A treatment guide to help your patients

START & STAY on KISQALI

NCCN CATEGORY 1 | National Comprehensive Cancer Network® (NCCN®) **differentiates ribociclib (KISQALI®) as the only Category 1 Preferred 1L treatment option** in combination with an AI for appropriate patients with HR+/HER2- mBC[1]

There is controversy on the choice of CDK4/6i as there are no head-to-head comparisons between the agents and there are some differences in the study populations in the phase III randomized studies. 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.

MONALEESA-2, statistically significant OS in 1L postmenopausal patients: At a median follow-up of 80 months, mOS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with placebo + letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004. OS was a secondary end point; PFS was the primary end point.[2-4]

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).[2,5]

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

eBC
mBC
SUMMARY
SUPPORT & RESOURCES

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 those with no nodal involvement

NATALEE was a randomized, multicenter, open-label, phase III clinical trial of KISQALI + AI (n=2549) vs AI alone* (n=2552) in the adjuvant treatment of HR+/HER2- eBC[2,6]

Study population[2,7]

- 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

Key end points[6]

Primary

- Invasive disease-free survival (iDFS)

Secondary

- Distant disease-free survival (DDFS)
- Health-related quality of life (HRQOL)
- Overall survival (OS) (ongoing)

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

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.

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

KISQALI® ribociclib 200 mg tablets

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

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

Patients were eligible for KISQALI even with up to 12 months of prior ET—the most inclusive ET eligibility window of any positive CDK4/6 inhibitor trial in eBC[7]

- NATALEE is the only positive trial of a CDK4/6 inhibitor to allow endocrine-based therapy for up to 12 months prior to randomization, so patients who began ET within the last year may still be candidates for treatment with KISQALI

Adjuvant dosing studied with the goal of balancing efficacy and adherence[7]

- The 400-mg starting dose and 3-year duration were chosen for the adjuvant setting 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)

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.

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

KISQALI® ribociclib 200 mg tablets

KISQALI—IDENTIFY & TREAT patients with confidence

KISQALI is proven to help the broadest range of patients with stage II/III HR+/HER2- eBC[5,7,8]

Patient portrayals.

Regardless of...

- NODAL STATUS
- TUMOR SIZE
- TUMOR GRADE
- AGE (≥18 YEARS)
- MENOPAUSAL STATUS

Consider KISQALI for your patients

Patients with stage IIA, T2N0 HR+/HER2- eBC must meet the following criteria to be eligible for treatment with KISQALI: grade 3, or grade 2 with Ki-67 ≥20% or high genomic risk.[7]

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.

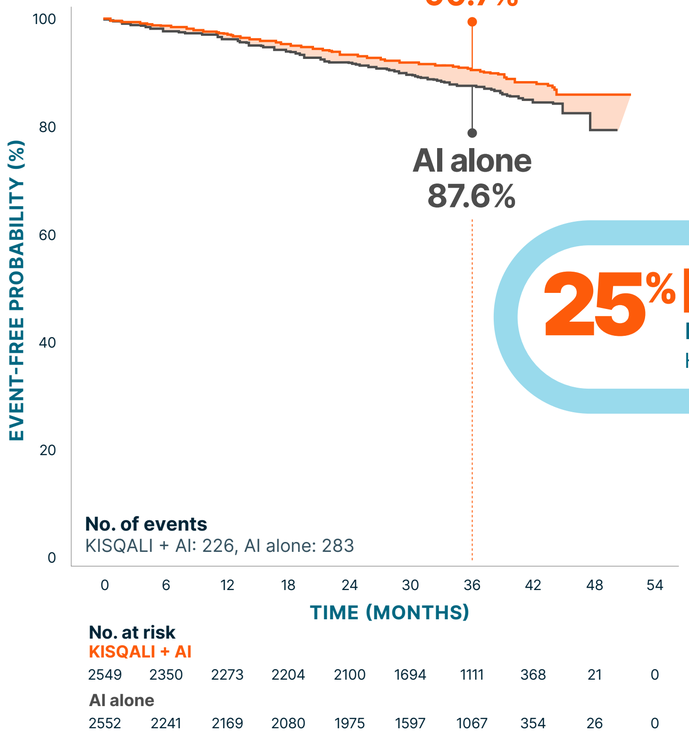
KISQALI® ribociclib 200 mg tablets

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

25% reduction in the risk of recurrence

NATALEE: KISQALI + AI vs AI alone

At a median follow-up of 33.3 months



Hazard ratio is based on stratified Cox model.[9]

Results were consistent across the key secondary end point of distant disease-free survival (DDFS) and all prespecified iDFS subgroups—regardless of anatomic stage, nodal or menopausal status, age, or grade[5,8]

- **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)[2]
- **DDFS was defined as** the time from randomization to the date of the first event of distant recurrence, second primary non-breast invasive cancer (excluding basal and squamous cell carcinomas of the skin), or death (any cause)[9]

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. 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). Prespecified subgroups included anatomic stage (stage II: HR=0.700 [95% CI: 0.496-0.986]; stage III: HR=0.755 [95% CI: 0.616-0.926]), nodal status (N0: HR=0.723 [95% CI: 0.412-1.268]; N1, N2, N3: HR=0.759 [95% CI: 0.631-0.912]), menopausal status (premenopausal/men: HR=0.688 [95% CI: 0.519-0.913]; postmenopausal: HR=0.806 [95% CI: 0.645-1.007]), age (<45 years: HR=0.652 [95% CI: 0.443-0.959]; 45 to 54 years: HR=0.799 [95% CI: 0.578-1.104]; 55 to 64 years: HR=0.871 [95% CI: 0.636-1.193]; ≥65 years: HR=0.662 [95% CI: 0.444-0.986]), histological grade at time of surgery (grade 1: HR=0.708 [95% CI: 0.303-1.657]; grade 2: HR=0.696 [95% CI: 0.548-0.885]; grade 3: HR=0.890 [95% CI: 0.658-1.204]). Grade 1 subgroup did not include patients with T2N0 disease. Results from the subgroup analysis included no prespecified statistical procedure controlling for type 1 error.[2,5,6,8]

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.

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

KISQALI® ribociclib 200 mg tablets

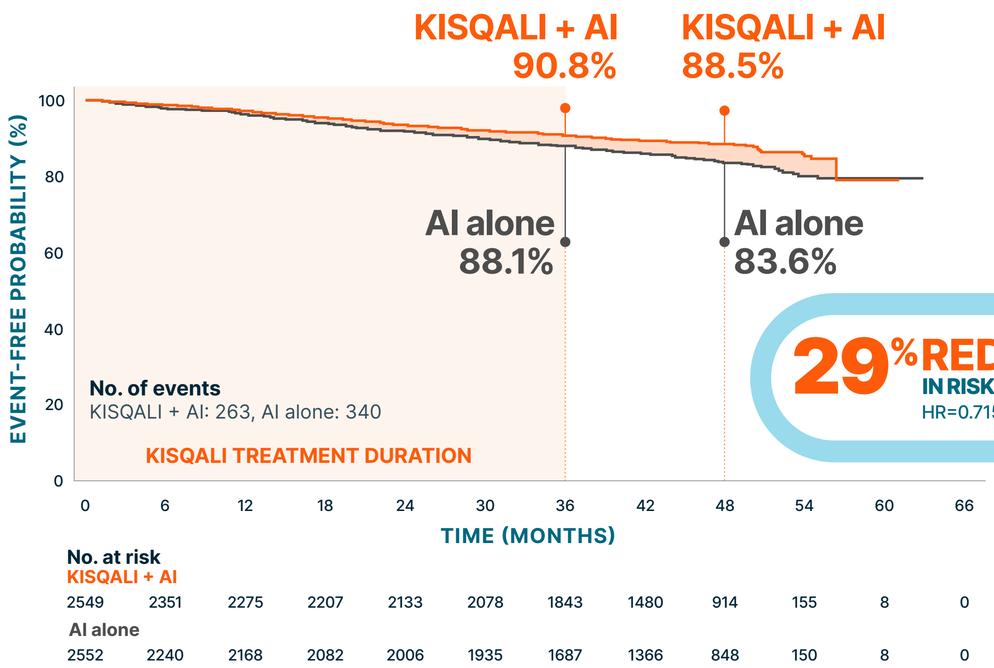
4-YEAR iDFS In patients with stage II/III HR+/HER2- eBC,

The iDFS benefit increased over time with KISQALI—beyond the 3-year treatment period

NATALEE: KISQALI + AI vs AI alone

At a median follow-up of 44 months

INVASIVE DISEASE-FREE SURVIVAL AT 4 YEARS | KISQALI + AI[10]



29% REDUCTION IN RISK OF RECURRENCE
HR=0.715 (95% CI: 0.609-0.840)

Hazard ratio is based on stratified Cox model.[9]

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).[2]

- **At 4 years, the absolute difference in iDFS was 4.9%[10]**
- 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[10]
- A statistically significant reduction in risk was achieved despite the greater challenge of showing clinical benefit in a broad range of patients[2,7]
- 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

For patients with HR+/HER2- eBC, KISQALI can help reduce the risk of recurrence, including recurrence with incurable metastatic disease

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.

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

KISQALI® ribociclib 200 mg tablets

In the adjuvant setting, for patients with stage II/III HR+/HER2- eBC,

Do more today to help protect their tomorrow

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

Please see safety section.

IN THE NATALEE TRIAL[2,5,7,8]

✓ SAFETY

No new safety signals were observed with KISQALI in the adjuvant setting.

✓ TOLERABILITY

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.

✓ ADHERENCE

Most ARs with KISQALI were manageable and reversible with dose reduction, which may have helped patients remain on therapy.

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 arm [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 and 0% with NSAI alone; rate of discontinuation due to ARs was 20.8% with KISQALI + NSAI and 5.5% with NSAI alone. The leading causes of KISQALI + NSAI 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%). No new safety signals were observed at 4 years of follow-up.[2,8,10]

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

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.

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[11,12]

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

Additional HRQOL outcomes from the EORTC QLQ-C30 in NATALEE [11,12]

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

- 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[11]
- 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

*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.
†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.
‡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.
§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.

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.

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	✓	✓	–	–	–

Assessment requirements based on a 28-day treatment cycle.

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

Speak with your Novartis Oncology Specialist or Clinical Educator about a simple solution for fast, easy, and accurate ECG testing with in-office or direct-to-patient options

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 monitoring may be required as clinically indicated.

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%).

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 ARs

(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	✓	✓	✓	✓	

Starting dose modification for severe renal impairment[2]

- The recommended starting dose is 200 mg once daily for patients with severe renal impairment

- 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 until disease progression or unacceptable toxicity
  - KISQALI can be taken with or without food
  - Store refrigerated at 2°C to 8°C (36°F to 46°F). Excursions permitted between 2°C and 15°C (36°F and 59°F)
  - After dispensing, patients may store at room temperature at 20°C to 25°C (68°F to 77°F) for up to 2 months
  - Store tablets in the original blister pack

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

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

KISQALI single-strength tablets make dose reduction simple and convenient

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

Starting dose

2 TABLETS (400 mg)

Reduction

1 TABLET (200 mg)

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 to manage ARs

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

Straightforward dose adjustments

ILD/PNEUMONITIS[2]

Grade 1 (asymptomatic)	No dose interruption or adjustment is required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 2 (symptomatic)	Interrupt dose until recovery to grade ≤1, then consider resuming KISQALI at the next lower dose level • If grade 2 recurs, discontinue
Grade 3 (severe symptomatic) **or grade 4**	Discontinue

- For grade 2 ILD/pneumonitis, an individualized benefit-risk assessment should be performed when considering resuming KISQALI

CUTANEOUS ADVERSE REACTIONS, INCLUDING SCARs[2]

Grade 1 or grade 2 (<10% or 10%-30% of BSA, respectively, with active skin toxicity, no signs of systemic involvement)	No dose adjustment is required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 3 (severe rash not responsive to medical management; >30% BSA with active skin toxicity, signs of systemic involvement present; SJS)	Interrupt KISQALI until the etiology of the reaction has been determined. If etiology is not a SCAR, • Interrupt dose until recovery to grade ≤1; resume at same dose level • If grade 3 reaction recurs, resume at next lower dose level If etiology is a SCAR, permanently discontinue KISQALI
Grade 4 (any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences; TEN)	Permanently discontinue

- SJS (grades 3 and 4) is skin sloughing covering <10% BSA and 10%-30% BSA, respectively, with associated signs. TEN (grade 4) is defined as skin sloughing covering ≥30% BSA with associated symptoms
  - Signs and symptoms of SJS and TEN include erythema, purpura, epidermal detachment, and mucous membrane detachment

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

KISQALI® ribociclib 200 mg tablets

Straightforward dose adjustments (continued)

NEUTROPENIA[2]

Grade 1 or grade 2 (ANC 1000/mm^3 - < LLN)	No dose adjustment required
Grade 3 (afebrile) (ANC 500/mm^3 - <1000/mm^3)	Interrupt dose until recovery to grade ≤2; resume at same dose level • If grade 3 recurs, interrupt dose until recovery; resume at next lower dose level
Grade 3 (febrile) **or grade 4** (ANC <500/mm^3)	Interrupt dose until recovery to grade ≤2; resume at next lower dose level

- Grade 3 febrile neutropenia is defined as a single episode of fever >38.3°C or ≥38°C for more than 1 hour and/or concurrent infection
- CBCs should be assessed prior to initiation of treatment. Repeat CBCs every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated

QT PROLONGATION[2]

QTcF prolongation >480 ms and ≤500 ms	Interrupt treatment until recovery to ≤480 ms; resume at same dose level • If QTcF >480 ms recurs, interrupt dose until recovery; resume at next lower dose level
QTcF prolongation >500 ms	Interrupt treatment until recovery to ≤480 ms; resume at next lower dose level • If QTcF >500 ms recurs, discontinue KISQALI • Permanently discontinue KISQALI if QTcF interval prolongation is either >500 ms or >60 ms change from baseline AND associated with torsade de pointes, polymorphic ventricular tachycardia, syncope, or signs/symptoms of serious arrhythmia

- ECGs should be assessed prior to initiation of treatment. Initiate treatment with KISQALI only in patients with QTcF values less than 450 ms. Repeat ECGs at approximately Day 14 of the first cycle and as clinically indicated. In case of QTcF prolongation at any given time during treatment, more frequent ECG monitoring is recommended
- Serum electrolytes (including potassium, calcium, phosphorus, and magnesium) should be assessed prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI therapy

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

KISQALI® ribociclib 200 mg tablets

Straightforward dose adjustments (continued)

ALT AND/OR AST ELEVATION[2]

Grade 1 (> ULN - 3 × ULN) **or grade 2 at baseline** (>3 - 5 × ULN)	No dose adjustment required
New grade 2 (>3 - 5 × ULN)	Interrupt dose until recovery to ≤ baseline grade; resume at same dose level • If grade 2 recurs, resume at next lower dose level
Grade 3 (>5 - 20 × ULN)	Interrupt dose until recovery to ≤ baseline grade; resume at next lower dose level • If grade 3 recurs, discontinue
Grade 4 (>20 × ULN) **or any grade with TB >2 × ULN without cholestasis**	Discontinue

- LFTs should be assessed prior to initiation of treatment. Repeat LFTs every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. If grade ≥2 abnormalities are noted, more frequent monitoring is recommended

OTHER TOXICITIES[2]

Grade 1 or grade 2	No dose adjustment required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 3	Interrupt dose until recovery to grade ≤1; resume at same dose level • If grade 3 recurs, resume at next lower dose level
Grade 4	Discontinue

- Grading criteria from CTCAE v4.03. Adverse reactions not requiring a dose adjustment are not shown. Initiate appropriate medical therapy as clinically indicated
- Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit-risk assessment

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

KISQALI® ribociclib 200 mg tablets

Considerations for KISQALI dosing and administration

SELECT DRUG INTERACTIONS[2]	
Strong CYP3A4 inhibitors	• Avoid concomitant use • If coadministration cannot be avoided, reduce KISQALI dose to 200 mg once daily
Strong CYP3A4 inducers	• Avoid concomitant use
CYP3A substrates	• For CYP3A substrates where minimal increases in the concentration may increase CYP3A substrate adverse reactions, monitor for increased adverse reactions of the CYP3A substrate during treatment with KISQALI • The dose of the sensitive CYP3A substrate may need to be reduced as KISQALI can increase its exposure
Drugs known to prolong QT Interval	• Avoid concomitant use of drugs such as antiarrhythmic medicines and other drugs that are known to prolong the QT interval • If concomitant use cannot be avoided, monitor ECG when initiating, during concomitant use, and as clinically indicated

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

KISQALI® ribociclib 200 mg tablets

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[7]

- 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]
- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatotoxicity, neutropenia, and embryo-fetal toxicity[2]
- In the NATALEE trial, no new safety signals were observed at 4 years of follow-up[10]

Grading according to CTCAE version 4.03.
*Infections included urinary and respiratory tract infections.[2]
†Only includes grade 3 ARs.[2]

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

KISQALI® ribociclib 200 mg tablets

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

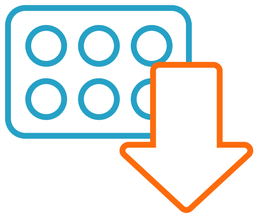
- Grade 4 increases in ALT (1.5%) and AST (0.8%) were reported in the KISQALI + AI arm[2]
- Drug-induced liver injury was reported in 9 patients (0.4%), of which 5 were grade ≥3, and 8 had resolved as of the data cutoff. There were 8 (0.3%) clinically confirmed Hy's Law cases (including 4 out of 9 drug-induced 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 safety signals were observed at 4 years of follow-up[10]

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

KISQALI® ribociclib 200 mg tablets

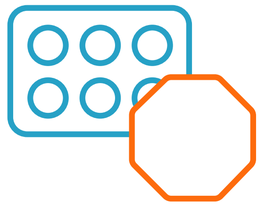
In stage II/III HR+/HER2- eBC,

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



Rate of dose reductions due to ARs[8]

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



Rate of discontinuation due to ARs[8]

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

- Median time to KISQALI discontinuation was 4.2 months[13]

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

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

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.

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[2,5]

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

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.

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

KISQALI® ribociclib 200 mg tablets

Abbreviations and references

Abbreviations: 1L=first line; AI=aromatase inhibitor; ALT=alanine aminotransferase; ANC=absolute neutrophil count; AR=adverse reaction; AST=aspartate aminotransferase; BSA=body surface area; CBC=complete blood count; CDK=cyclin-dependent kinase; CTCAE=Common Terminology Criteria for Adverse Events; CYP3A4=cytochrome P450, family 3, subfamily A, member 4; DDFS=distant disease-free survival; eBC=early breast cancer; ECG=electrocardiogram; EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ET=endocrine therapy; HR=hazard ratio; HRQOL=health-related quality of life; iDFS=invasive disease-free survival; ILD=interstitial lung disease; IV=intravenous; LFT=liver function test; LHRH=luteinizing hormone-releasing hormone; LLN=lower limit of normal; mBC=metastatic breast cancer; mOS=median overall survival; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PFS=progression-free survival; QOL=quality of life; QTcF=QT interval corrected by Fridericia's formula; SCAR=severe cutaneous adverse reaction; SD=standard deviation; SJS=Stevens-Johnson syndrome; TB=total bilirubin; TEN=toxic epidermal necrolysis; ULN=upper limit of normal.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed July 8, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **3.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med*. 2016;375(18):1738-1748. doi:10.1056/NEJMoa1609709 **4.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. *N Engl J Med*. 2022;386(10):942-950. doi:10.1056/NEJMoa2114663 **5.** Hortobagyi GN, Stroyakovskiy D, Yardley DA, et al. Ribociclib + nonsteroidal aromatase inhibitor as adjuvant treatment in patients with HR+/HER2- early breast cancer: final invasive disease-free survival analysis from the NATALEE trial. Presented at: San Antonio Breast Cancer Symposium; December 5-9, 2023; San Antonio, TX. **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.** 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 **8.** Data on file. CLEE011O12301C (NATALEE) final iDFS analysis results. Novartis Pharmaceuticals Corp; 2023. **9.** 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 **10.** 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. **11.** Fasching PA, Slamon DJ, Nowecki Z, et al. Health-related quality of life in the phase 3 NATALEE study of adjuvant ribociclib plus a NSAI vs NSAI alone in patients with HR+/HER2- early breast cancer. Presented at: ESMO Virtual Plenary with AACR Expert Commentary; September 14-15, 2023. **12.** Cocks K, King MT, Velikova G, et al. Evidence-based guidelines for interpreting change scores for the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. *Eur J Cancer*. 2012;48(11):1713-1721. doi:10.1016/j.ejca.2012.02.059 **13.** Barrios C, Harbeck N, Hortobagyi G, et al. NATALEE update: safety and treatment duration of ribociclib + nonsteroidal aromatase inhibitor in patients with HR+/HER2- early breast cancer. Presented at: ESMO Breast Cancer 2024; May 15-17, 2024; Berlin, Germany.

IMPORTANT SAFETY INFORMATION (continued)

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.**

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

KISQALI® ribociclib 200 mg tablets

Newly diagnosed patients with HR+/HER2- mBC look for a treatment that can deliver on their goals

Majority of patients reported that overall survival is their #1 treatment goal[1]

"I want to be here for my daughter growing up. I want to spend many more years with my husband."

—**Dee,** Patient on KISQALI

"I have so much going on in my life. I'm a legal assistant, I am a travel agent, I am a minister. I'm a grandmother...it's very important that I'm able to keep going and doing all those things."

—**Lisa,** Patient on KISQALI

MONALEESA-2 was a randomized, double-blind, placebo-controlled phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 80 months, mOS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with placebo + letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[2-4]

Dee and Lisa have taken KISQALI and have been compensated for their time.

IMPORTANT SAFETY INFORMATION (continued)

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.

KISQALI® ribociclib 200 mg tablets

Medical experts are endorsing KISQALI as their preferred first-line CDK4/6 inhibitor

NCCN CATEGORY 1

National Comprehensive Cancer Network® (NCCN®) **differentiates ribociclib (KISQALI®) as the only Category 1 Preferred 1L treatment option** in combination with an AI for appropriate patients with HR+/HER2- mBC[5]

There is controversy on the choice of CDK4/6i as there are no head-to-head comparisons between the agents and there are some differences in the study populations in the phase III randomized studies.

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.

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 HR+/HER2- mBC,

KISQALI was studied across menopausal statuses and endocrine combination partners

MONALEESA-2

- A randomized, double-blind, placebo-controlled, phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334)[2-4]
- Included postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease
- PFS was the primary end point; OS was a secondary end point

MONALEESA-3

- A randomized, double-blind, placebo-controlled, phase III study of KISQALI + fulvestrant (n=484) vs placebo + fulvestrant (n=242)[2,6,7]
- Included postmenopausal patients with HR+/HER2- mBC who had received no or only 1 line of prior ET for advanced disease
- Efficacy results are from a 1L subgroup analysis of 365 patients who received KISQALI (n=237) or placebo (n=128) with fulvestrant and were not powered to show statistical significance
- PFS was the primary end point; OS was a secondary end point

MONALEESA-7

- A randomized, double-blind, placebo-controlled, phase III study of KISQALI + ET (NSAI or tamoxifen) + goserelin (n=337) vs placebo + ET (NSAI or tamoxifen) + goserelin (n=335) (ITT)[2,8,9]
- Included premenopausal patients with HR+/HER2- mBC who received no prior ET for advanced disease
- **KISQALI is not indicated for concomitant use with tamoxifen**
- Efficacy results are from a prespecified subgroup analysis of 495 patients who received KISQALI (n=248) or placebo (n=247) with an NSAI + goserelin and were not powered to show statistical significance
- PFS was the primary end point; OS was a secondary end point

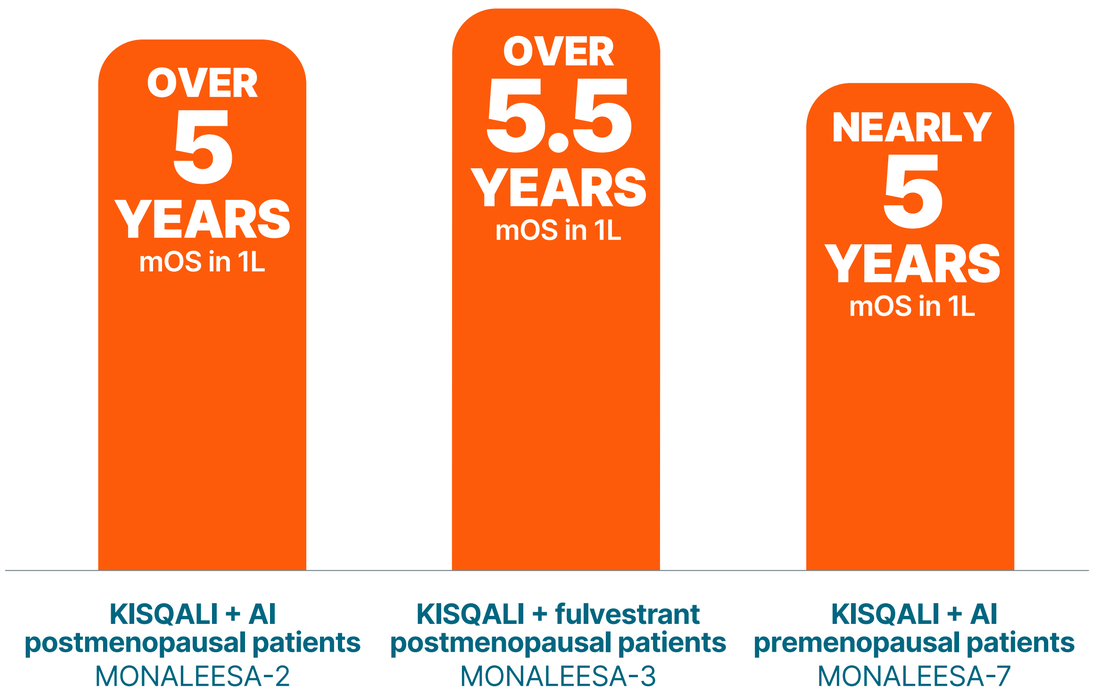
IMPORTANT SAFETY INFORMATION (continued)

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.

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

KISQALI® ribociclib 200 mg tablets

KISQALI is the only CDK4/6 inhibitor to achieve statistically significant OS in a broad range of patients across 3 phase III trials



1L refers to patients with mBC across all trials.

MONALEESA-2: At a median follow-up of 80 months, mOS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with placebo + letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004. OS was a secondary end point; PFS was the primary end point.[2-4]

MONALEESA-3: In an exploratory analysis of a 1L subgroup of patients receiving KISQALI + fulvestrant (n=237) or placebo + fulvestrant (n=128), at a median follow-up of 71 months mOS was 67.6 months with KISQALI + fulvestrant (95% CI: 59.6-NR) vs 51.8 months with placebo + fulvestrant (95% CI: 40.4-61.2); HR=0.673 (95% CI: 0.504-0.899). OS was a secondary end point; PFS was the primary end point. At a median follow-up of 39 months, statistical significance was established for overall survival in the ITT population; HR=0.724 (95% CI: 0.568-0.924); *P*=0.00455. Results from the 71-month analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[2,6,7,10]

MONALEESA-7: Efficacy results are from a prespecified subgroup analysis of 495 patients who received KISQALI (n=248) or placebo (n=247) with an NSAI + goserelin and were not powered to show statistical significance. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 54 months (exploratory analysis), mOS was 58.7 months with KISQALI + NSAI + goserelin (95% CI: 48.5-NR) vs 47.7 months with placebo + NSAI + goserelin (95% CI: 41.2-55.4); HR=0.798 (95% CI: 0.615-1.035). At a median follow-up of 35 months, statistical significance was established for overall survival in the ITT population; HR=0.71 (95% CI: 0.54-0.95); *P*=0.00973. Results from the 54-month analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[2,8,9,11,12]

KISQALI delivers on OS for a broad range of patients with HR+/HER2- mBC

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.

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

KISQALI® ribociclib 200 mg tablets

Patient portrayal.

MONALEESA-2

- **1L postmenopausal patients with an AI**
- **Only CDK4/6 inhibitor trial to demonstrate a statistically significant OS benefit in this population**

Study design: MONALEESA-2 was a randomized, double-blind, placebo-controlled, phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 80 months, mOS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with placebo + letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[2-4]

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.

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

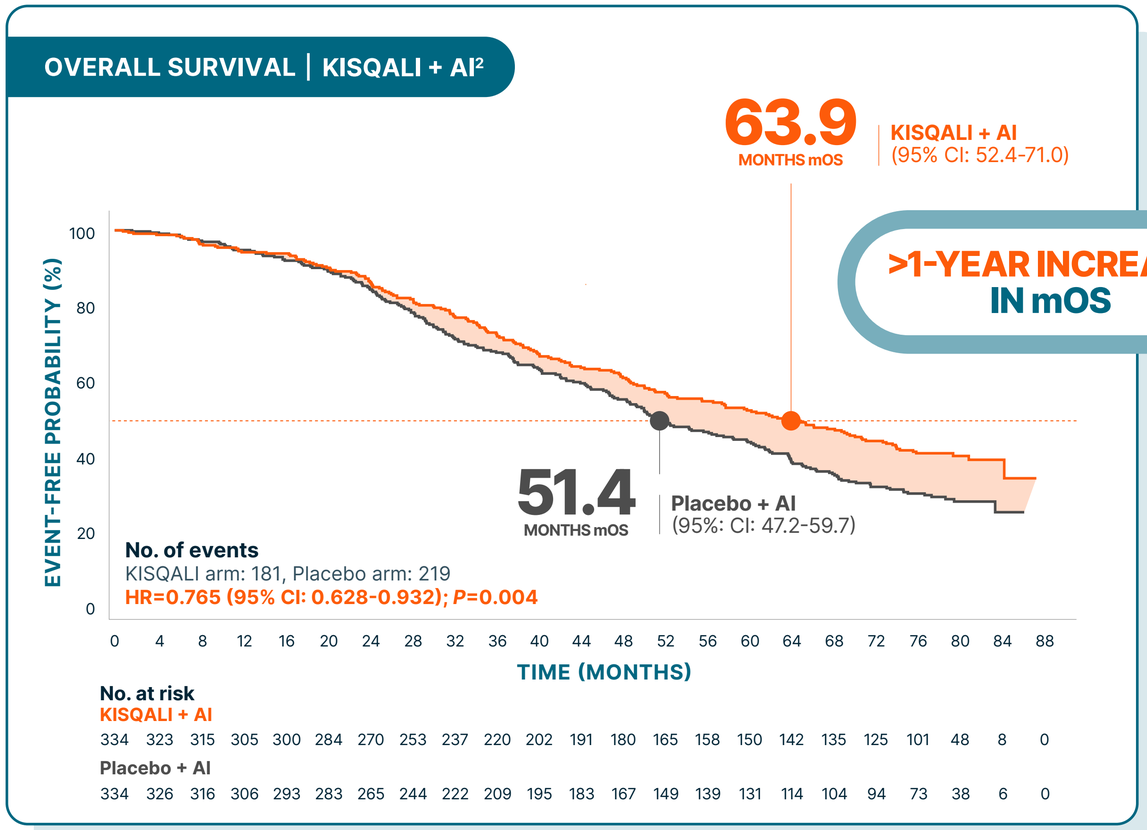
KISQALI® ribociclib 200 mg tablets

In HR+/HER2- mBC,

Over 5 years median overall survival for 1L postmenopausal patients with an AI

MONALEESA-2: KISQALI + AI in 1L postmenopausal patients

At a median follow-up of 80 months



OS benefit with KISQALI increased over time

- At 6 years, the survival rate of patients receiving KISQALI + letrozole was 44% vs 32% with placebo + letrozole[3]

"To have now a significant prolongation of overall survival and reaching the...5-year mark in overall survival in breast cancer is amazing."

—Gabriel Hortobagyi, MD

Hazard ratio is based on stratified Cox model.[3]

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.

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

KISQALI® ribociclib 200 mg tablets

In HR+/HER2- mBC,

Patient-reported health-related quality of life outcomes with KISQALI + ET and ET alone

Time to deterioration (TTD) ≥10% across the MONALEESA trials[13-15]

MONALEESA-2: KISQALI + AI in 1L postmenopausal patients	**Median TTD ≥10%** At a median follow-up of 26 months • **KISQALI: 27.7 months** • **Placebo: 27.6 months**	**HR=0.944** (95% CI: 0.720-1.237)[16,17]
MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients	**Median TTD ≥10%** At a median follow-up of 39 months • **KISQALI: 35.9 months** • **Placebo: 33.1 months**	**HR=0.81** (95% CI: 0.62-1.06)[10,14]
MONALEESA-7: KISQALI + AI + goserelin in 1L premenopausal patients	**Median TTD ≥10%** At a median follow-up of 35 months • **KISQALI: 34.2 months** • **Placebo: 23.3 months**	**HR=0.69** (95% CI: 0.52-0.91)[12,15]

HRQOL was assessed using the EORTC QLQ-C30 questionnaire—a validated tool used worldwide to assess quality of life in patients with cancer.[13-15,18,19]

- HRQOL was a secondary end point measured by patient-reported outcomes and was assessed at baseline and every 8 to 12 weeks throughout treatment
- TTD was defined as a decline of at least 10% of the global health status/QOL scale score or death due to any cause
- There was no prespecified statistical procedure controlling for type 1 error
- The EORTC QLQ-C30 is not all inclusive and does not include adequate assessment of all expected treatment-related symptoms. TTD may be confounded by events not related to disease/treatment

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.

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

KISQALI® ribociclib 200 mg tablets

Median time to chemotherapy was delayed ≥4 years across all 3 phase III trials with KISQALI

MONALEESA-2: KISQALI + AI in 1L postmenopausal patients	**OVER 4-YEAR DELAY**	At a median follow-up of 80 months, mTTC was 50.6 months with KISQALI + letrozole vs 38.9 months with placebo + letrozole; HR=0.742 (95% CI: 0.606-0.909)[3,20]
MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients	**4-YEAR DELAY**	At a median follow-up of 56 months, mTTC was 48.1 months with KISQALI + fulvestrant vs 28.8 months with placebo + fulvestrant; HR=0.704 (95% CI: 0.566-0.876)[21]
MONALEESA-7: KISQALI + AI in 1L premenopausal patients	**OVER 4-YEAR DELAY**	At a median follow-up of 54 months, mTTC was 50.9 months with KISQALI + NSAI + goserelin vs 36.0 months with placebo + NSAI + goserelin; HR=0.659 (95% CI: 0.509-0.851)[11]

- Time to chemotherapy was an exploratory end point and was defined as the time from randomization to the beginning of the first chemotherapy after discontinuing study treatment[10,12,13]
- There was no prespecified statistical procedure controlling for type 1 error

"That's a long time to have metastatic breast cancer and not have to have the side effects of chemotherapy."

—Timothy J. Pluard, MD
Saint Luke's Cancer Institute,
Kansas City, Missouri

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.

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 HR+/HER2- mBC,

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	✓	✓	–	–	–

Assessment requirements based on a 28-day treatment cycle.

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

Speak with your Novartis Oncology Specialist or Clinical Educator about a simple solution for fast, easy, and accurate ECG testing with in-office or direct-to-patient options

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 monitoring may be required as clinically indicated.

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.

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 HR+/HER2- mBC,

Start with KISQALI 600 mg—the starting dose with proven outcomes

(28-day cycle)[2]	Week 1	Week 2	Week 3	Week 4	Subsequent cycles
KISQALI: 3 tablets (3 x 200 mg)	✓	✓	✓	–	↻ Repeat 28-day cycle
AI	✓	✓	✓	✓	
or					
KISQALI: 3 tablets (3 x 200 mg)	✓	✓	✓	–	↻ Repeat 28-day cycle
Fulvestrant	✓ Day 1 injection	–	✓ Day 15 injection (Cycle 1 only)	–	✓ Once monthly

- KISQALI can be taken with or without food
- Store refrigerated at 2°C to 8°C (36°F to 46°F). Excursions permitted between 2°C and 15°C (36°F and 59°F)
- After dispensing, patients may store at room temperature at 20°C to 25°C (68°F to 77°F) for up to 2 months
- Store tablets in the original blister pack

Starting dose modifications for hepatic or severe renal impairment[2]:

- The recommended starting dose is 400 mg once daily for patients with moderate or severe (Child-Pugh class B or C) hepatic impairment
- The recommended starting dose is 200 mg once daily for patients with severe renal impairment

- KISQALI is given as 600 mg (3 x 200-mg tablets) orally, once daily (3 weeks on, 1 week off) with either[2]:
  - An AI once daily (continuously); in men and premenopausal women, an LHRH agonist should also be administered according to current clinical practice guidelines; or
  - Fulvestrant 500 mg intramuscularly on Days 1, 15, and 29, and once monthly thereafter; in men and premenopausal women, an LHRH agonist should also be administered according to current clinical practice guidelines
- Patients should continue treatment until disease progression or unacceptable toxicity

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%).

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 HR+/HER2- mBC,

KISQALI single-strength tablets make dose reduction simple and convenient

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

Starting dose

3 TABLETS (600 mg)

1st reduction

2 TABLETS (400 mg)

2nd reduction

1 TABLET (200 mg)

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

"...the single-tablet strength allows for simple dose adjustments, and to me, that is game changing."

—Nick McAndrew, MD
University of California, Los Angeles

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.

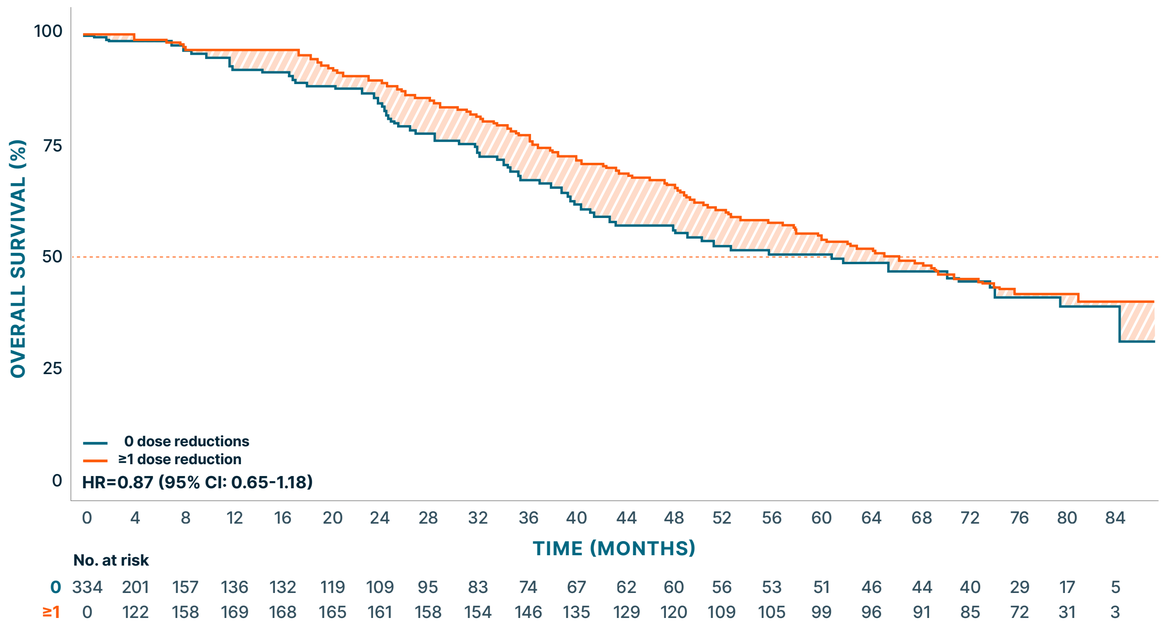
KISQALI® ribociclib 200 mg tablets

For your patients with HR+/HER2- mBC,

KISQALI maintained overall survival in patients requiring dose reductions across 3 phase III trials

MONALEESA-2 POSTMENOPAUSAL[22,23] | **MONALEESA-3** POSTMENOPAUSAL[24,25] | **MONALEESA-7** PREMENOPAUSAL[24,26]

62.6% of patients (209/334) had ≥1 dose reduction



Time-varying Cox regression analysis of OS by dose reduction. Results are based on a post hoc analysis; efficacy in the placebo comparator arms was not assessed and should be interpreted with caution.

6.5 MONTHS LONGER ON THERAPY

In MONALEESA-2, managing ARs with dose reductions helped patients stay on therapy an average of 6.5 months longer than those without dose reductions.[23]

Lowering the dose of KISQALI **can help address side effects and, in clinical studies, did not impact efficacy.**

"It's very reassuring to see that the overall survival benefit was maintained despite dose reduction."

—Lubna N. Chaudhary, MD
Medical College of Wisconsin

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.

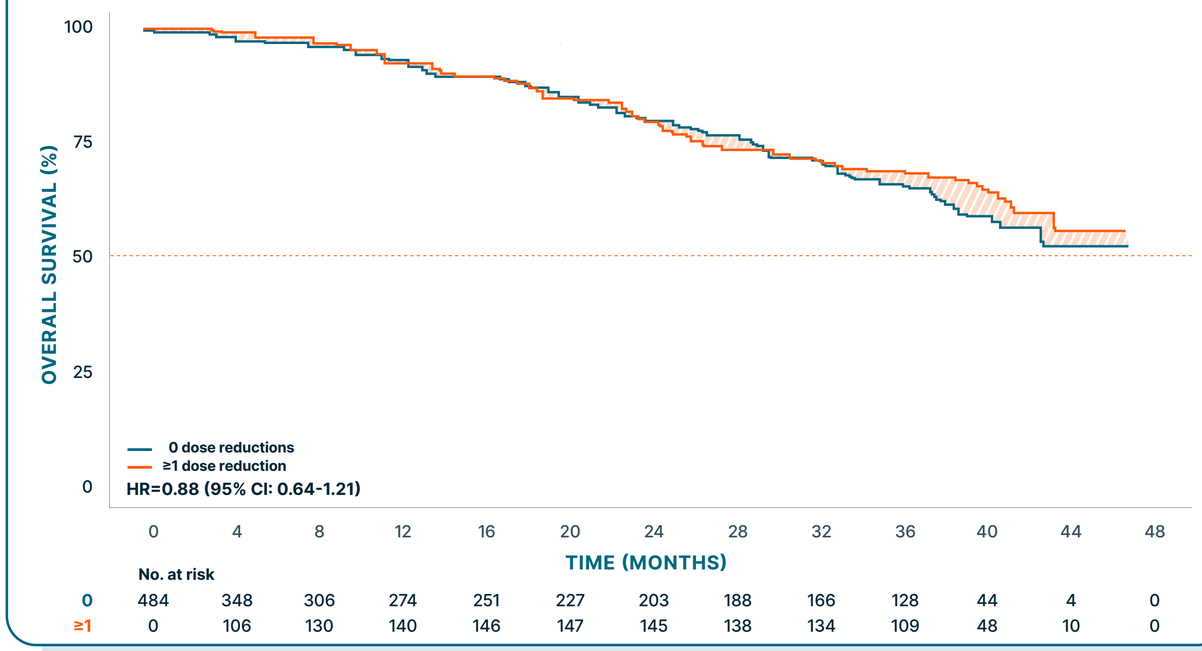
KISQALI® ribociclib 200 mg tablets

For your patients with HR+/HER2- mBC,

KISQALI maintained overall survival in patients requiring dose reductions across 3 phase III trials

MONALEESA-2 POSTMENOPAUSAL[22,23] | **MONALEESA-3** POSTMENOPAUSAL[24,25] | **MONALEESA-7** PREMENOPAUSAL[24,26]

40.7% of patients (197/484) had ≥1 dose reduction



Time-varying Cox regression analysis of OS by dose reduction. Results are based on a post hoc analysis; efficacy in the placebo comparator arms was not assessed and should be interpreted with caution.

6.5 MONTHS LONGER ON THERAPY

In MONALEESA-2, managing ARs with dose reductions helped patients stay on therapy an average of 6.5 months longer than those without dose reductions.[23]

Lowering the dose of KISQALI **can help address side effects and, in clinical studies, did not impact efficacy.**

"It's very reassuring to see that the overall survival benefit was maintained despite dose reduction."

—Lubna N. Chaudhary, MD
Medical College of Wisconsin

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.

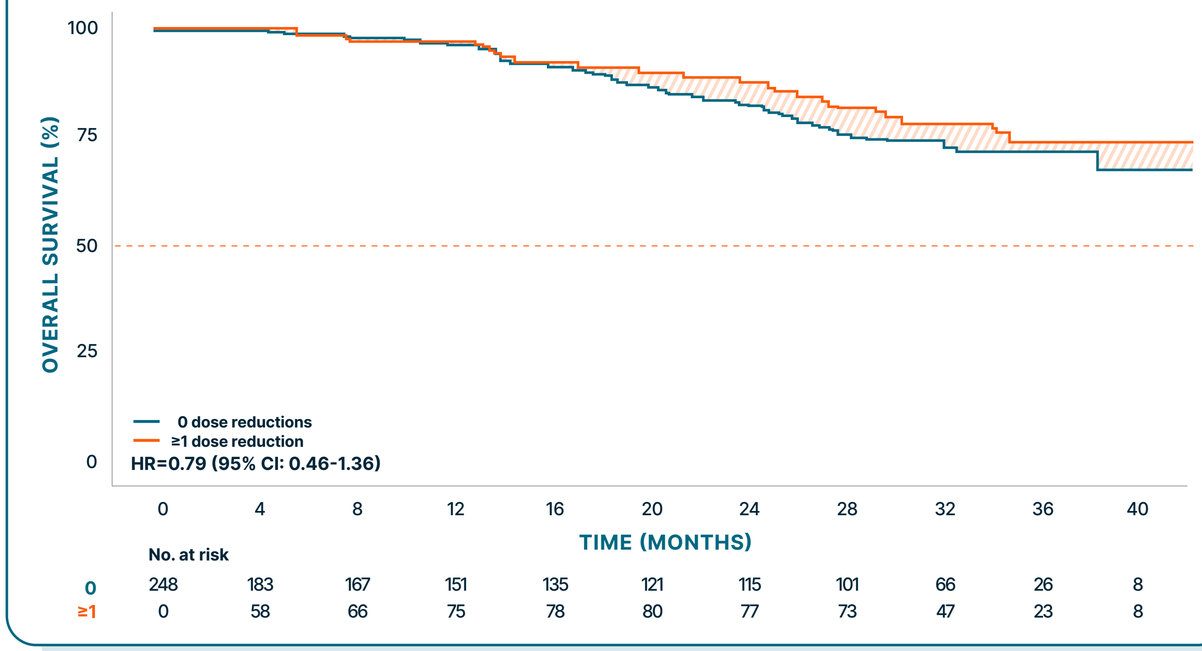
KISQALI® ribociclib 200 mg tablets

For your patients with HR+/HER2- mBC,

KISQALI maintained overall survival in patients requiring dose reductions across 3 phase III trials

MONALEESA-2 POSTMENOPAUSAL[22,23] | **MONALEESA-3** POSTMENOPAUSAL[24,25] | **MONALEESA-7** PREMENOPAUSAL[24,26]

40.7% of patients (101/248) had ≥1 dose reduction



Time-varying Cox regression analysis of OS by dose reduction. Results are based on a post hoc analysis; efficacy in the placebo comparator arms was not assessed and should be interpreted with caution.

6.5 MONTHS LONGER ON THERAPY

In MONALEESA-2, managing ARs with dose reductions helped patients stay on therapy an average of 6.5 months longer than those without dose reductions.[23]

Lowering the dose of KISQALI **can help address side effects and, in clinical studies, did not impact efficacy.**

"It's very reassuring to see that the overall survival benefit was maintained despite dose reduction."

—Lubna N. Chaudhary, MD
Medical College of Wisconsin

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

Straightforward dose adjustments

ILD/PNEUMONITIS[2]	
Grade 1 (asymptomatic)	No dose interruption or adjustment is required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 2 (symptomatic)	Interrupt dose until recovery to grade ≤1, then consider resuming KISQALI at the next lower dose level • If grade 2 recurs, discontinue
Grade 3 (severe symptomatic) **or grade 4**	Discontinue

- For grade 2 ILD/pneumonitis, an individualized benefit-risk assessment should be performed when considering resuming KISQALI

CUTANEOUS ADVERSE REACTIONS, INCLUDING SCARs[2]	
Grade 1 or grade 2 (<10% or 10%-30% of BSA, respectively, with active skin toxicity, no signs of systemic involvement)	No dose adjustment is required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 3 (severe rash not responsive to medical management; >30% BSA with active skin toxicity, signs of systemic involvement present; SJS)	Interrupt KISQALI until the etiology of the reaction has been determined. If etiology is not a SCAR, • Interrupt dose until recovery to grade ≤1; resume at same dose level • If grade 3 reaction recurs, resume at next lower dose level If etiology is a SCAR, permanently discontinue KISQALI
Grade 4 (any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences; TEN)	Permanently discontinue

- SJS (grades 3 and 4) is skin sloughing covering <10% BSA and 10%-30% BSA, respectively, with associated signs. TEN (grade 4) is defined as skin sloughing covering ≥30% BSA with associated symptoms
  - Signs and symptoms of SJS and TEN include erythema, purpura, epidermal detachment, and mucous membrane detachment

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

KISQALI® ribociclib 200 mg tablets

Straightforward dose adjustments (continued)

NEUTROPENIA[2]	
Grade 1 or grade 2 (ANC 1000/mm^3 - < LLN)	No dose adjustment required
Grade 3 (afebrile) (ANC 500/mm^3 - <1000/mm^3)	Interrupt dose until recovery to grade ≤2; resume at same dose level • If grade 3 recurs, interrupt dose until recovery; resume at next lower dose level
Grade 3 (febrile) **or grade 4** (ANC <500/mm^3)	Interrupt dose until recovery to grade ≤2; resume at next lower dose level

- Grade 3 febrile neutropenia is defined as a single episode of fever >38.3°C or ≥38°C for more than 1 hour and/or concurrent infection

QT PROLONGATION[2]	
QTcF prolongation >480 ms and ≤500 ms	Interrupt treatment until recovery to ≤480 ms; resume at next lower dose level • If QTcF >480 ms recurs, interrupt dose until recovery; resume at next lower dose level
QTcF prolongation >500 ms	Interrupt treatment until recovery to ≤480 ms; resume at next lower dose level • If QTcF >500 ms recurs, discontinue KISQALI • Permanently discontinue KISQALI if QTcF interval prolongation is either >500 ms or >60 ms change from baseline AND associated with torsade de pointes, polymorphic ventricular tachycardia, syncope, or signs/symptoms of serious arrhythmia

- ECGs should be assessed prior to initiation of treatment. Initiate treatment with KISQALI only in patients with QTcF values less than 450 ms. Repeat ECGs at approximately Day 14 of the first cycle and as clinically indicated. In case of QTcF prolongation at any given time during treatment, more frequent ECG monitoring is recommended
- Serum electrolytes (including potassium, calcium, phosphorus, and magnesium) should be assessed prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI therapy

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

KISQALI® ribociclib 200 mg tablets

Straightforward dose adjustments (continued)

ALT AND/OR AST ELEVATION[2]	
Grade 1 (> ULN - 3 × ULN) **or grade 2 at baseline** (>3 - 5 × ULN)	No dose adjustment required
New grade 2 (>3 - 5 × ULN)	Interrupt dose until recovery to ≤ baseline grade; resume at same dose level • If grade 2 recurs, resume at next lower dose level
Grade 3 (>5 - 20 × ULN)	Interrupt dose until recovery to ≤ baseline grade; resume at next lower dose level • If grade 3 recurs, discontinue
Grade 4 (>20 × ULN) **or any grade with TB >2 × ULN without cholestasis**	Discontinue

OTHER TOXICITIES[2]	
Grade 1 or grade 2	No dose adjustment required • Initiate appropriate medical therapy and monitor as clinically indicated
Grade 3	Interrupt dose until recovery to grade ≤1; resume at same dose level • If grade 3 recurs, resume at next lower dose level
Grade 4	Discontinue

- Grading criteria from CTCAE v4.03. Adverse reactions not requiring a dose adjustment are not shown. Initiate appropriate medical therapy as clinically indicated
- Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit-risk assessment

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

KISQALI® ribociclib 200 mg tablets

Considerations for KISQALI dosing and administration

SELECT DRUG INTERACTIONS[2]	
Strong CYP3A4 inhibitors	• Avoid concomitant use • If coadministration cannot be avoided, reduce KISQALI dose to 400 mg once daily
Strong CYP3A4 inducers	• Avoid concomitant use
CYP3A substrates	• For CYP3A substrates where minimal increases in the concentration may increase CYP3A substrate adverse reactions, monitor for increased adverse reactions of the CYP3A substrate during treatment with KISQALI • The dose of the sensitive CYP3A substrate may need to be reduced as KISQALI can increase its exposure
Drugs known to prolong QT Interval	• Avoid concomitant use of drugs such as antiarrhythmic medicines and other drugs that are known to prolong the QT interval • If concomitant use cannot be avoided, monitor ECG when initiating, during concomitant use, and as clinically indicated

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

KISQALI® ribociclib 200 mg tablets

KISQALI + letrozole safety profile

MONALEESA-2: KISQALI + letrozole in 1L postmenopausal patients

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[2]

	KISQALI + letrozole (n=334)		Placebo + letrozole (n=330)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
GASTROINTESTINAL DISORDERS				
Nausea	52	2.4*	29	0.6*
Diarrhea	35	1.2*	22	0.9*
Vomiting	29	3.6*	16	0.9*
Constipation	25	1.2*	19	0
Stomatitis	12	0.3*	7	0
Abdominal pain	11	1.2*	8	0
GENERAL DISORDERS AND ADMINISTRATION-SITE CONDITIONS				
Fatigue	37	2.4	30	0.9
Pyrexia	13	0.3*	6	0
Peripheral edema	12	0	10	0
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Alopecia	33	0	16	0
Rash	17	0.6*	8	0
Pruritus	14	0.6*	6	0
NERVOUS SYSTEM DISORDERS				
Headache	22	0.3*	19	0.3*
Insomnia	12	0.3*	9	0
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Back pain	20	2.1*	18	0.3*
METABOLISM AND NUTRITION DISORDERS				
Decreased appetite	19	1.5*	15	0.3*
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS				
Dyspnea	12	1.2*	9	0.6*
INFECTIONS AND INFESTATIONS				
Urinary tract infection	11	0.6*	8	0

- Dose reductions due to ARs: 45% with KISQALI + letrozole
- Permanent discontinuations: 7% with KISQALI + letrozole
- The most common ARs (≥20% on the KISQALI arm and ≥2% higher than placebo), including laboratory abnormalities, were decrease in neutrophils, decrease in leukocytes, decrease in hemoglobin, nausea, decrease in lymphocytes, increase in ALT, increase in AST, fatigue, diarrhea, alopecia, vomiting, decrease in platelets, constipation, headache, and back pain
- Fatal ARs occurred in 1.8% of patients who received KISQALI. Fatal ARs in ≥0.1% of patients receiving KISQALI included acute respiratory failure (0.6%), acute myocardial infarction, sudden death (with grade 3 hypokalemia and grade 2 QT prolongation), unknown cause, and pneumonia (0.3% each)

The majority of adverse reactions with KISQALI were manageable and reversible

Grading according to CTCAE version 4.03.
*Only includes grade 3 ARs.

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

KISQALI® ribociclib 200 mg tablets

KISQALI + letrozole safety profile (continued)

MONALEESA-2: KISQALI + letrozole in 1L postmenopausal patients

LABORATORY ABNORMALITIES OCCURRING IN ≥10% OF PATIENTS[2]

	KISQALI + letrozole (n=334)		Placebo + letrozole (n=330)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
HEMATOLOGY				
Leukocyte count decreased	93	34	29	1.5
Neutrophil count decreased	93	60	24	1.2
Hemoglobin decreased	57	1.8	26	1.2
Lymphocyte count decreased	51	14	22	3.9
Platelet count decreased	29	0.9	6	0.3
CHEMISTRY				
ALT increased	46	10	36	1.2
AST increased	44	7	32	1.5
Creatinine increased	20	0.6	6	0
Phosphorus decreased	13	5	4	0.6
Potassium decreased	11	1.2	7	1.2

- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatotoxicity, neutropenia, and embryo-fetal toxicity

The majority of adverse reactions with KISQALI were manageable and reversible

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

KISQALI® ribociclib 200 mg tablets

KISQALI + fulvestrant safety profile

MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[2]

	KISQALI + fulvestrant (n=483)		Placebo + fulvestrant (n=241)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
GASTROINTESTINAL DISORDERS				
Nausea	45	1.4‡	28	0.8‡
Diarrhea	29	0.6‡	20	0.8‡
Vomiting	27	1.4‡	13	0
Constipation	25	0.8‡	12	0
Abdominal pain	17	1.4‡	13	0.8‡
INFECTIONS AND INFESTATIONS				
Infections*,†	42	4.6‡	30	1.7‡
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Rash	23	0.8‡	8	0
Pruritus	20	0.2‡	7	0
Alopecia	19	0	5	0
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS				
Cough	22	0	15	0
Dyspnea	15	1.4	12	1.7
METABOLISM AND NUTRITION DISORDERS				
Decreased appetite	16	0.2‡	13	0
GENERAL DISORDERS AND ADMINISTRATION-SITE CONDITIONS				
Peripheral edema	15	0	7	0
Pyrexia	11	0.2‡	7	0
NERVOUS SYSTEM DISORDERS				
Dizziness	13	0.2‡	8	0

- Dose reductions due to ARs: 32% with KISQALI + fulvestrant
- Permanent discontinuations: 8% with KISQALI + fulvestrant
- The most common ARs (≥20% on the KISQALI arm and ≥2% higher than placebo), including laboratory abnormalities, were decrease in leukocytes, decrease in neutrophils, decrease in lymphocytes, increase in creatinine, decrease in hemoglobin, increase in AST, nausea, increase in ALT, infections, decrease in platelets, diarrhea, vomiting, constipation, decrease in glucose serum, cough, rash, and pruritus
- Fatal ARs occurred in 1.2% of patients who received KISQALI. Fatal ARs in ≥0.1% of patients receiving KISQALI included cardiac failure, ventricular arrhythmia, pneumonia, acute respiratory distress, pulmonary embolism, and hemorrhagic shock (0.2% each)

The majority of adverse reactions with KISQALI were manageable and reversible

Grading according to CTCAE version 4.03.
*Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (1%).
†Includes the following fatal adverse reactions: pneumonia (n=1).
‡Only includes grade 3 ARs.

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

KISQALI® ribociclib 200 mg tablets

KISQALI + fulvestrant safety profile (continued)

MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients

LABORATORY ABNORMALITIES OCCURRING IN ≥10% OF PATIENTS [2]

	KISQALI + fulvestrant (n=483)		Placebo + fulvestrant (n=241)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
HEMATOLOGY				
Leukocyte count decreased	95	26	26	0.4
Neutrophil count decreased	92	53	21	0.8
Lymphocyte count decreased	69	16	35	4.1
Hemoglobin decreased	60	4.3	35	2.9
Platelet count decreased	33	1.9	11	0
CHEMISTRY				
Creatinine increased	65	1	33	0.4
GGT increased	52	8	49	10
AST increased	50	7	43	2.9
ALT increased	44	11	37	1.7
Glucose serum decreased	23	0	18	0
Phosphorus decreased	18	4.6	8	0.8
Albumin decreased	12	0	8	0

- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatotoxicity, neutropenia, and embryo-fetal toxicity

The majority of adverse reactions with KISQALI were manageable and reversible

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

KISQALI® ribociclib 200 mg tablets

KISQALI + NSAI + goserelin safety profile

MONALEESA-7: KISQALI + NSAI + goserelin in 1L premenopausal patients

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[2]

	KISQALI + NSAI + goserelin (n=248)		Placebo + NSAI + goserelin (n=247)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
INFECTIONS AND INFESTATIONS				
Infections*	36	1.6†	24	0.4†
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
Arthralgia	34	0.8†	29	1.2†
GASTROINTESTINAL DISORDERS				
Nausea	32	0	20	0
Constipation	16	0	12	0
Stomatitis	10	0	8	0.4†
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Alopecia	21	0	13	0
Rash	17	0.4†	9	0
Pruritus	11	0	4	0
GENERAL DISORDERS AND ADMINISTRATION-SITE CONDITIONS				
Pyrexia	17	0.8†	7	0
Pain in extremity	10	0	8	1.2†
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS				
Cough	15	0	10	0

- Dose reductions due to ARs: 33% with KISQALI + NSAI + goserelin
- Permanent discontinuations: 3% with KISQALI + NSAI + goserelin
- The most common ARs (≥20% on the KISQALI arm and ≥2% higher than placebo), including laboratory abnormalities, were decrease in leukocytes, decrease in neutrophils, decrease in hemoglobin, decrease in lymphocytes, increase in gamma-glutamyl transferase, increase in AST, infections, arthralgia, increase in ALT, nausea, decrease in platelets, and alopecia

The majority of adverse reactions with KISQALI were manageable and reversible

Grading according to CTCAE version 4.03.
*Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (<1%).
†Only includes grade 3 ARs.

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

KISQALI® ribociclib 200 mg tablets

KISQALI + NSAI + goserelin safety profile (continued)

MONALEESA-7: KISQALI + NSAI + goserelin in 1L premenopausal patients

LABORATORY ABNORMALITIES OCCURRING IN ≥10% OF PATIENTS[2]

	KISQALI + NSAI + goserelin (n=248)		Placebo + NSAI + goserelin (n=247)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
HEMATOLOGY				
Leukocyte count decreased	93	36	30	0.8
Neutrophil count decreased	92	63	27	2.4
Hemoglobin decreased	84	2.4	51	0.4
Lymphocyte count decreased	55	14	18	2.8
Platelet count decreased	26	0.4	9	0.4
CHEMISTRY				
GGT increased	42	7	42	9
AST increased	37	4.8	35	1.6
ALT increased	33	6	31	1.6
Phosphorus decreased	14	1.6	11	0.8
Potassium decreased	11	1.2	14	1.2
Glucose serum decreased	10	0.4	10	0.4
Creatinine increased	8	0	2	0

- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatotoxicity, neutropenia, and embryo-fetal toxicity

The majority of adverse reactions with KISQALI were manageable and reversible

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

KISQALI® ribociclib 200 mg tablets

In patients with HR+/HER2- mBC,

Incidence of QT prolongation was low across all KISQALI clinical trials, and most cases were moderate in nature

ECG changes were reversible with dose interruption and the majority occurred within the first 4 weeks of treatment.

In a pooled analysis across 3 phase III trials of 1054 pre- and postmenopausal patients treated with KISQALI + an AI or fulvestrant[2]:

- **1.4%** had a >500 ms postbaseline QTcF value
- **6%** experienced a >60 ms increase from baseline in QTcF interval
- There were **no reported cases** of torsades de pointes

"I think it's time to come out of that comfort zone and really start using ribociclib."

—Lubna N. Chaudhary, MD
Medical College of Wisconsin

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.

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

KISQALI® ribociclib 200 mg tablets

Abbreviations and references

Abbreviations: 1L=first line; 2L=second line; AI=aromatase inhibitor; ALT=alanine aminotransferase; ANC=absolute neutrophil count; AR=adverse reaction; AST=aspartate aminotransferase; BSA=body surface area; CBC=complete blood count; CDK=cyclin-dependent kinase; CTCAE=Common Terminology Criteria for Adverse Events; CYP3A4=cytochrome P450, family 3, subfamily A, member 4; ECG=electrocardiogram; EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ET=endocrine therapy; GGT=gamma-glutamyl transferase; HR=hazard ratio; HRQOL=health-related quality of life; ILD=interstitial lung disease; ITT=intent to treat; IV=intravenous; LFT=liver function test; LHRH=luteinizing hormone-releasing hormone; LLN=lower limit of normal; mBC=metastatic breast cancer; mOS=median overall survival; mTTC=median time to chemotherapy; NR=not reached; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PFS=progression-free survival; QOL=quality of life; QTcF=QT interval corrected by Fridericia's formula; SCAR=severe cutaneous adverse reaction; SJS=Stevens-Johnson syndrome; TB=total bilirubin; TEN=toxic epidermal necrolysis; TTD=time to deterioration; ULN=upper limit of normal.

References: 1. Pfizer, Inc. Meaningful goals in the management of mBC. White paper. June 2017. **2.** Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **3.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. *N Engl J Med.* 2022;386(10):942-950. doi:10.1056/NEJMoa2114663 **4.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med.* 2016;375(18):1738-1748. doi:10.1056/NEJMoa1609709 **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed March 20, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **6.** Neven P, Fasching PA, Chia S, et al. Updated overall survival from the MONALEESA-3 trial in postmenopausal women with HR+/HER2- advanced breast cancer receiving first-line ribociclib plus fulvestrant. *Breast Cancer Res.* 2023;25(1):103. doi:10.1186/s13058-023-01701-9 **7.** Slamon DJ, Neven P, Chia S, et al. Phase III randomized study of ribociclib and fulvestrant in hormone receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer: MONALEESA-3. *J Clin Oncol.* 2018;36(24):2465-2472. doi:10.1200/JCO.2018.78.9909 **8.** Tripathy D, Im S-A, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomised phase 3 trial. *Lancet Oncol.* 2018;19(7):904-915. doi:10.1016/S1470-2045(18)30292-4 **9.** Lu YS, Im SA, Colleoni M, et al. Updated overall survival of ribociclib plus endocrine therapy versus endocrine therapy alone in pre- and perimenopausal patients with HR+/HER2- advanced breast cancer in MONALEESA-7: a phase III randomized clinical trial. *Clin Cancer Res.* 2022;28(5):851-859. doi:10.1158/1078-0432.CCR-21-3032 **10.** Slamon DJ, Neven P, Chia S, et al. Overall survival with ribociclib plus fulvestrant in advanced breast cancer. *N Engl J Med.* 2020;382(6):514-524. doi:10.1056/NEJMoa1911149 **11.** Data on file. CLEE011E2301. Novartis Pharmaceuticals Corp; 2020. **12.** Im S-A, Lu Y-S, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Engl J Med.* 2019;381(4):307-316. doi:10.1056/NEJMoa1903765 **13.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med.* 2016;375(18):1738-1748;(protocol). doi:10.1056/NEJMoa1609709 **14.** Fasching PA, Beck JT, Chan A, et al. Ribociclib plus fulvestrant for advanced breast cancer: health-related quality-of-life analyses from the MONALEESA-3 study. *Breast.* 2020;54:148-154. doi:10.1016/j.breast.2020.09.008 **15.** Harbeck N, Franke F, Villanueva-Vazquez R, et al. Health-related quality of life in premenopausal women with hormone-receptor-positive, HER2-negative advanced breast cancer treated with ribociclib plus endocrine therapy: results from a phase III randomized clinical trial (MONALEESA-7). *Ther Adv Med Oncol.* 2020;12:1758835920943065. doi:10.1177/1758835920943065 **16.** Data on file. CLEE011A2301 additional analyses. Novartis Pharmaceuticals Corp; 2017. **17.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. *Ann Oncol.* 2018;29(7):1541-1547. doi:10.1093/annonc/mdy155 **18.** Im S-A, Lu Y-S, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Engl J Med.* 2019;381(4):307-316;(protocol). doi:10.1056/NEJMoa1903765 **19.** Fayers PM, Aaronson NK, Bjordal K, et al, on behalf of the EORTC Quality of Life Group. *EORTC QLQ-C30 Scoring Manual (3rd edition).* EORTC; 2001. **20.** Data on file. MONALEESA-2 final overall survival analysis. Novartis Pharmaceuticals Corp; 2021. **21.** Slamon DJ, Neven P, Chia S, et al. Ribociclib plus fulvestrant for postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer in the phase III randomized MONALEESA-3 trial: updated overall survival. *Ann Oncol.* 2021;32(8):1015-1024. doi:10.1016/j.annonc.2021.05.353 **22.** Data on file. M2 OS by dose reduction. Novartis Pharmaceuticals Corp; 2021. **23.** Data on file. CLEE011A2301 additional analysis. Novartis Pharmaceuticals Corp; 2021. **24.** Data on file. OS by dose reduction poster. Novartis Pharmaceuticals Corp. 2020. **25.** Data on file. CLEE011F2301 additional analysis. Novartis Pharmaceuticals Corp; 2020. **26.** Data on file. CLEE011E2301 additional analysis. Novartis Pharmaceuticals Corp; 2020.

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.

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

KISQALI® ribociclib 200 mg tablets

Do more today to help protect their tomorrow: KISQALI is now proven to help reduce the risk of recurrence in the broadest range of patients with stage II or III HR+/HER2- eBC—so they can live the lives they love

Stage II/III HR+/HER2- eBC: KISQALI can help prevent recurrence in the broadest population of patients, without sacrificing tolerability[1,2]

RESULTS FROM THE PHASE III NATALEE TRIAL[1,3-5]

Risk of recurrence and risk of distant recurrence

3 YEARS	4 YEARS
25% REDUCTION	**29% REDUCTION**

- **At 3 years, the absolute difference was 3.1% for iDFS and 2.7% for DDFS; at 4 years, the absolute difference was 4.9% for iDFS and 4.5% for DDFS[1,3-5]**
- **At 3 years, improvement in iDFS was consistent across subgroups, regardless of anatomic stage, nodal or menopausal status, age, or grade[3,6,*]**
- The majority of ARs with KISQALI were manageable and reversible[1,6]
- 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[1]

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). **DDFS was defined as** the time from randomization to the date of the first event of distant recurrence, second primary non-breast invasive cancer (excluding basal and squamous cell carcinomas of the skin), or death (any cause).[1,7]

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. 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). Prespecified subgroups included anatomic stage (stage II: HR=0.700 [95% CI: 0.496-0.986]; stage III: HR=0.755 [95% CI: 0.616-0.926]), nodal status (N0: HR=0.723 [95% CI: 0.412-1.268]; N1, N2, N3: HR=0.759 [95% CI: 0.631-0.912]), menopausal status (premenopausal/men: HR=0.688 [95% CI: 0.519-0.913]; postmenopausal: HR=0.806 [95% CI: 0.645-1.007]), age (<45 years: HR=0.652 [95% CI: 0.443-0.959]; 45 to 54 years: HR=0.799 [95% CI: 0.578-1.104]; 55 to 64 years: HR=0.871 [95% CI: 0.636-1.193]; ≥65 years: HR=0.662 [95% CI: 0.444-0.986]), and histological grade at time of surgery (grade 1: HR=0.708 [95% CI: 0.303-1.657]; grade 2: HR=0.696 [95% CI: 0.548-0.885]; grade 3: HR=0.890 [95% CI: 0.658-1.204]). Grade 1 subgroup did not include patients with T2N0 disease. Results from the subgroup analysis included no prespecified statistical procedure controlling for type 1 error. In an exploratory analysis, at a median follow-up of 44 months, with 603 iDFS events in the study (263 [10.3%] in the KISQALI arm and 340 [13.3%] in the NSAI-alone arm), iDFS at the 4-year landmark was 88.5% for KISQALI + NSAI vs 83.6% for NSAI alone **(absolute difference 4.9%)**; there was a 28.5% relative reduction in the risk of an iDFS event; HR=0.715 (95% CI: 0.609-0.840). With 551 DDFS events in the study (240 [9.4%] in the KISQALI arm and 311 [12.2%] in the NSAI-alone arm), DDFS at the 4-year landmark was 89.4% for KISQALI + NSAI vs 84.9% for NSAI alone **(absolute difference 4.5%)**; there was a 28.5% relative reduction in the risk of a DDFS event; HR=0.715 (95% CI: 0.604-0.847). Results from the 4-year analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[1,3-6,8]

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 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 + NSAI 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%). No new safety signals were observed at 4 years of follow-up.[1,4,6]

*Histological grade at time of surgery.[3]
†Infections included urinary and respiratory tract infections.[1]
‡Only includes grade 3 ARs.[1]

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

KISQALI® ribociclib 200 mg tablets

More life for living: KISQALI is proven to help a broad range of patients with HR+/HER2- mBC live longer—and that means more time doing what they love

HR+/HER2- mBC: KISQALI is the only CDK4/6 inhibitor to achieve statistically significant OS in first line in combination with an AI[1]

PROVEN RESULTS ACROSS ALL 3 PHASE III MONALEESA TRIALS[1,9,10]

Postmenopausal patients		Premenopausal patients
MONALEESA-2 **Over 5 years mOS in 1L**	**MONALEESA-3** **Over 5.5 years mOS in 1L**	**MONALEESA-7** **Nearly 5 years mOS in 1L**

1L refers to patients with mBC across all trials.

MONALEESA-2 was a randomized, double-blind, placebo-controlled, phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 80 months, mOS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with placebo + letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[1,11,12]

MONALEESA-3 was a randomized, double-blind, placebo-controlled, phase III study of KISQALI + fulvestrant (n=484) vs placebo + fulvestrant (n=242) in postmenopausal patients with HR+/HER2- mBC who received no or only 1 line of prior ET for advanced disease. OS was a secondary end point; PFS was the primary end point. In an exploratory analysis of a 1L subgroup of patients receiving KISQALI + fulvestrant (n=237) or placebo + fulvestrant (n=128), at a median follow-up of 71 months mOS was 67.6 months with KISQALI + fulvestrant (95% CI: 59.6-NR) vs 51.8 months with placebo + fulvestrant (95% CI: 40.4-61.2); HR=0.673 (95% CI: 0.504-0.899). At a median follow-up of 39 months, statistical significance was established for overall survival in the ITT population; HR=0.724 (95% CI: 0.568-0.924); *P*=0.00455. Results from the 71-month analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[1,9,13,14]

MONALEESA-7 was a randomized, double-blind, placebo-controlled, phase III study of KISQALI + ET (NSAI or tamoxifen) + goserelin (n=335) vs placebo + ET (NSAI or tamoxifen) + goserelin (n=337) (ITT) in premenopausal patients with HR+/HER2- mBC who received no prior ET for advanced disease. **KISQALI is not indicated for concomitant use with tamoxifen.** Efficacy results are from a prespecified subgroup analysis of 495 patients who received KISQALI (n=248) or placebo (n=247) with an NSAI + goserelin and were not powered to show statistical significance. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 54 months (exploratory analysis), mOS was 58.7 months with KISQALI + NSAI + goserelin (95% CI: 48.5-NR) vs 47.7 months with placebo + NSAI + goserelin (95% CI: 41.2-55.4); HR=0.798 (95% CI: 0.615-1.035). At a median follow-up of 35 months, statistical significance was established for overall survival in the ITT population; HR=0.71 (95% CI: 0.54-0.95); *P*=0.00973. Results from the 54-month analysis were not prespecified and were observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error.[1,10,15-17]

IMPORTANT SAFETY INFORMATION (continued)

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.**

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

KISQALI® ribociclib 200 mg tablets

Give your patients with HR+/HER2- eBC or mBC

Confidence to start and stay on KISQALI

A few standard assessments help to ensure your patients start right away[1]

Assessments	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 and 2 required ECG assessments for eBC and mBC, completed within the first 2 weeks of treatment[1]

- KISQALI should only be initiated in patients with QTcF <450 ms
- Monitor serum electrolytes prior to the initiation of treatment, at the beginning of the first 6 cycles, and as clinically indicated. Correct any electrolyte abnormalities before initiating treatment
- Monitor CBC and LFTs prior to the initiation of treatment, every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. For LFT, if grade ≥2 abnormalities are noted, more frequent monitoring is recommended

Speak with your Novartis Oncology Specialist or Clinical Educator about a simple solution for fast, easy, and accurate ECG testing with in-office or direct-to-patient options

IMPORTANT SAFETY INFORMATION (continued)

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.

KISQALI® ribociclib 200 mg tablets

Give your patients with HR+/HER2- eBC or mBC

Confidence to start and stay on KISQALI

KISQALI single-strength tablets help simplify management of adverse reactions with straightforward dose reductions[1]

	eBC	mBC
Starting dose	2 TABLETS (400 mg)	3 TABLETS (600 mg)
1st reduction	1 TABLET (200 mg)	2 TABLETS (400 mg)
2nd reduction	—	1 TABLET (200 mg)

- KISQALI is given as 400 mg (2 x 200-mg tablets) and 600 mg (3 x 200-mg tablets) orally once daily (3 weeks on, 1 week off) for HR+/HER2- eBC and HR+/HER2- mBC, respectively, with either:
  - An AI once daily (continuously); in men and premenopausal women, an LHRH agonist should also be administered according to current clinical practice guidelines; or
  - In mBC only: fulvestrant 500 mg intramuscularly on Days 1, 15, and 29, and once monthly thereafter; in men and premenopausal women, an LHRH agonist should also be administered according to current clinical practice guidelines
- Metastatic breast cancer patients should continue treatment until disease progression or unacceptable toxicity
- Early breast cancer patients should continue treatment for 3 years or until disease recurrence or unacceptable toxicity
- Dose adjustments for ARs should be made stepwise by reducing the number of tablets taken
- Dose modification is recommended based on individual safety and tolerability
- If dose reduction below 200 mg/day is required, discontinue treatment
- KISQALI can be taken with or without food
- Store refrigerated at 2°C to 8°C (36°F to 46°F). Excursions permitted between 2°C and 15°C (36°F and 59°F)
- After dispensing, patients may store at room temperature at 20°C to 25°C (68°F to 77°F) for up to 2 months
- Store tablets in the original blister pack

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

Abbreviations and references

Abbreviations: 1L=first line; AI=aromatase inhibitor; ALT=alanine aminotransferase; AR=adverse reaction; AST=aspartate aminotransferase; CBC=complete blood count; CDK=cyclin-dependent kinase; DDFS=distant disease-free survival; eBC=early breast cancer; ECG=electrocardiogram; ET=endocrine therapy; HR=hazard ratio; iDFS=invasive disease-free survival; ITT=intent to treat; LFT=liver function test; LHRH=luteinizing hormone-releasing hormone; mBC=metastatic breast cancer; mOS=median overall survival; NR=not reached; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PFS=progression-free survival; QTcF=QT interval corrected by Fridericia's formula.

References: 1. Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **2.** 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 **3.** Hortobagyi GN, Stroyakovskiy D, Yardley DA, et al. Ribociclib + nonsteroidal aromatase inhibitor as adjuvant treatment in patients with HR+/HER2- early breast cancer: final invasive disease-free survival analysis from the NATALEE trial. Presented at: San Antonio Breast Cancer Symposium; December 5-9, 2023; San Antonio, TX. **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.** Data on file. NATALEE (LEE011O1). Novartis Pharmaceuticals Corp; 2024. **6.** Data on file. CLEE011O12301C (NATALEE) final iDFS analysis results. Novartis Pharmaceuticals Corp; 2023. **7.** 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 **8.** 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 **9.** Neven P, Fasching PA, Chia S, et al. Updated overall survival from the MONALEESA-3 trial in postmenopausal women with HR+/HER2- advanced breast cancer receiving first-line ribociclib plus fulvestrant. *Breast Cancer Res.* 2023;25(1):103. doi:10.1186/s13058-023-01701-9 **10.** Lu YS, Im S-A, Colleoni M, et al. Updated overall survival of ribociclib plus endocrine therapy versus endocrine therapy alone in pre- and perimenopausal patients with HR+/HER2- advanced breast cancer in MONALEESA-7: a phase III randomized clinical trial. *Clin Cancer Res.* 2022;28(5):851-859. doi:10.1158/1078-0432.CCR-21-3032 **11.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. *N Engl J Med.* 2022;386(10):942-950. doi:10.1056/NEJMoa2114663 **12.** Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med.* 2016;375(18):1738-1748. doi:10.1056/NEJMoa1609709 **13.** Slamon DJ, Neven P, Chia S, et al. Phase III randomized study of ribociclib and fulvestrant in hormone receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer: MONALEESA-3. *J Clin Oncol.* 2018;36(24):2465-2472. doi:10.1200/JCO.2018.78.9909 **14.** Slamon DJ, Neven P, Chia S, et al. Overall survival with ribociclib plus fulvestrant in advanced breast cancer. *N Engl J Med.* 2020;382(6):514-524. doi:10.1056/NEJMoa1911149 **15.** Tripathy D, Im S-A, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomised phase 3 trial. *Lancet Oncol.* 2018;19(7):904-915. doi:10.1016/S1470-2045(18)30292-4 **16.** Data on file. CLEE011E2301. Novartis Pharmaceuticals Corp; 2020. **17.** Im S-A, Lu Y-S, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Engl J Med.* 2019;381(4):307-316. doi:10.1056/NEJMoa1903765

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.

Please see 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 you and your patients

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

Your practice and patients will have access to a Novartis Patient Support team committed to providing the support you need, including:

Insurance Support

Dedicated assistance with access and reimbursement

Financial Support

Assistance with relevant savings options for your eligible patients

Clinical Testing and Support

Personalized support for your patients on therapy

Ongoing Support

Single points of contact for you and your patients

Download the Start Form to get your patients started with KISQALI, today

To learn more, contact your dedicated Novartis Patient Support Team at 1-866-433-8000,
Monday-Friday, 8:00 AM - 8:00 PM ET, excluding holidays

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.

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

KISQALI® ribociclib 200 mg tablets

Novartis Patient Support

Insurance support

Benefits Verification

Once you've enrolled your patients in Novartis Patient Support, our team will conduct a benefits verification to help you better understand your patients' coverage, including:

- Work with your patients' health plan to understand coverage for KISQALI
- Inform your practice about additional requirements, such as prior authorization
- Identify savings options available to your patients

Prior Authorizations (PAs) and Appeals

Novartis Patient Support can help with PA requests or letters of appeal by working directly with you or your office, including:

- Provide best practices and timely updates via phone
- Share helpful resources about the PA and appeals process including:
  - Access and Support Guide, which includes the following:
    - Checklists and sample letters to help your office prepare and follow up on requests to health plans
    - Links to available resources to help your patients get started on and afford their KISQALI treatment
- ICD-10-CM Flashcard which includes information on potential codes for KISQALI

9 out of 10 patients
have favorable coverage for KISQALI for approved metastatic indications[1]

Unrestricted or single-step edit coverage from KISQALI MMIT data as of June 2024.

For information on benefits verification, PA or appeals processes and health plan requirements, contact your Dedicated Novartis Associate Director, Access & Reimbursement (ADAR), or download the Start Form

Reference: 1. Data on file. Kisqali MMIT data June 2024. Novartis Pharmaceuticals Corp; 2024.

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

KISQALI® ribociclib 200 mg tablets

Novartis Patient Support

Financial support

$0 Co-Pay Plus Offer*

- Patients may be eligible for immediate co-pay savings on their next prescription of KISQALI tablets and/or FEMARA® (including generic letrozole)
- Eligible patients with private insurance may pay $0 per month for KISQALI*
- Novartis will pay the remaining co-pay, up to $15,000 per calendar year, per product*

The Bridge Program†

- Up to 5 free treatment cycles of KISQALI while health plan coverage is pursued
- Once patients enroll in Novartis Patient Support, we automatically identify if they are eligible for the Bridge Program based on the results of the benefits verification
- Privately insured patients waiting for their coverage to take effect for KISQALI may be eligible for an additional supply of KISQALI that could continue for up to 5 treatment cycles

Free Trial Offer‡

- Your patients are eligible to receive a 1-treatment-cycle supply of KISQALI and/or FEMARA® (including generic letrozole) at no cost
- No purchase required of KISQALI and/or FEMARA (including generic letrozole)
- This offer is available for patients with a valid prescription for KISQALI and/or FEMARA (including generic letrozole), including patients who have not been prescribed KISQALI or another Novartis product

The Novartis Patient Assistance Foundation, Inc (NPAF)

- If uninsured or underinsured patients express financial hardship, Novartis Patient Support can help connect them with Novartis Patient Assistance Foundation (NPAF)
- NPAF is an independent 501(c)(3) non-profit, non-commercial entity
- Patients who cannot afford the cost of their Novartis medications may be eligible to receive them from NPAF at no cost

For more information on NPAF, visit www.PAP.Novartis.com or call 1-800-277-2254, then select option 2.

***Limitations apply.** Valid only for those with private insurance. The Program includes the Co-Pay Plus offer, Plus Card (if applicable), and Rebate, with a combined annual limit up to $15,000. Patient is responsible for any costs once limit is reached in a calendar year. Program not valid (i) under Medicare, Medicaid, TRICARE, VA, DoD, or any other federal or state health care program, (ii) where patient is not using insurance coverage at all, (iii) where the patient's insurance plan reimburses for the entire cost of the drug, or (iv) where product is not covered by patient's insurance. The value of this program is exclusively for the benefit of patients and is intended to be credited towards patient out-of-pocket obligations and maximums, including applicable co-payments, coinsurance, and deductibles. Program is not valid where prohibited by law. Patient may not seek reimbursement for the value received from this program from other parties, including any health insurance program or plan, flexible spending account, or health care savings account. Patient is responsible for complying with any applicable limitations and requirements of their health plan related to the use of the Program. Valid only in the United States and Puerto Rico. For purchases of FEMARA only, this offer is NOT valid for Massachusetts patients and is only valid for California patients that meet additional eligibility criteria. This Program is not health insurance. Program may not be combined with any third-party rebate, coupon, or offer. Proof of purchase may be required. Novartis reserves the right to rescind, revoke, or amend the Program and discontinue support at any time without notice.

†**The Bridge Program applies to KISQALI only.** Eligible patients must have private insurance, a valid prescription for KISQALI, and a denial of insurance coverage based on a prior authorization requirement. Program requires the submission of a prior authorization and/or appeal of the coverage denial within the first 90 days of enrollment to remain eligible. Program provides KISQALI for free to eligible patients for up to 5 months, or until they receive insurance coverage approval, whichever occurs earlier. A valid prescription consistent with FDA-approved labeling is required. Program is not available to patients whose medications are reimbursed in whole or in part by Medicare, Medicaid, TRICARE, or any other federal or state program. Patients may be asked to reverify insurance coverage status during the course of the program. No purchase necessary. Program is not health insurance, nor is participation a guarantee of insurance coverage. Additional limitations may apply. Novartis Pharmaceuticals Corporation reserves the right to rescind, revoke, or amend this Program without notice.

‡**No purchase required.** This free trial is not health insurance. Void where prohibited by law. Product dispensed pursuant to terms and conditions of voucher. Valid only in the US and Puerto Rico. For Massachusetts residents, offer is valid for one of the following: the KISQALI FEMARA Co-Pack or KISQALI and/or generic letrozole. Claims shall not be submitted to any public or private third-party payer or any federal or state health care program for reimbursement. Offer not valid if reproduced or submitted to any other payer. It is illegal for any person to sell, purchase or trade, or offer to sell, purchase or trade, or to counterfeit, this voucher. Prescriber ID# required on prescription. This is the property of Novartis Pharmaceuticals Corporation and must be returned upon request. Novartis Pharmaceuticals Corporation reserves the right to rescind, revoke, or amend this offer without notice.

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

KISQALI® ribociclib 200 mg tablets

Novartis Patient Support

Clinical testing and support

We provide workflow support and options for testing, including:

- **Clinical educators** to support you and your office with questions about testing needs for KISQALI
- **ECG device program** your patients can receive their ECG assessment in seconds in your office or at home

There is no direct cost to you or your patients for participating in this program.

To learn more, contact your dedicated Novartis Patient Support Team at 1-866-433-8000, Monday-Friday, 8:00 AM - 8:00 PM ET, excluding holidays.

Download the Start Form to fill out applicable information for ECG testing support

Limitations apply. KISQALI ECG Device Monitoring Program is only permitted to be used for monitoring or evaluating a patient for the current or potential administration of ribociclib. The equipment or services are not permitted to be used for any purpose outside of the scope of the program. You must not bill any entity or person for any equipment or services relating to the provision or interpretation of the ECG. In the event that you fail to abide by the rules of the KISQALI ECG Device Monitoring Program, your participation in the program may be terminated or modified at any time without prior notice, and you may be subject to additional remedies. Additional terms and conditions apply.

Sunshine Act costs may apply.

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

KISQALI® ribociclib 200 mg tablets

Novartis Patient Support

Ongoing support

Novartis Patient Support provides patients with ongoing help to stay on track with their KISQALI treatment plan, including:

- A dedicated Novartis Patient Support Team member to answer their questions at every step
- Information on financial support options
- Help navigating health care changes
- Tips for setting up a routine that can help patients stay on track with their medication dosing
- Educational resources about KISQALI and living with breast cancer
- Email communications tailored to their treatment journey
- A choice of texts and calls, including tips to keep them on track

To learn more, contact your dedicated Novartis Patient Support Team at 1-866-433-8000, Monday-Friday, 8:00 AM - 8:00 PM ET, excluding holidays

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

KISQALI® ribociclib 200 mg tablets

Downloadable resources

Novartis offers additional resources to support providers and patients.

These indication-specific and dual-indication resources are available for download at KISQALI-HCP.COM.

Resources for HR+/HER2- early breast cancer

Resources for HR+/HER2- metastatic breast cancer

Ask your Novartis Oncology Specialist or Clinical Educator about
available offerings and resources for KISQALI

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

KISQALI® ribociclib 200 mg tablets

Expert perspectives for treating with KISQALI

View expert videos at
KISQALI-HCP.COM

KISQALI for HR+/HER2- early breast cancer

KISQALI for HR+/HER2- metastatic breast cancer

The health care professionals quoted in this piece have been compensated by Novartis Pharmaceuticals Corporation.

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

KISQALI® ribociclib 200 mg tablets

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.

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.

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

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 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 **(continued)** 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.

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.

NOVARTIS

KISQALI® ribociclib 200 mg tablets

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

9/24

FA-11259592