NCCN CATEGORY 1

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**.[1]

KISQALI is approved for use in combination with an AI; node-positive disease excludes patients with microscopic nodal involvement.[1,2]

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.[1,2]

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.[1]

#1 PRESCRIBED in eBC

KISQALI is the #1 prescribed CDK4/6 inhibitor in new-to-brand prescriptions in HR+/HER2- eBC[3]

July 2025 IQVIA custom breast cancer market sizing report.

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).[2,4]

AI, aromatase inhibitor; CDK, cyclin-dependent kinase; eBC, early breast cancer; HER2-, human epidermal growth factor receptor 2-negative; HR, hazard ratio; HR+, hormone receptor-positive; iDFS, invasive disease-free survival; NSAI, nonsteroidal aromatase inhibitor.

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
- for the treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer (mBC) in combination with:
  - an aromatase inhibitor as initial endocrine-based therapy; or
  - fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy

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).

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, MONALEESA-7), 1.6% of patients had ILD/pneumonitis of any grade, 0.4% had grade 3/4, and 0.1% had a fatal outcome. Additional cases of ILD/pneumonitis have occurred in the postmarketing setting, some resulting in death.

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

KISQALI® ribociclib 200 mg tablets

In stage II and III HR+ eBC,

Risk of recurrence is a significant lifelong concern

Despite treatment with adjuvant ET, patients remain at risk of recurrence with incurable metastatic disease—including those patients with no to low nodal involvement[5-8]

RISK BY NODAL STATUS[6-9]

	Within 3 years, up to		Within 20 years
	1 in 9	with N0 disease (no nodal involvement)	1 in 3
	1 in 8	with N1 disease (1-3 nodes)	1 in 3
	1 in 4	with N2/N3 disease (4+ nodes)	1 in 2

RISK BY STAGE[6-8]

	Within 3 years, up to	Within 20 years
Stage II	12%	27%-37%
Stage III	21%	46%-57%

The 3- and 20-year risk of recurrence rates are derived from distinct data sets gathered from unique patient populations; there was no longitudinal follow-up between patient groups or points in time. These data reflect recent outcomes published for patients with HR+ eBC who may be appropriate for treatment with CDK4/6 inhibitors, 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.**[2,6,7,9]

3-year risk of recurrence rates are based on iDFS outcomes among patients with HR+/HER2- eBC who received ET in select CDK4/6 inhibitor clinical trials. Data are from control arms only; no comparisons should be made between results from CDK4/6 inhibitor arms. The 3-year data listed for stage III also include some patients with stage IIB disease, due to differentiated data breakouts between trials.[6,7]

20-year risk of recurrence rates are based on rates of distant recurrence in a meta-analysis of 78 randomized trials in the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) database of 74,194 women with ER+ breast cancer who had 5 years of scheduled ET. Rates include patients with T1/T2 disease and <10 involved nodes.[9]

ER+, estrogen receptor-positive; ET, endocrine therapy; N, nodal status; T, tumor size.

IMPORTANT SAFETY INFORMATION (continued)

Interstitial lung disease/pneumonitis (continued). 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 treatment with KISQALI in patients with severe ILD/pneumonitis or any recurrent symptomatic ILD/pneumonitis.

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KISQALI® ribociclib 200 mg tablets

In stage II/III HR+/HER2- eBC,

NATALEE—a positive study of KISQALI efficacy and safety in the broadest range of patients at risk of recurrence, including all those with node-positive or high-risk node-negative disease

NATALEE was a randomized, multicenter, open-label, phase III clinical trial of KISQALI + AI vs AI alone for the adjuvant treatment of HR+/HER2- eBC[2,5,10,11]

STUDY POPULATION (N=5101)

- Adults with HR+/HER2- eBC
- Pre- and postmenopausal women, men
- Diagnosed ≤18 months prior
- Anatomic stage II or III
- All high-risk node-negative or node-positive
  - N0: T2 (G2 + high genomic risk or Ki-67 ≥20% or G3), T3, T4
  - All N1
  - All N2
  - All N3

1:1 randomization

STUDY TREATMENT (3 YEARS)

KISQALI 400 mg/day (3 weeks on/1 week off) + AI* (n=2549)

AI alone* (n=2552)

AI continued for ≥5 years

LONG-TERM FOLLOW-UP
(up to ~91 months)

Select exclusion criteria[5]

- Prior treatment with a CDK4/6 inhibitor
- ECOG performance status ≥2
- Major surgery, chemotherapy, or radiotherapy within 14 days prior to randomization
- Treatment with tamoxifen, raloxifene, or AIs for reduction in risk of breast cancer and/or treatment for osteoporosis within the last 2 years

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.

ECOG, Eastern Cooperative Oncology Group; G, grade.
*Men and premenopausal women also received goserelin.[10]

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KISQALI® ribociclib 200 mg tablets

Reducing the risk of recurrence—including distant recurrence with incurable metastatic disease—was the primary treatment goal in NATALEE

Invasive disease-free survival (iDFS), the primary end point in NATALEE, includes local and distant recurrence and death, while distant disease-free survival (DDFS) excludes local recurrence[2,12]

EVENTS INCLUDED IN END POINTS

	PRIMARY	SECONDARY
	iDFS	DDFS
Invasive ipsilateral breast tumor recurrence	✓	–
Local/regional invasive recurrence	✓	–
Invasive contralateral breast cancer	✓	–
Distant recurrence	✓	✓
Death from breast cancer	✓	✓
Death from non–breast cancer cause	✓	✓
Death from unknown cause	✓	✓
Second primary non-breast invasive cancer (excluding basal and squamous cell carcinomas of the skin)	✓	✓

- iDFS and DDFS were defined as the time from randomization to the date of the first event[2,12]
- Overall survival (OS) is a secondary end point in NATALEE. At the time of iDFS final analysis, OS data were immature and analysis is ongoing[2]
- Health-related quality of life (HRQOL) is an additional secondary end point in NATALEE[12]

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.

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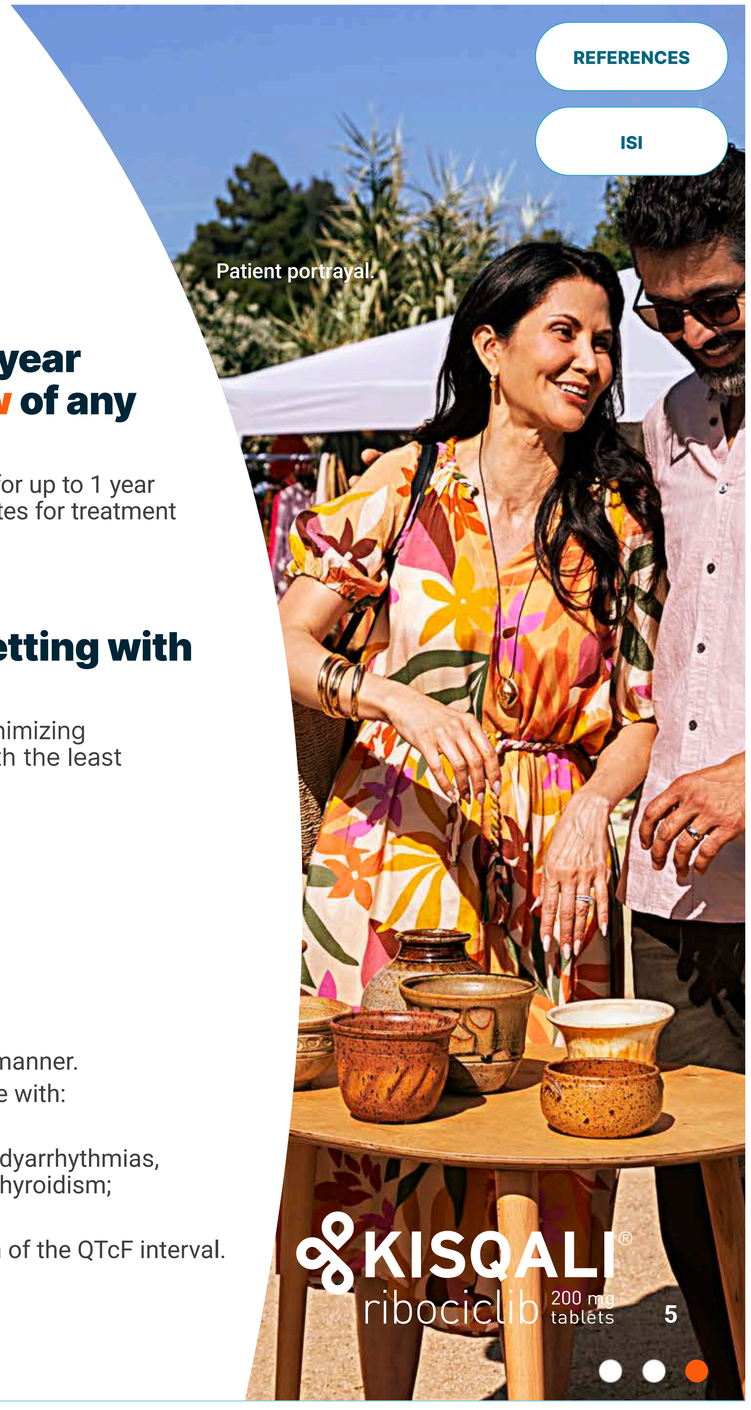
KISQALI® ribociclib 200 mg tablets

For stage II/III HR+/HER2- eBC,

The NATALEE trial was designed to help patients START & STAY on KISQALI + AI—whether new to adjuvant therapy or already on ET



Patients were eligible for KISQALI even with up to 1 year of prior ET—the most inclusive ET eligibility window of any positive CDK4/6 inhibitor trial in eBC[5-7]

- NATALEE is the only positive trial of a CDK4/6 inhibitor to allow endocrine-based therapy for up to 1 year prior to randomization, so patients who began ET within the last year may still be candidates for treatment with KISQALI

Dosing was intentionally chosen for the adjuvant setting with the goal of balancing efficacy and safety[5]

- NATALEE studied the 400-mg starting dose and 3-year duration with the goal of minimizing dose-dependent adverse reactions and adherence issues related to tolerability—with the least possible impact on efficacy

IMPORTANT SAFETY INFORMATION (continued)

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.

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

KISQALI is the only CDK4/6 inhibitor proven and FDA approved for all stage II/III node-positive and high-risk node-negative disease

KISQALI ELIGIBILITY IN STAGE II/III HR+/HER2- eBC BY NODAL STATUS[5]

N0	Without high-risk features	Tumor >2 cm and ≤5 cm G1 or G2 + no additional risk factors	–
	With high-risk features	Tumor >2 cm and ≤5 cm: G3 or G2 + Ki-67 ≥20% or HGR	✓
		Tumor >5 cm or tumor of any size with extension to the chest wall and/or skin	✓
N1		G1/G2 and tumor size <5 cm	✓
		G3 or tumor size ≥5 cm	✓
N2		All patients	✓
N3		All patients	✓

~50% of patients with stage II/III HR+/HER2- eBC have these characteristics[13]

KISQALI is the only FDA-approved CDK4/6 inhibitor for these patients

High genomic risk may be determined by any of the following test scores[10]:

- Oncotype DX®: ≥26
- Prosigna® PAM50: High risk
- MammaPrint®: High risk
- EndoPredict®: High risk

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.

FDA, US Food and Drug Administration; HGR, high genomic risk.

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.

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

KISQALI® ribociclib 200 mg tablets

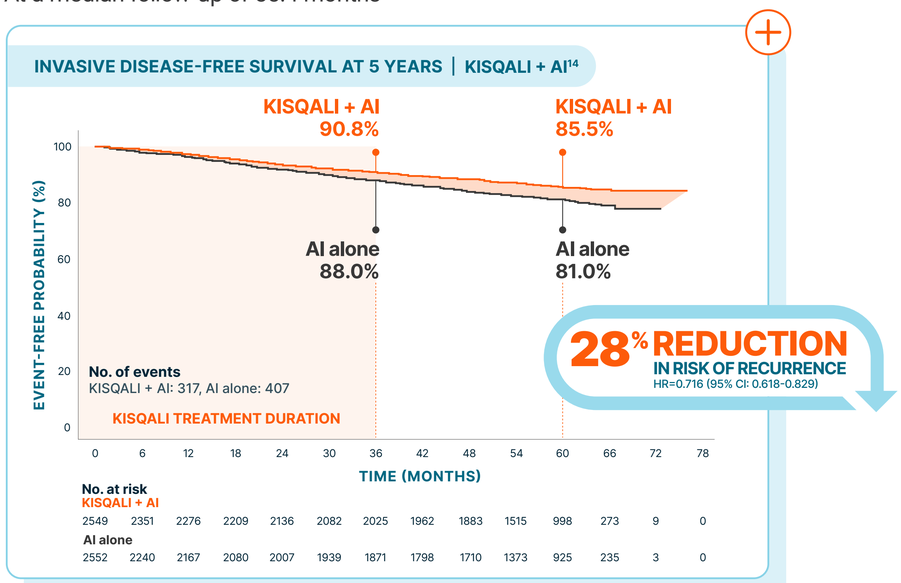
iDFS In patients with stage II/III HR+/HER2- eBC,

Over 5 years, KISQALI delivered a 28% reduction in the risk of recurrence

The iDFS benefit deepened over time with KISQALI + AI, beyond the 3-year treatment period[14]

NATALEE: KISQALI + AI vs AI alone

At a median follow-up of 55.4 months



Hazard ratio is based on stratified Cox model.[12]

In the 5-year prespecified analysis[14]:

- **At 3 years: 2.7% absolute difference***
- **At 5 years: 4.5% absolute difference**
- At the time of data cutoff, only 12.4% of patients receiving KISQALI + AI had experienced an iDFS event vs 15.9% of patients treated with AI alone
- The 5-year analysis was prespecified and observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error

In the 3-year final analysis (median follow-up of 33.3 months)[2,4]:

- **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)**

In an interim analysis, at a median follow-up of 28 months, a statistically significant reduction in risk was achieved despite the greater challenge of showing clinical benefit in a broad range of patients.[2,5,15]

KISQALI can help reduce the risk of recurrence, including distant recurrence with incurable metastatic disease

*The difference between percentages does not equal 2.7 due to rounding.[14]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI. There were no reported cases of torsades de pointes.

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, and MONALEESA-7) who received 600 mg KISQALI plus NSAI or fulvestrant, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >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.

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iDFS In patients with stage II/III HR+/HER2- eBC,

Over 5 years, KISQALI delivered a 28% reduction in the risk of recurrence

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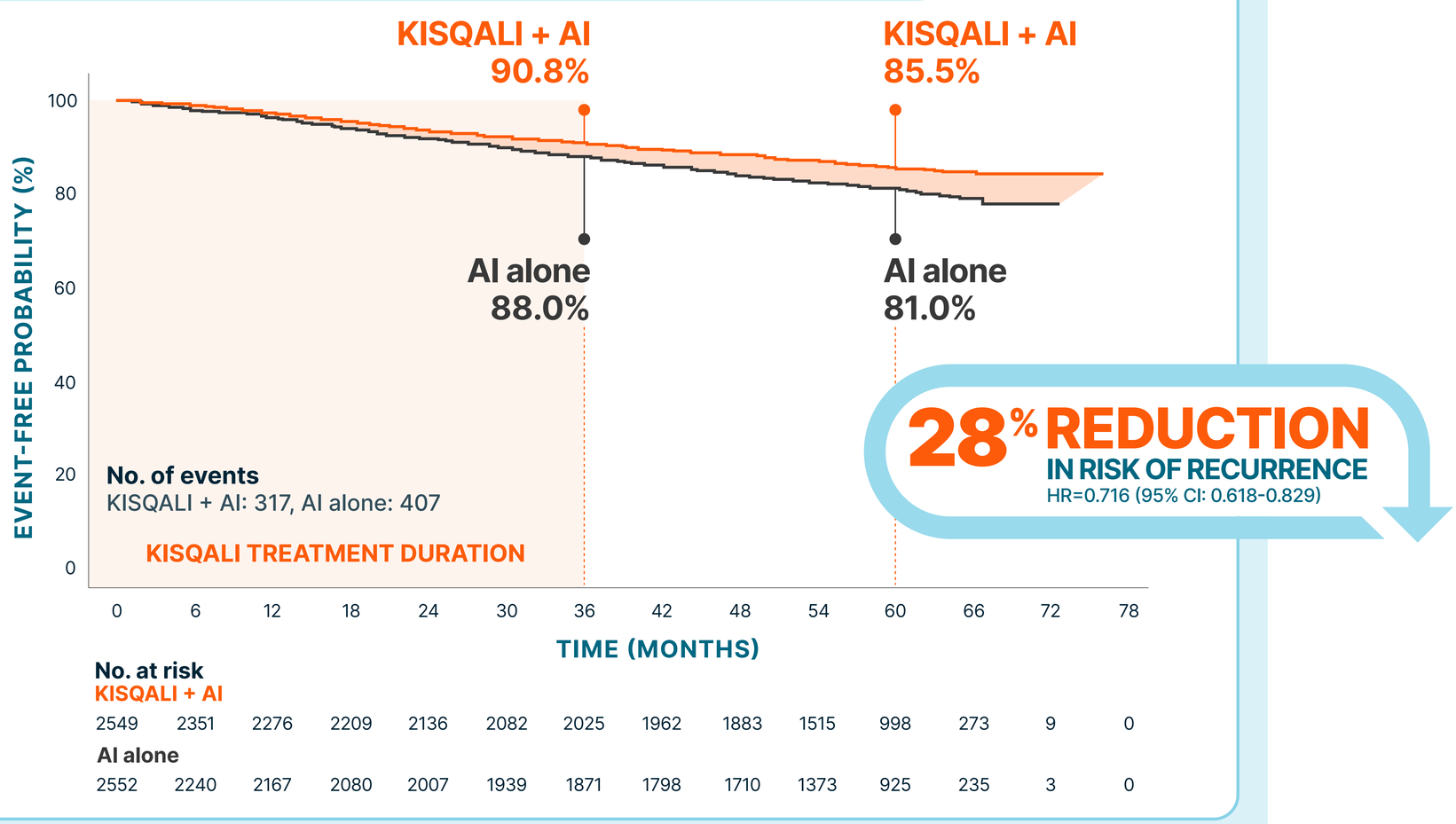
INVASIVE DISEASE-FREE SURVIVAL AT 5 YEARS | KISQALI + AI[14]



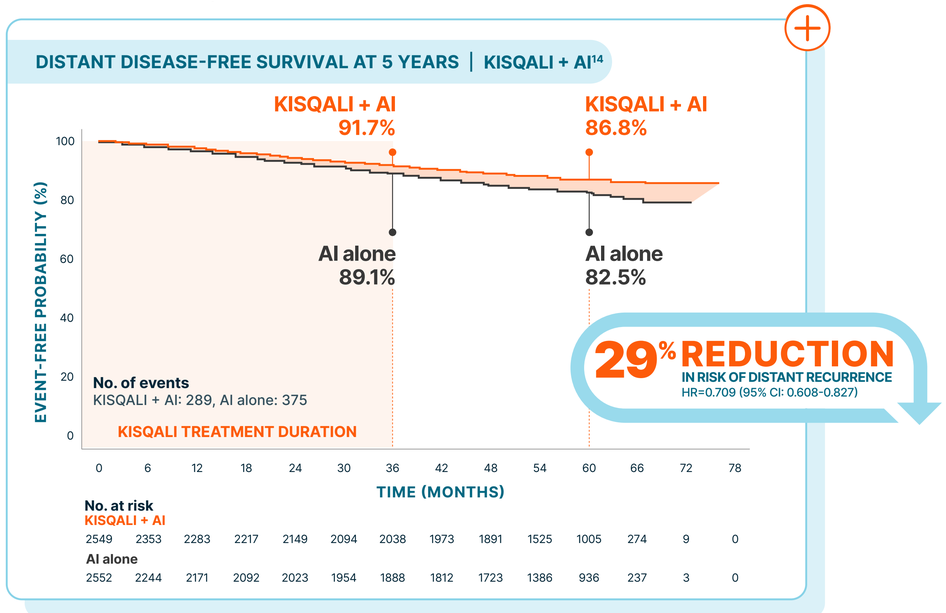
DDFS In patients with stage II/III HR+/HER2- eBC,

Over 5 years, KISQALI showed a 29% reduction in the risk of distant recurrence

The DDFS benefit was consistent with iDFS and increased over time with KISQALI + AI, beyond the treatment period[14]

NATALEE: KISQALI + AI vs AI alone

At a median follow-up of 55.5 months



In the 5-year prespecified analysis[14]:

- **At 3 years: 2.6% absolute difference**
- **At 5 years: 4.3% absolute difference**
- At the time of data cutoff, only 11.3% of patients receiving KISQALI + AI had experienced a DDFS event vs 14.7% of patients treated with AI alone
- The 5-year analysis was prespecified and observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error

KISQALI can help reduce the risk of distant recurrence with incurable metastatic disease

Hazard ratio is based on stratified Cox model.[12]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). There were no reported cases of torsades de pointes. In MONALEESA-2, in the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-7 or MONALEESA-3.

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.

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DDFS In patients with stage II/III HR+/HER2- eBC,

Over 5 years, KISQALI showed a 29% reduction in the risk of di

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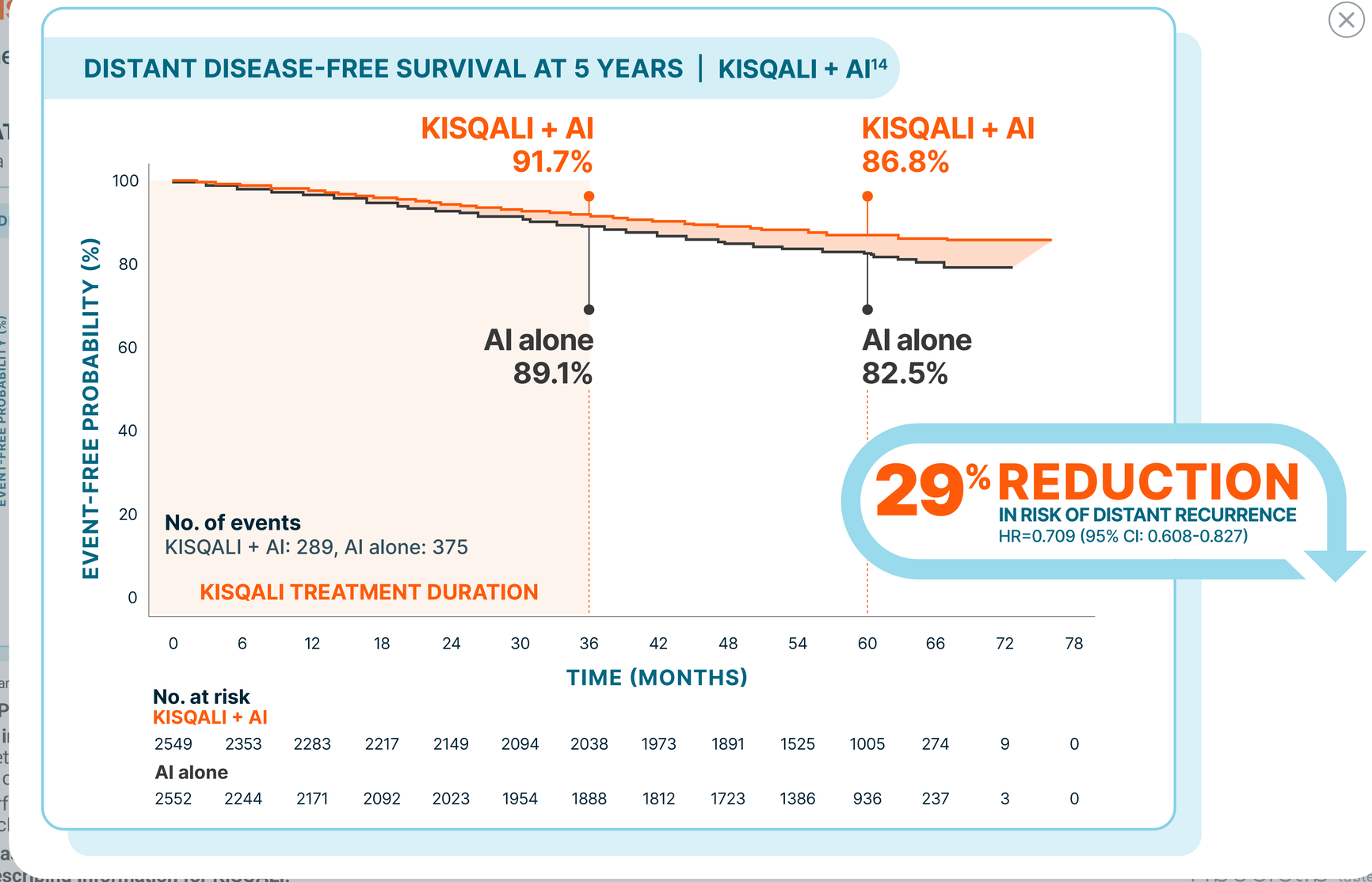

5-YEAR iDFS SUBGROUPS

In patients with stage II/III HR+/HER2- eBC,

KISQALI + AI consistently improved iDFS across subgroups, regardless of stage, nodal status, or menopausal status

iDFS results favored KISQALI across prespecified subgroups, including no nodal involvement[14]

ANATOMIC STAGE		
Stage II	✓	HR=0.660 (95% CI: 0.493-0.884)
Stage III	✓	HR=0.730 (95% CI: 0.615-0.865)
NODAL STATUS*		
N0	✓	HR=0.606 (95% CI: 0.372-0.986)
N1, N2, N3	✓	HR=0.737 (95% CI: 0.631-0.860)
MENOPAUSAL STATUS		
Premenopausal/men	✓	HR=0.714 (95% CI: 0.565-0.902)
Postmenopausal	✓	HR=0.734 (95% CI: 0.608-0.887)

In the NATALEE trial, KISQALI consistently reduced the threat of recurrence in the broadest range of patients, including those with no nodal involvement

Results from the subgroup analysis included no prespecified statistical procedure controlling for type 1 error.

AJCC, American Joint Committee on Cancer.
Hazard ratios reported as KISQALI + AI vs AI alone.
*Nodal status classification according to AJCC staging. Nodal status is from the worst stage derived per surgical specimen or at diagnosis.[14]

With 33.3 months of follow-up, in the adjuvant setting, for patients with stage II/III HR+/HER2- eBC,

No new safety signals were observed with KISQALI

ADVERSE REACTIONS (≥10% AND ≥2% HIGHER THAN AI-ALONE ARM) IN NATALEE[2]

	KISQALI + AI (n=2526)		AI alone (n=2441)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
INFECTIONS AND INFESTATIONS				
Infections*	37	2	27	0.9
NERVOUS SYSTEM DISORDERS				
Headache	23	0.4†	17	0.2†
GASTROINTESTINAL DISORDERS				
Nausea	23	0.2†	8	0.1†
Diarrhea	15	0.6†	6	0.1†
Constipation	13	0.2†	5	0
Abdominal pain	11	0.5†	7	0.4†
GENERAL DISORDERS AND ADMINISTRATION-SITE CONDITIONS				
Fatigue	22	0.8†	13	0.2†
Asthenia	17	0.6†	12	0.1†
Pyrexia	11	0.2†	6	0.1†
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Alopecia	15	0	4.6	0
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS				
Cough	13	0.1†	8	0.1†

The NATALEE trial was designed to maximize the efficacy benefit of KISQALI while minimizing dose-dependent ARs and adherence issues related to tolerability[5]

- 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[2]
- 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[2]
- 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%)[2]
- In the NATALEE trial, no new safety signals were observed at 5 years of follow-up[14]

Grading according to CTCAE version 4.03.
*Infections included urinary and respiratory tract infections.
†Only includes grade 3 ARs.

ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events.

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KISQALI® ribociclib 200 mg tablets

With 33.3 months of follow-up, in the adjuvant setting, for patients with stage II/III HR+/HER2- eBC,

No new lab abnormalities were observed with KISQALI

SELECT LABORATORY ABNORMALITIES (≥10%) IN NATALEE[2]

	KISQALI + AI (n=2526)		AI alone (n=2441)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
HEMATOLOGY				
Lymphocyte count decreased	97	19	88	6
Leukocyte count decreased	95	27	45	0.6
Neutrophil count decreased	94	45	35	1.7
Hemoglobin decreased	47	0.6	26	0.3
Platelet count decreased	28	0.4	13	0.3
CHEMISTRY				
ALT increased	45	8	35	1
AST increased	44	5	33	1
Creatinine increased	33	0.3	11	0

- Grade 4 increases in ALT (1.5%) and AST (0.8%) were reported in the KISQALI + AI arm[2]
- 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 of which were improving, all after discontinuation of KISQALI[2]
- In the NATALEE trial, no new lab abnormalities were observed at 5 years of follow-up[14]

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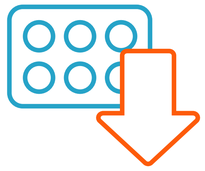
KISQALI® ribociclib 200 mg tablets

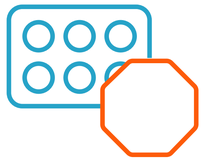
In stage II/III HR+/HER2- eBC,

With KISQALI, most adverse reactions were manageable and reversible with dose reduction, which may have helped patients remain on therapy



Rate of dose reductions due to ARs[16]

KISQALI + AI: 23.2% | **AI alone: 0%**



Rate of discontinuation due to ARs[16]

KISQALI + AI: 20.8% | **AI alone: 5.5%**

- Median time to KISQALI discontinuation was 4.2 months[17]

In NATALEE, the leading cause of discontinuation was asymptomatic laboratory findings such as increases in ALT or AST, not symptomatic ARs such as diarrhea, fatigue, and nausea

In NATALEE, the leading causes of KISQALI + AI discontinuation (occurring in ≥2% of patients) were increases in ALT or AST (8%).[2]

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity. In patients with eBC and advanced or mBC, 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%).

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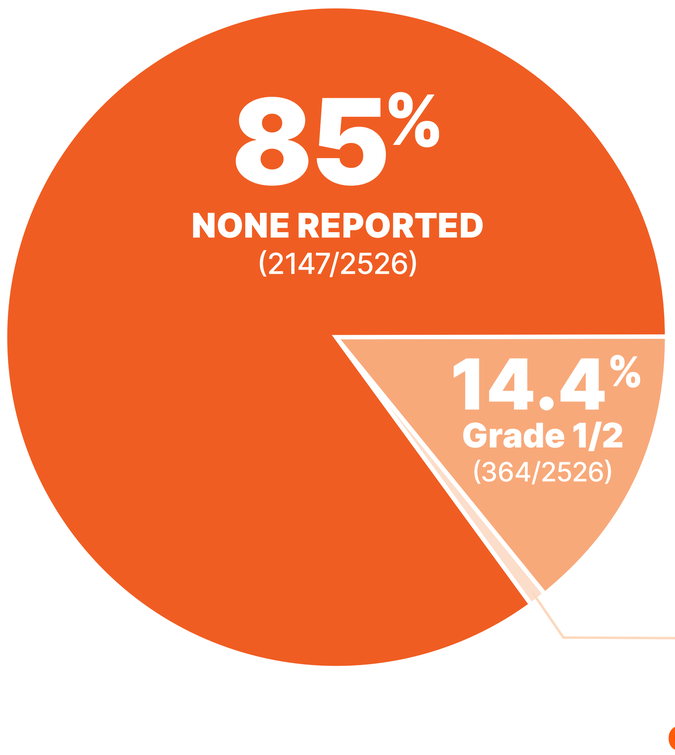
In the NATALEE clinical trial,

Reported rates of diarrhea were low with KISQALI

Diarrhea rates in NATALEE[2]



Diarrhea can be disruptive in many ways—from a daily, unpredictable inconvenience to a debilitating, even life-threatening condition[18]

- **Grade 1:** <4 stools/day over baseline; mild increase in ostomy output
- **Grade 2:** 4 to 6 stools per day over baseline; moderate increase in ostomy output; limiting instrumental ADL
- **Grade 3:** ≥7 stools per day over baseline; hospitalizations indicated; severe increase in ostomy output; limiting self-care ADL
- **Grade 4:** Life-threatening; urgent intervention indicated
- **Grade 5:** Death

ADL, activities of daily living.

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity (continued). In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) treated with KISQALI, grade 3 or 4 increases in ALT and AST occurred in 11% and 8%, respectively. Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 92 days for the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. The median time to resolution to grade ≤2 was 21 days in the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST >3x ULN and total bilirubin >2x ULN, with normal alkaline phosphatase, in the absence of cholestasis (Hy's Law) occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI.

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

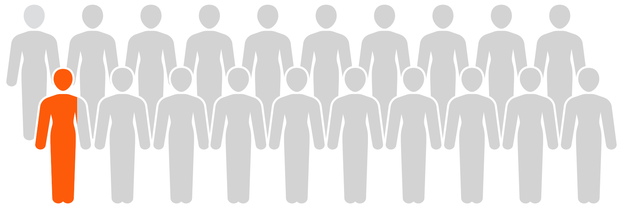
KISQALI® ribociclib 200 mg tablets

In patients with stage II/III HR+/HER2- eBC,

Incidence of QT prolongation observed with KISQALI was low

INCIDENCE OF QT PROLONGATION IN THE NATALEE TRIAL[2,19]

All grades: **4.3%**



Grade ≥3: **0.3%**

Most cases of QT prolongation were moderate and reversible, and the majority occurred within the first 4 weeks of treatment

Among cases of QT prolongation[2]:

- **0.3%** had a >500 ms postbaseline QTcF value
- **2%** had a >60 ms increase from baseline in QTcF interval
- There were **no reported cases** of torsades de pointes

QTcF, QT interval corrected by Fridericia's formula.

IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity (continued). 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.

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

KISQALI® ribociclib 200 mg tablets

In stage II/III HR+/HER2- eBC,

Patient-reported health-related quality of life with KISQALI + AI vs AI alone

In NATALEE, physical functioning from the EORTC QLQ-C30 was the prespecified primary HRQOL outcome of interest[20,21]

Physical functioning	**Change from baseline (median follow-up 34 months)*:** **KISQALI + AI: -1.50** AI alone: -1.34 Range of -5 to 2 equates to no clinically meaningful difference according to established threshold for interpreting changes in physical functioning score

- HRQOL was a secondary end point measured by patient-reported outcomes and was assessed at baseline, every 12 weeks for the first 24 months of treatment and every 24 weeks after that, at end of treatment, at confirmation of first recurrence, and every 12 or 24 weeks after confirmation of distant recurrence[20]
- There was no prespecified statistical procedure controlling for type 1 error
- The HRQOL measures used in the NATALEE trial are not all inclusive and do not include assessment of all disease- or treatment-related symptoms

Additional HRQOL outcomes from the EORTC QLQ-C30 in NATALEE[20,21]

MEASURE	CHANGE FROM BASELINE (median follow-up 34 months)
Global health status	**Change from baseline†:** **KISQALI + AI: -3.10** AI alone: -1.96 Range of -5 to 5 equates to no clinically meaningful difference according to established threshold for interpreting changes in global health status score
Social functioning	**Change from baseline‡:** **KISQALI + AI: 0.26** AI alone: 1.39 Range of -6 to 3 equates to no clinically meaningful difference according to established threshold for interpreting changes in social functioning score
Emotional functioning	**Change from baseline§:** **KISQALI + AI: -4.52** AI alone: -3.97 Range of -3 to 6 equates to no clinically meaningful difference according to established threshold for interpreting changes in emotional functioning score

*Standard deviation from baseline values was 14.87 for KISQALI + AI treatment arm and 14.87 for AI alone; all changes were within 0.5 SD of baseline values.[20]
†Standard deviation from baseline values was 17.67 for KISQALI + AI treatment arm and 17.77 for AI alone; all changes were within 0.5 SD of baseline values.[20]
‡Standard deviation from baseline values was 22.55 for KISQALI + AI treatment arm and 22.36 for AI alone; all changes were within 0.5 SD of baseline values.[20]
§Standard deviation from baseline values was 20.07 for KISQALI + AI treatment arm and 19.51 for AI alone; all changes were within 0.5 SD of baseline values.[20]

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; SD, standard deviation.

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia (continued). In patients with advanced or metastatic breast cancer (MONALEESA-2, MONALEESA-7, and MONALEESA-3) who received KISQALI plus NSAI or fulvestrant, 75% had neutropenia, 62% had grade 3/4 decrease in neutrophil count (based on laboratory findings), and 1.7% had febrile neutropenia. The median time to grade ≥2 neutropenia was 17 days. The median time to resolution of grade ≥3 neutropenia to grade <3 was 12 days. Treatment discontinuation due to neutropenia was required in 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.

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

KISQALI® ribociclib 200 mg tablets

For your patients with stage II/III HR+/HER2- eBC,

Complete most of the scheduled assessments for KISQALI within the first 2 months of therapy—with none beyond Cycle 6

Assessment[2]	Baseline	Cycle 1	Cycle 2		Cycles 3-6
		Day 14	Day 1	Day 14	Day 1
CBC and LFT	✓	✓	✓	✓	✓
Electrolytes	✓	–	✓	–	✓
ECG	✓	✓	–	–	–

Routine monitoring for lab abnormalities[2]

- Blood tests are performed at baseline, on Day 14 of Cycle 1, on Days 1 and 14 of Cycle 2, on Day 1 of Cycles 3 through 6, and as clinically indicated
- Additional monitoring may be required as clinically indicated

2 required ECG assessments completed within the first 2 weeks of treatment[2]

- ECGs are performed at baseline, on Day 14 of Cycle 1, and as clinically indicated
- KISQALI should only be initiated in patients with QTcF <450 ms
- In case of QTcF prolongation during therapy, more frequent assessments are recommended
- Additional assessments may be required as clinically indicated

CBC, complete blood count; ECG, electrocardiogram; LFT, liver function test.

IMPORTANT SAFETY INFORMATION (continued)

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 in early breast cancer patients. Most common (incidence ≥20%) adverse reactions include infections, nausea, headache, and fatigue.

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

KISQALI® ribociclib 200 mg tablets

For your patients with stage II/III HR+/HER2- eBC,

Start with KISQALI 400 mg—the starting dose chosen to reduce both the risk of recurrence and dose-dependent adverse reactions

(28-day cycle)[2]	Week 1	Week 2	Week 3	Week 4	Subsequent cycles
KISQALI: 2 tablets (2 x 200 mg)	✓	✓	✓	-	Repeat 28-day cycle
AI	✓	✓	✓	✓	

- 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[2]
  - Review the full Prescribing Information for recommended dosing of selected AI
  - An LHRH agonist should be used concomitantly with AI in men and premenopausal women
  - Patients should continue treatment for 3 years or until disease recurrence or unacceptable toxicity
  - KISQALI can be taken with or without food
  - Store at room temperature at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F)
  - Store in the original blister package in order to protect from moisture

LHRH, luteinizing hormone-releasing hormone.

IMPORTANT SAFETY INFORMATION (continued)

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**.

Adverse reactions in advanced or metastatic breast cancer patients. Most common (incidence ≥20%) adverse reactions include infections, nausea, fatigue, diarrhea, vomiting, headache, constipation, alopecia, cough, rash, and back pain.

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

For your patients with stage II/III HR+/HER2- eBC,

KISQALI single-strength tablets make dose reduction SIMPLE & CONVENIENT

Dose reductions with KISQALI mean no need for new mid-cycle prescriptions or additional costs[2]

Dose adjustments for ARs should be made by reducing the number of tablets taken[2]

- If dose reduction below 200 mg/day is required, discontinue treatment
- KISQALI dose modification is recommended based on individual safety and tolerability
- KISQALI can be taken with or without food

In the NATALEE trial, iDFS benefit was maintained for patients who required KISQALI dose reduction

Lowering the dose of KISQALI can help address side effects and, in the NATALEE trial, did not impact efficacy.[2,22]

- 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])[22]

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.

IMPORTANT SAFETY INFORMATION (continued)

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, AST increased, gamma-glutamyl transferase increased, ALT increased, creatinine increased, platelets decreased, and glucose serum decreased**.

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

KISQALI® ribociclib 200 mg tablets

KISQALI—broad access and coverage to help make treatment available for more of your patients

For the majority of patients with prescription drug insurance coverage, all or nearly all of the cost of KISQALI is covered, and prior authorizations are approved within 1 day

For Medicare members, nearly

85% of KISQALI out-of-pocket costs were between **$0** and **$20** per month[23]

For patients with commercial insurance, nearly

80% of KISQALI out-of-pocket costs were between **$0** and **$50** per month[23]

More than

85% of KISQALI PAs are approved in less than **24 hours**[24]

More than 9 out of 10 patients have preferred formulary coverage for KISQALI[25]

Unrestricted coverage from MMIT data as of July 2025.

PA, prior authorization.
Novartis does not guarantee payment or coverage for any product or service. Actual coverage and reimbursement decisions are made by individual payers following receipt of claims. Coverage is subject to change by the relevant payer.

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

KISQALI® ribociclib 200 mg tablets

Novartis Patient Support™—a dedicated team for your patients

Novartis Patient Support is a comprehensive program that is designed to help your eligible patients start, stay, and save on KISQALI

We support your patient's journey with:

Insurance Support
Help navigating the insurance process, including benefits verification

Financial Support
Assistance with connecting patients to relevant savings options

Clinical Testing and Support
Workflow support and options for testing

Ongoing Support
Dedicated assistance from our team and educational resources

To learn more, contact your dedicated Novartis Patient Support team at 866-433-8000

Monday-Friday, 8:00 AM - 8:00 PM ET, excluding holidays

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

Do MORE today to help protect their tomorrow

KISQALI + AI is proven to help reduce the risk of recurrence in patients with stage II or III HR+/HER2- eBC at high risk of recurrence—so they can live the lives they love

Patient portrayal.

REFERENCES

ISI

- The only CDK4/6 inhibitor FDA approved for all patients with stage II/III node-positive and high-risk node-negative HR+/HER2- eBC[2,5]
- Reduced risk of recurrence, including distant recurrence with incurable metastatic disease—a benefit that increased over time, beyond the 3-year treatment period[14]
- Consistently improved iDFS across subgroups, regardless of stage, nodal status, or menopausal status[14,16]
- No new safety signals observed in the adjuvant setting[2]

#1 PRESCRIBED

KISQALI is the most prescribed CDK4/6 inhibitor in HR+/HER2- breast cancer[26]

July 2025 IQVIA custom breast cancer market sizing report.

NATALEE was a randomized, multicenter, open-label, phase III study of KISQALI + 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). At a median follow-up of 33.3 months, with 509 iDFS (primary end point) events in the study (226 [8.9%] in the KISQALI arm and 283 [11.1%] in the NSAI-alone arm), iDFS 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). With 460 DDFS (secondary end point) events in the study (204 [8%] in the KISQALI arm and 256 [10%] in the NSAI-alone arm), DDFS at the 3-year landmark was 92.9% for KISQALI + NSAI vs 90.2% for NSAI alone **(absolute difference 2.7%)**; there was a 25.1% relative reduction in the risk of a DDFS event; HR=0.749 (95% CI: 0.623-0.900). In the 5-year prespecified analysis, prespecified subgroups included anatomic stage (stage II: HR=0.660 [95% CI: 0.493-0.884]; stage III: HR=0.730 [95% CI: 0.615-0.865]), nodal status (N0: HR=0.606 [95% CI: 0.372-0.986]; N1, N2, N3: HR=0.737 [95% CI: 0.631-0.860]), and menopausal status (premenopausal/men: HR=0.714 [95% CI: 0.565-0.902]; postmenopausal: HR=0.734 [95% CI: 0.608-0.887]). Results from the subgroup analysis included no prespecified statistical procedure controlling for type 1 error. In the 5-year prespecified analysis, at a median follow-up of 55.4 months, with 724 iDFS events in the study (317 [12.4%] in the KISQALI arm and 407 [15.9%] in the NSAI-alone arm), iDFS at the 5-year landmark was 85.5% for KISQALI + NSAI vs 81.0% for NSAI 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). At a median follow-up of 55.5 months, with 664 DDFS events in the study (289 [11.3%] in the KISQALI arm and 375 [14.7%] in the NSAI-alone arm), DDFS at the 5-year landmark was 86.8% for KISQALI + NSAI vs 82.5% for NSAI 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). The 5-year analysis was prespecified and observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[2,4,10,14]

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 5 years of follow-up.[2,14,16]

*Infections included urinary and respiratory tract infections.[2]
†Only includes grade 3 ARs.[2]

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.

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

KISQALI® ribociclib 200 mg tablets

References

References: 1. 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 April 17, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **3.** Data on file. mBC and eBC NBRx share data from IQVIA market sizing report. Novartis Pharmaceuticals Corp; 2025. **4.** 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 **5.** Slamon DJ, Fasching PA, Hurvitz S, et al. 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Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI.

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
- for the treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer (mBC) in combination with:
  - an aromatase inhibitor as initial endocrine-based therapy; or
  - fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy

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).

In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, MONALEESA-7), 1.6% of patients had ILD/pneumonitis of any grade, 0.4% had grade 3/4, and 0.1% had a fatal outcome. Additional cases of ILD/pneumonitis have occurred in the postmarketing setting, some resulting in death.

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 treatment with 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.

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). In patients with advanced or mBC (MONALEESA-2, MONALEESA-3, and MONALEESA-7) who received 600 mg KISQALI plus NSAI or fulvestrant, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >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. In MONALEESA-2, in the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-7 or MONALEESA-3.

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.

Hepatotoxicity. In patients with eBC and advanced or mBC, 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%).

In patients with advanced or mBC (MONALEESA-2, MONALEESA-7, and MONALEESA-3) treated with KISQALI, grade 3 or 4 increases in ALT and AST occurred in 11% and 8%, respectively. Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 92 days for the KISQALI plus aromatase inhibitor or fulvestrant treatment arms. The median time to resolution to grade ≤2 was 21 days in the KISQALI plus aromatase inhibitor or fulvestrant treatment arms.

In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST >3x ULN and total bilirubin >2x ULN, with normal alkaline phosphatase, in the absence of cholestasis (Hy's Law) occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI.

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.

In patients with advanced or metastatic breast cancer (MONALEESA-2, MONALEESA-7, and MONALEESA-3) who received KISQALI plus NSAI or fulvestrant, 75% had neutropenia, 62% had grade 3/4 decrease in neutrophil count (based on laboratory findings), and 1.7% had febrile neutropenia. The median time to grade ≥2 neutropenia was 17 days. The median time to resolution of grade ≥3 neutropenia to grade <3 was 12 days. Treatment discontinuation due to neutropenia was required in 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.

IMPORTANT SAFETY INFORMATION (continued)

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 in early breast cancer patients. 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**.

Adverse reactions in advanced or metastatic breast cancer patients. Most common (incidence ≥20%) adverse reactions include infections, nausea, fatigue, diarrhea, vomiting, headache, constipation, alopecia, cough, rash, and back pain.

Laboratory abnormalities. Across clinical trials of patients with advanced or metastatic breast cancer, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, AST increased, gamma-glutamyl transferase increased, ALT increased, creatinine increased, platelets decreased, and glucose serum decreased**.

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

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