MORE LIFE for living

KISQALI may help your patients, including elderly patients, live longer—and that could mean more time doing what they love

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 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]

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.

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

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

PATIENT PROFILE | EFFICACY | ELDERLY PATIENT OS | SAFETY | DOSING AND ADJUSTMENTS | COVERAGE

Meet Susan, a 68-year-old patient with HR+/HER2- mBC

Susan has HR+/HER2- mBC. Now that she is a grandmother, she wants to be able to spend as much time as possible with her family—and needs a treatment option that can give her more life for living.

How could your treatment choice help make a difference in Susan's life?

KISQALI can help patients like Susan achieve their treatment goals:

✓ **OVERALL SURVIVAL**
KISQALI demonstrated an overall survival benefit vs placebo, including in elderly patients

✓ **ESTABLISHED SAFETY**
Safety was generally consistent across all age groups, including in elderly patients[5]

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]

Pooled safety from MONALEESA trials (N=1065): In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were leukocytes decreased (95%), neutrophils decreased (93%), hemoglobin decreased (68%), lymphocytes decreased (66%), aspartate aminotransferase increased (55%), gamma-glutamyl transferase increased (53%), alanine aminotransferase increased (52%), infections (47%), nausea (47%), creatinine increased (42%), fatigue (35%), platelets decreased (34%), diarrhea (33%), vomiting (29%), headache (27%), constipation (25%), alopecia (25%), cough (24%), rash (24%), back pain (24%), and glucose serum decreased (20%). In MONALEESA-2, adverse reactions which resulted in permanent discontinuation of both KISQALI and letrozole in ≥2% of patients were alanine aminotransferase increased (5%), aspartate aminotransferase increased (3%), and vomiting (2%).[2]

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.

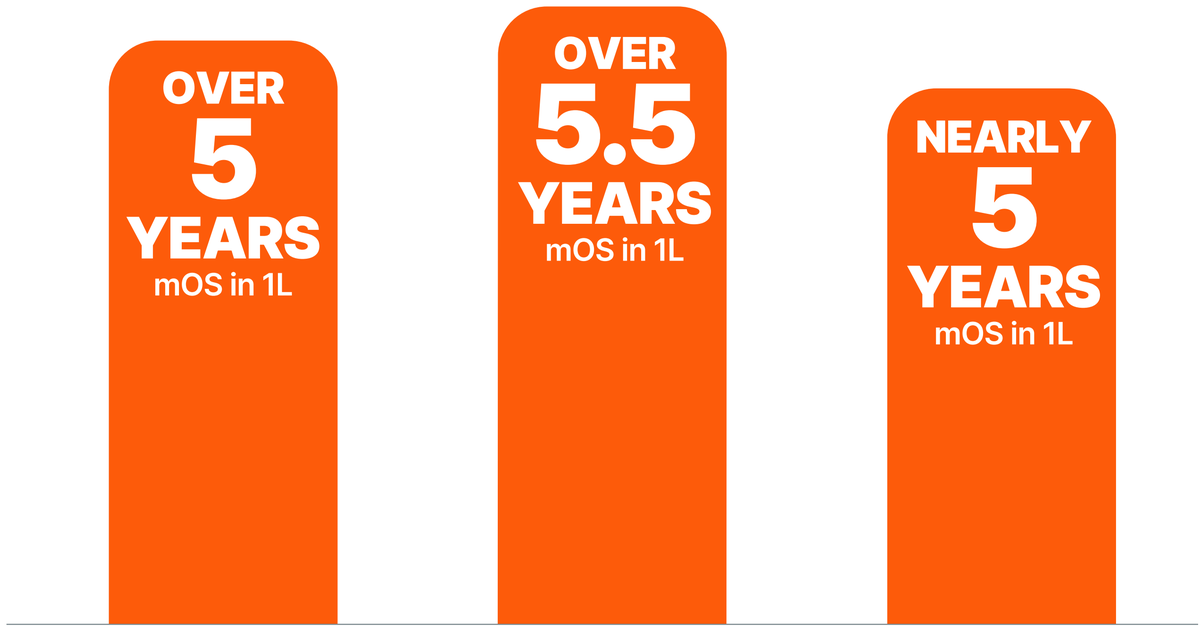
If SJS, TEN, or DiHS/DRESS is confirmed, permanently discontinue KISQALI. Do not reintroduce KISQALI in patients who have experienced SCARs or other life-threatening cutaneous reactions during KISQALI treatment.

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

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

PATIENT PROFILE | EFFICACY | ELDERLY PATIENT OS | SAFETY | DOSING AND ADJUSTMENTS | COVERAGE

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



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.[2-4]

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.[2,6-8]

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.[2,9-12]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued)

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.

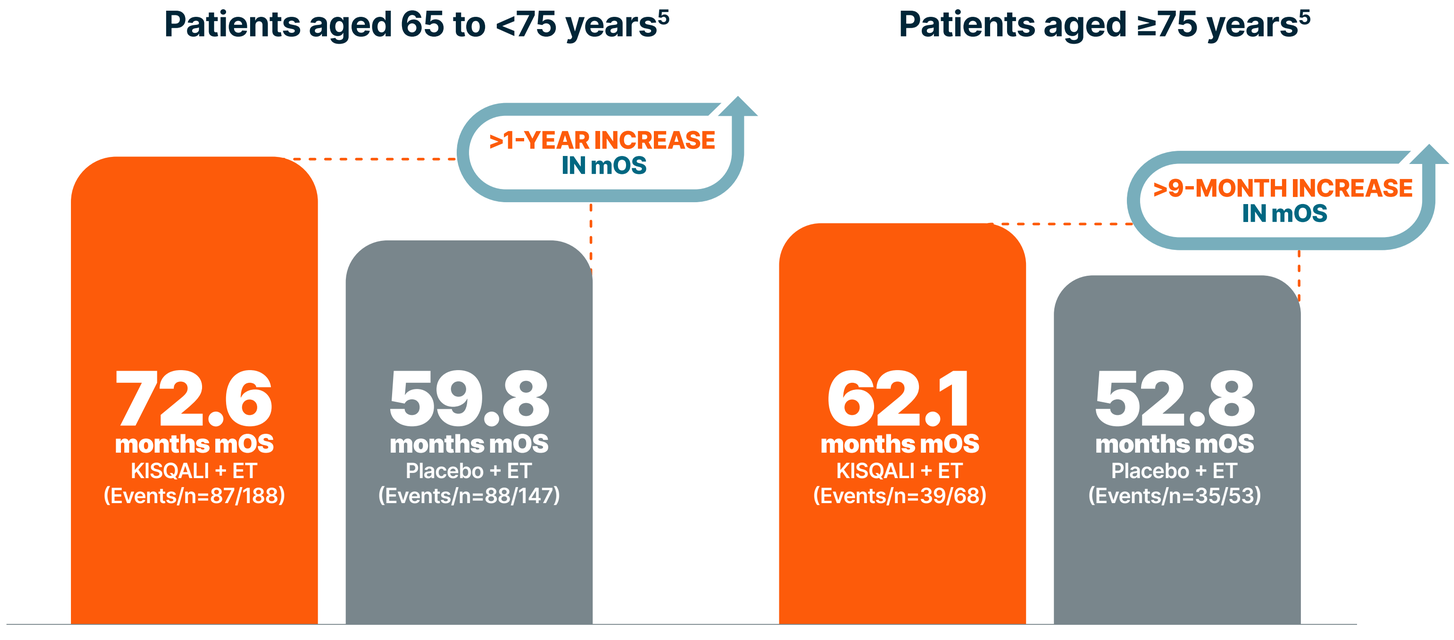
Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

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

KISQALI® ribociclib 200 mg tablets

An exploratory, pooled, post hoc analysis of the MONALEESA-2, MONALEESA-3, and MONALEESA-7 studies

A consistent overall survival benefit across age groups, including in elderly patients



- Median follow-up of 77.3 months[5]
- Increase of 12.8 months (HR=0.79 [95% CI: 0.58-1.07])[5]

- Median follow-up of 76.0 months[5]
- Increase of 9.3 months (HR=0.75 [95% CI: 0.46-1.21])[5]

KISQALI prolonged mOS by 15.9 months (HR=0.69 [95% CI: 0.56-0.84]) in patients <65 years old.

At a median follow-up of 71.2 months, mOS was[5]:

- 67.6 months with KISQALI + ET (Events/n=182/419)
- 51.7 months with placebo + ET (Events/n=194/354)

Data was pooled from patients within the first-line setting in the MONALEESA-2, MONALEESA-3, and MONALEESA-7 studies. In MONALEESA-7, only the nonsteroidal aromatase inhibitor cohort was included, and patients with early relapse (≤12 months after [neo]adjuvant ET) were excluded, as their prognoses were closer to those of patients in the second-line setting.[5]

This pooled dataset included a total of 1229 patients across 3 different age groups; 773 (63%) were <65 years, 335 (27%) were 65 to <75 years, and 121 (10%) were ≥75 years.[5]

The 65 to <75 and ≥75 years age groups consisted of patients from the MONALEESA-2 and MONALEESA-3 studies. The <65 years age group consisted of patients from the MONALEESA-2, MONALEESA-3, and MONALEESA-7 studies.[5]

This exploratory analysis evaluated PFS, OS, time to first subsequent chemotherapy, and safety across age groups.[5]

The ≥75 years age group has a small sample size, and data should be interpreted with caution.

These results are exploratory and hypothesis-generating; as such, there was no statistical procedure controlling for type 1 error.

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued)

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

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

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

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

KISQALI® ribociclib 200 mg tablets

Safety was generally consistent across all age groups, including in elderly patients

ADVERSE EVENTS OF SPECIAL INTEREST (AESIs) BY AGE[5]

	Patients <65 years				Patients 65 to <75 years				Patients ≥75 years			
	KISQALI + ET (n=419)		Placebo + ET (n=350)		KISQALI + ET (n=188)		Placebo + ET (n=147)		KISQALI + ET (n=68)		Placebo + ET (n=52)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
Neutropenia	79	67	8	3	77	64	6	0	63	53	4	2
– Febrile neutropenia	1	1	0.3	0.3	1	1	0	0	3	3	0	0
Infections	60	7	50	3	64	11	53	5	56	7	62	6
Hepatobiliary toxicity	31	15	21	6	25	10	17	3	32	19	19	8
QT interval prolongation	9	3	3	1	11	4	4	2	16	13	2	2
Interstitial lung disease	1	0	1	0	3	1	1	0	7	3	0	0

No grade 5 AEs were reported.

IMPORTANT SAFETY INFORMATION (continued)

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

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KISQALI® ribociclib 200 mg tablets

Safety was generally consistent across all age groups, including in elderly patients (continued)

Pooled safety from pivotal MONALEESA trials (N=1065): In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were leukocytes decreased (95%), neutrophils decreased (93%), hemoglobin decreased (68%), lymphocytes decreased (66%), aspartate aminotransferase increased (55%), gamma-glutamyl transferase increased (53%), alanine aminotransferase increased (52%), infections (47%), nausea (47%), creatinine increased (42%), fatigue (35%), platelets decreased (34%), diarrhea (33%), vomiting (29%), headache (27%), constipation (25%), alopecia (25%), cough (24%), rash (24%), back pain (24%), and glucose serum decreased (20%). In MONALEESA-2, adverse reactions which resulted in permanent discontinuation of both KISQALI and letrozole in ≥2% of patients were alanine aminotransferase increased (5%), aspartate aminotransferase increased (3%), and vomiting (2%).[2]

Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See the Warnings and Precautions section of the KISQALI Prescribing Information for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatobiliary toxicity, neutropenia, and embryo-fetal toxicity.[2]

MONALEESA-2

- Dose reductions due to ARs occurred in 45% of patients receiving KISQALI + letrozole[2]
- Permanent discontinuations due to AEs: 7.5% with KISQALI + letrozole; 2.1% with placebo + letrozole[3]

MONALEESA-3

- Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (1%)[2]
- Dose reductions due to ARs occurred in 32% of patients receiving KISQALI + fulvestrant[2]
- Permanent discontinuations due to AEs: 8.5% with KISQALI + fulvestrant; 4.1% with placebo + fulvestrant[6]

MONALEESA-7

- Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (<1%)[2]
- Dose reductions due to ARs occurred in 33% of patients receiving KISQALI + NSAI + goserelin[2]
- Permanent discontinuations due to AEs in the ITT population: 4% with KISQALI + ET (NSAI or tamoxifen) + goserelin; 3% with placebo + ET (NSAI or tamoxifen) + goserelin[9]
- **KISQALI is not indicated for concomitant use with tamoxifen[2]**

IMPORTANT SAFETY INFORMATION (continued)

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.

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

KISQALI® ribociclib 200 mg tablets

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

	mOS for patients with ≥1 dose reduction	mOS for patients without dose reductions
MONALEESA-2: 62.6% of patients (209/334) had ≥1 dose reduction[13,14]	**66.0 months** (95% CI: 57.6-75.7)	**60.6 months** (95% CI: 42.5-79.2)
	HR=0.87 (95% CI: 0.65-1.18)	
MONALEESA-3: 40.7% of patients (197/484) had ≥1 dose reduction[15,16]	**NOT REACHED** (95% CI: 43-NR)	**NOT REACHED** (95% CI: 41.1-NR)
	HR=0.88 (95% CI: 0.64-1.21)	
MONALEESA-7: 40.7% of patients (101/248) had ≥1 dose reduction[16,17]	**NOT REACHED** (95% CI: NR-NR)	**NOT REACHED** (95% CI: NR-NR)
	HR=0.79 (95% CI: 0.46-1.36)	

In the MONALEESA trials, which included elderly patients, the efficacy of KISQALI was maintained regardless of dose reduction[2,13-17]

Results are based on a post hoc analysis; efficacy in the placebo comparator arms was not assessed and should be interpreted with caution.

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 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.

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KISQALI® ribociclib 200 mg tablets

Only KISQALI offers single-strength tablets for simple dose reductions

Eliminate the need for new mid-cycle prescriptions and additional costs[2]

Recommended starting dose

3 TABLETS (600 mg)

1st reduction

2 TABLETS (400 mg)

2nd reduction

1 TABLET (200 mg)

- 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[2]; 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[2]
- Patients should continue treatment until disease progression or unacceptable toxicity[2]

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

- If dose reduction below 200 mg/day is required, discontinue treatment[2]
- KISQALI dose modification is recommended based on individual safety and tolerability[2]
- KISQALI can be taken with or without food[2]
- 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)[2]
- After dispensing, patients may store at room temperature at 20°C to 25°C (68°F to 77°F) for up to 2 months[2]
- Store tablets in the original blister pack[2]

IMPORTANT SAFETY INFORMATION (continued)

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

Adverse reactions. 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

With KISQALI, most elderly patients are covered

97% of Medicare Part D patients have favorable coverage for KISQALI for approved metastatic indications[18]

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

For more information about patient support programs visit:
KISQALI-support.com

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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Patient portrayal.

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KISQALI® ribociclib 200 mg tablets

Important Safety Information

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.

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

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

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

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

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

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

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

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

In patients with 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.**

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KISQALI® ribociclib 200 mg tablets

Abbreviations and references

Abbreviations: 1L=first line; AE=adverse event; AI=aromatase inhibitor; AR=adverse reaction; CBC=complete blood count; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; ECG=electrocardiogram; ET=endocrine therapy; HR=hazard ratio; ILD=interstitial lung disease; 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; SCAR=severe cutaneous adverse reaction.

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.** Hart L, Im SA, Tolaney SM, et al. Efficacy, safety, and quality of life with ribociclib + endocrine therapy in elderly patients with HR+/HER2− advanced breast cancer across the MONALEESA-2, -3, and -7 trials. Poster presented at: San Antonio Breast Cancer Symposium; December 5-9, 2023; San Antonio, TX. Poster PS02-01. **6.** 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 **7.** 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 **8.** 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 **9.** 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 **10.** 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 **11.** Data on file. CLEE011E2301 additional analysis. 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.** Data on file. ML2 OS by dose reduction. Novartis Pharmaceuticals Corp; 2021. **14.** Data on file. CLEE011A2301 additional analysis. Novartis Pharmaceuticals Corp; 2021. **15.** Data on file. CLEE011F2301 additional analysis. Novartis Pharmaceuticals Corp; 2020. **16.** Data on file. OS by dose reduction poster. Novartis Pharmaceuticals Corp; 2020. **17.** Data on file. CLEE011E2301 additional analysis. Novartis Pharmaceuticals Corp; 2020. **18.** Data on file. Kisqali MMIT data June 2024. Novartis Pharmaceuticals Corp; 2024.

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

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