359231178125 **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.** Crown J, Stroyakovskii D, Yardley DA, et al. Adjuvant ribociclib plus nonsteroidal aromatase inhibitor therapy in patients with HR-positive/HER2-negative early breast cancer: 5-year follow-up of NATALEE efficacy outcomes and updated overall survival. *ESMO Open.* Published online October 17, 2025. doi:10.1016/j.esmoop.2025.105858 **9.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.4.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed October 13, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **10.** Data on file. CLEE011O12301C (NATALEE) final iDFS analysis results. Novartis Pharmaceuticals Corp; 2023. **11.** Hamilton E, Decker T, Rugo HS, et al. Impact of ribociclib dose reduction on efficacy in patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative early breast cancer in NATALEE. Poster presented at: San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, TX. P1-11-16. **12.** Razavi P, O'Shaughnessy J, Ahmed M, et al. Risk of recurrence among patients with HR+/HER2- early breast cancer involving 1-3 axillary lymph nodes: a real-world evaluation. Poster presented at: European Society for Medical Oncology Breast Cancer Annual Congress; May 14-17, 2025; Munich, Germany. Poster #211P. **13.** Data on file. mBC and eBC NBRx share data from IQVIA market sizing report. Novartis Pharmaceuticals Corp; 2025.

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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.

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.

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.

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KISQALI® ribociclib 200 mg tablets

IMPORTANT SAFETY INFORMATION (continued)

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.

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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