Patient portrayal.

For premenopausal patients with HR+/HER2- mBC,

MORE LIFE for living

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.

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MONALEESA-7: 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. OS was a secondary end point; PFS was the primary end point. **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.**[2-6]

1L, first line; AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; HER2-, human epidermal growth factor receptor 2-negative; HR, hazard ratio; HR+, hormone receptor-positive; ITT, intent to treat; mBC, metastatic breast cancer; mOS, median overall survival; NR, not reached; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PFS, progression-free survival.

Indications

KISQALI is indicated for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (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 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

Patient portrayal.

Younger women who are diagnosed with HR+/HER2- mBC face a poorer prognosis[7]

MONALEESA-7

- **A statistically significant OS benefit in this population[6]**
- **The only CDK4/6 inhibitor trial dedicated to premenopausal patients with HR+/HER2- mBC[4]**
  - Almost 20 years passed between the publication of the last phase III trial dedicated to the treatment of premenopausal women with HR+/HER2- mBC* and MONALEESA-7[7]

*Not testing only ovarian suppression modalities.

MONALEESA-7 was a randomized, double-blind, placebo-controlled, phase III study of KISQALI 600 mg (dosed orally, once daily for the first 21 days followed by 7 days off, resulting in a complete cycle of 28 days) + 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. Patients continued treatment until disease progression or unacceptable toxicity. **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).[2-5]

CDK, cyclin-dependent kinase; ET, endocrine therapy.

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 KISQALI in patients with severe ILD/pneumonitis or any recurrent symptomatic ILD/pneumonitis.

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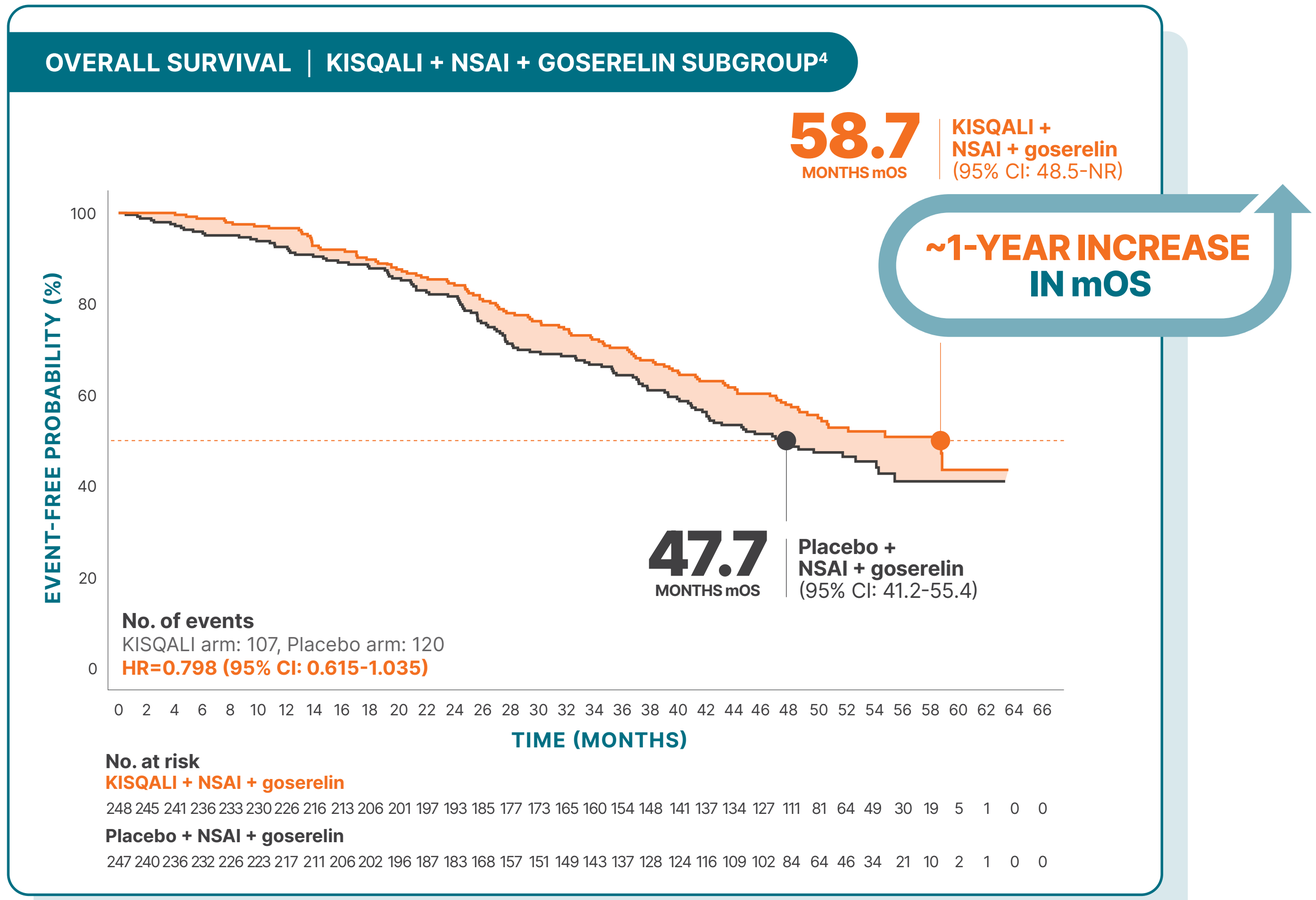
KISQALI® ribociclib 200 mg tablets

Nearly 5 years median overall survival for 1L premenopausal patients—which means MORE life for living

MONALEESA-7: KISQALI + NSAI + goserelin in 1L premenopausal patients
At a median follow-up of 54 months



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

- 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

At a median follow-up of 35 months:

- **Statistical significance was established for OS in the 1L ITT population; HR=0.71 (95% CI: 0.54-0.95); *P*=0.00973[6]**
- **In the subgroup of patients who received tamoxifen, an increased risk for QT prolongation was observed. KISQALI is not indicated for concomitant use with tamoxifen[2]**

"MONALEESA-7 is the only study specifically designed for premenopausal and perimenopausal women with HR+/HER2- mBC, a population that we usually consider higher risk."

—Aixa Soyano, MD
Moffitt Cancer Center, Tampa, Florida

Dr Soyano has been compensated for her time by Novartis Pharmaceuticals Corporation.

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.

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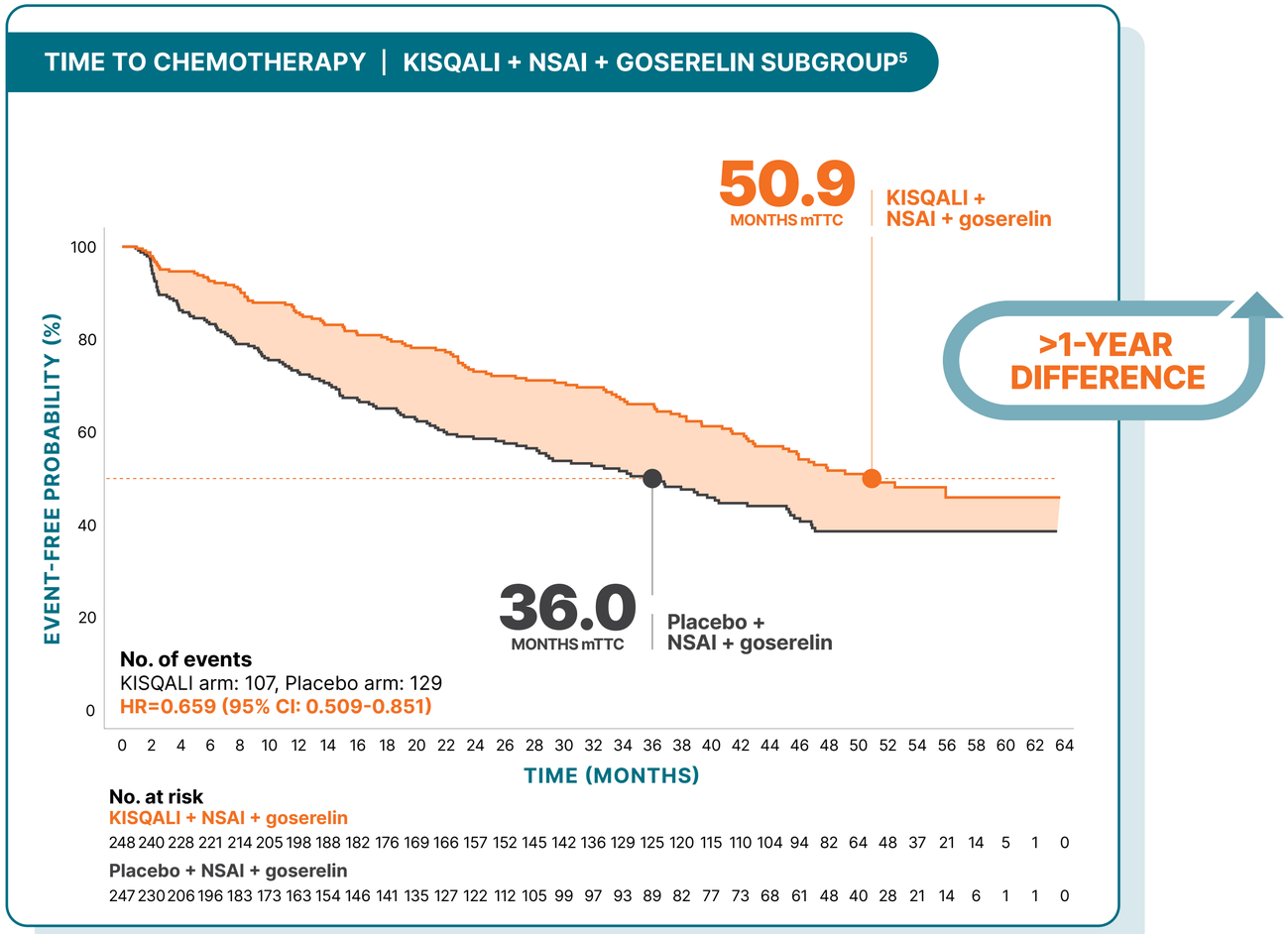
KISQALI® ribociclib 200 mg tablets

KISQALI + AI means more time living without chemotherapy

MONALEESA-7: Median time to chemotherapy delayed over 4 years for 1L premenopausal patients
At a median follow-up of 54 months



- **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)[5]**
- **Time to chemotherapy was evaluated in a post hoc exploratory analysis** and was defined as the time from randomization to the beginning of the first chemotherapy after discontinuing study treatment[6]
- There was no prespecified statistical procedure controlling for type 1 error

mTTC, median time to chemotherapy.

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.

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

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KISQALI® ribociclib 200 mg tablets

MONALEESA-7: KISQALI + NSAI + goserelin safety 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

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

- 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
- 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

ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; CBC, complete blood count; CTCAE, Common Terminology Criteria for Adverse Events; ECG, electrocardiogram; GGT, gamma-glutamyl transferase; ILD, interstitial lung disease; LFT, liver function test; SCAR, severe cutaneous adverse reaction.

Grading according to CTCAE version 4.03.

*Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (<1%).

†Only includes grade 3 ARs.

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KISQALI® ribociclib 200 mg tablets

In the only phase III CDK4/6 inhibitor trial dedicated to this population with HR+/HER2- mBC, KISQALI + NSAI + goserelin demonstrated

Nearly 5 years median overall survival for 1L premenopausal patients

#1 PRESCRIBED in mBC

KISQALI is the #1 prescribed CDK4/6 inhibitor in new-to-brand prescriptions in HR+/HER2- mBC, including in premenopausal patients.[8,9]

January and February 2025 IQVIA custom breast cancer market sizing reports.

See MORE trial data for KISQALI

MONALEESA-7: 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. **KISQALI is not indicated for concomitant use with tamoxifen due to an increased risk for QT prolongation.** OS was a secondary end point; PFS was the primary end point. **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.**[2-6]

IMPORTANT SAFETY INFORMATION

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

Most common (incidence ≥20%) adverse reactions include infections, nausea, fatigue, diarrhea, vomiting, headache, constipation, alopecia, cough, rash, and back pain.

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Patient portrayal.

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Important Safety Information

Indications

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

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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 advanced or mBC (MONALEESA-2, MONALEESA-3, and MONALEESA-7) who received 600 mg KISQALI plus NSAI or fulvestrant, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >60 ms QTcF increase from baseline. QTcF prolongation was reversible with dose interruption. The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI. There were no reported cases of torsades de pointes. In MONALEESA-2, in the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation. No cases of sudden death were reported in MONALEESA-7 or MONALEESA-3.

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

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

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

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

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 the ULN and total bilirubin >2x the 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 advanced or mBC (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. 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 click here for full Prescribing Information for KISQALI.

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References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.4.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 17, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Kisqali. Prescribing information. Novartis Pharmaceuticals Corp. **3.** 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 **4.** Lu Y-S, 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 **5.** Data on file. CLEE011E2301 additional analysis. Novartis Pharmaceuticals Corp; 2020. **6.** 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 **7.** Bardia A, Hurvitz S. Targeted therapy for premenopausal women with HR+, HER2- advanced breast cancer: focus on special considerations and latest advances. *Clin Cancer Res.* 2018;24(21):5206-5218. doi:10.1158/1078-0432.CCR-18-0162 **8.** Data on file. mBC NBRx share data from IQVIA market sizing report. Novartis Pharmaceuticals Corp; 2025. **9.** Data on file. mBC new patient – premenopausal share data from IQVIA market sizing report. Novartis Pharmaceuticals Corp; 2025.

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