Learn MORE about KISQALI

in 1L patients with HR+/HER2- mBC who have aggressive disease

Aggressive disease is characterized by rapidly growing cancer cells that are more likely to spread (metastasize) to other parts of the body. Aggressive breast cancer is generally associated with a higher risk of recurrence and poorer prognosis.[1]

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.

KISQALI® ribociclib 200 mg tablets

Meet Kate, a patient with HR+/HER2- mBC with visceral metastases

With visceral metastases, we know that Kate has a more challenging journey ahead. Kate's life has already been affected by her aggressive disease, and she is not feeling her best.

Living longer is an important treatment goal for patients like Kate with visceral disease, but she also needs a treatment with a tolerable safety profile. KISQALI can deliver on Kate's goals:

✓ **Overall survival**

✓ **Tolerable safety profile**

View safety table

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.

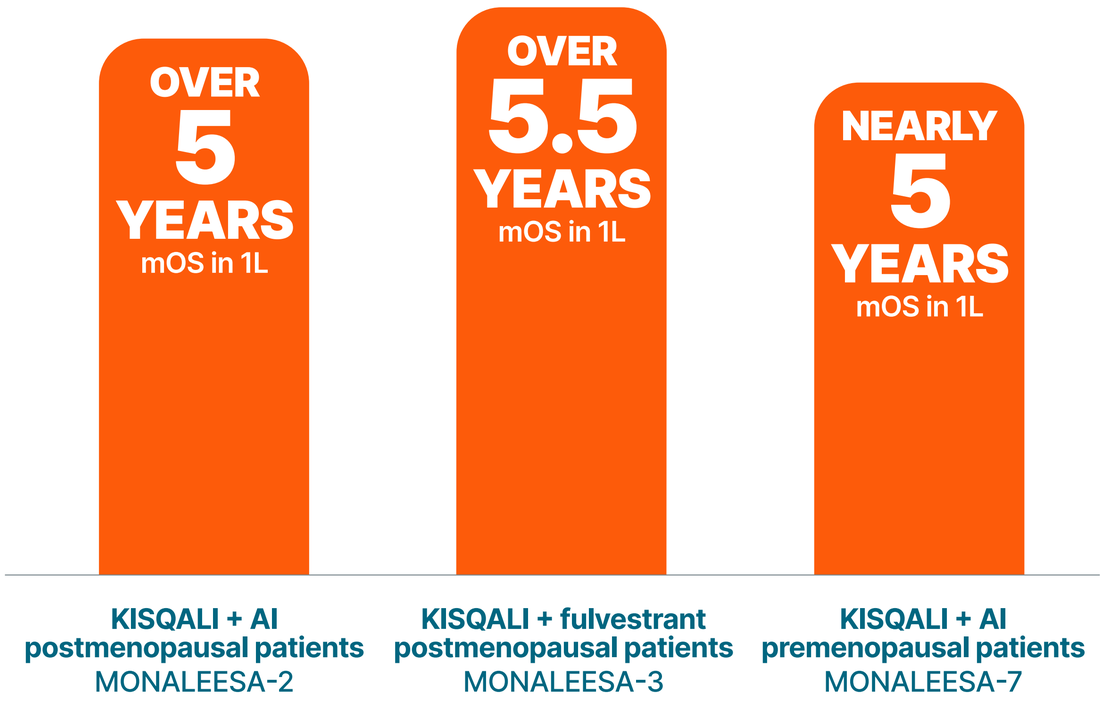
If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Early consultation with a dermatologist is recommended to ensure greater diagnostic accuracy and appropriate management.

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.

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

Patient portrayal.

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.**[2,5-7]

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.**[2,8-11]

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.

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KISQALI® ribociclib 200 mg tablets

KISQALI + AI + goserelin was studied in patients with aggressive disease

RIGHT Choice trial

Study design[12,13]

- Randomized, phase II, open-label, multicenter trial
- Primary end point: PFS
- Select secondary end points: OS and ORR
- Treatment arms
  - KISQALI + AI (letrozole or anastrozole) + goserelin (n=112)
  - Combination chemotherapy (either of docetaxel + capecitabine, paclitaxel + gemcitabine, or capecitabine + vinorelbine) (n=110)
  - As determined by the investigators, 106 patients presented with visceral crisis and 116 patients presented without visceral crisis
  - Visceral crisis, defined subjectively as severe organ dysfunction, as assessed by signs and symptoms, laboratory studies, and rapid progression of the disease, in patients with mBC often requires a treatment with rapid efficacy

Key inclusion criteria[12]

- Pre-/perimenopausal patients with HR+/HER2- mBC who received no prior systemic therapy for advanced disease
- >10% ER+
- Patients must have met at least 1 of the following criteria, for which combination chemotherapy was clinically indicated:
  - Symptomatic visceral metastases
  - Markedly symptomatic nonvisceral disease if the treating physician opted to give chemotherapy for rapid palliation of patients' symptoms
  - Rapid progression of disease or impending visceral compromise

RIGHT CHOICE: SELECT BASELINE CHARACTERISTICS[12]

	KISQALI + AI + goserelin (n=112)	Combination chemotherapy (n=110)
Median age, years	44	43
De novo disease	63%	66%
AGGRESSIVE DISEASE CHARACTERISTICS		
Symptomatic visceral metastases	66%	69%
Rapid progression	21%	16%
Symptomatic nonvisceral disease	13%	15%
METASTATIC SITES		
Liver	48%	48%
Lung	55%	50%
Liver or lung	78%	75%

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 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.

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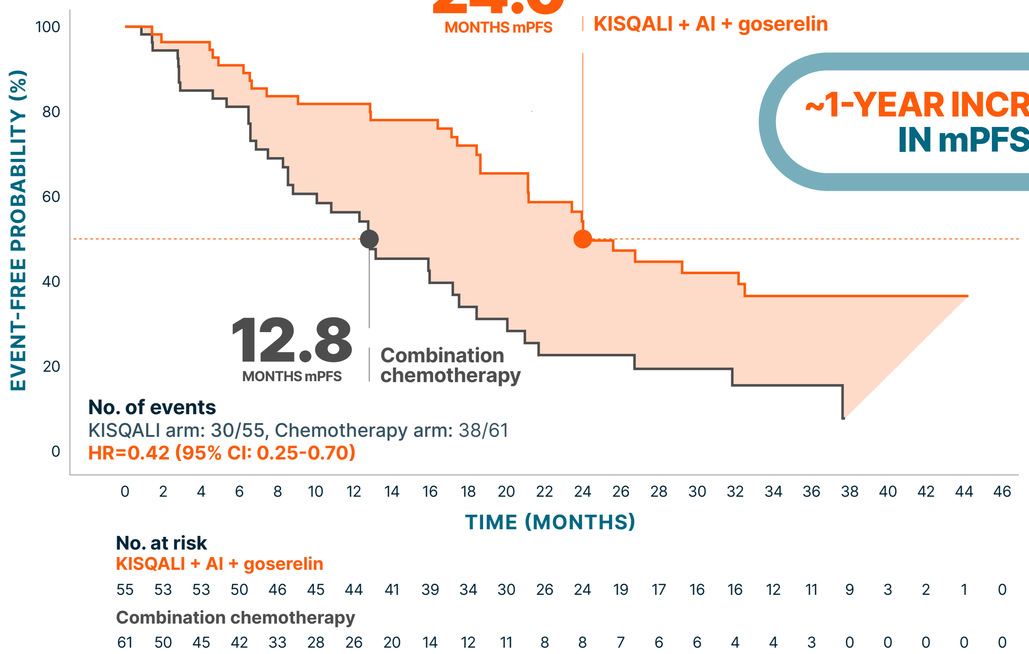
KISQALI® ribociclib 200 mg tablets

KISQALI + AI + goserelin vs combination chemotherapy in aggressive HR+/HER2- advanced breast cancer: subgroup analysis of patients without visceral crisis

The RIGHT Choice trial: a phase II trial evaluating KISQALI + an AI + goserelin for 1L treatment of pre- or perimenopausal patients with HR+/HER2- mBC who have aggressive disease[12]

PFS | KISQALI + AI + GOSERELIN SUBGROUP WITHOUT VISCERAL CRISIS[14]



KISQALI + AI + goserelin tumor response rates were consistent with combination chemotherapy[14,15]

- KISQALI + AI + goserelin ORR: 60.0% (95% CI: 45.9-73.0)
- Combination chemotherapy ORR: 62.3% (95% CI: 49.0-74.4)

Due to the nature of the study, results should be interpreted with caution. These results from a subgroup analysis of patients with aggressive disease who did not have visceral crisis are exploratory and hypothesis-generating; as such, there was no statistical procedure controlling for type 1 error.

Overall survival is being evaluated, but is ongoing and not yet mature.[12]

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.

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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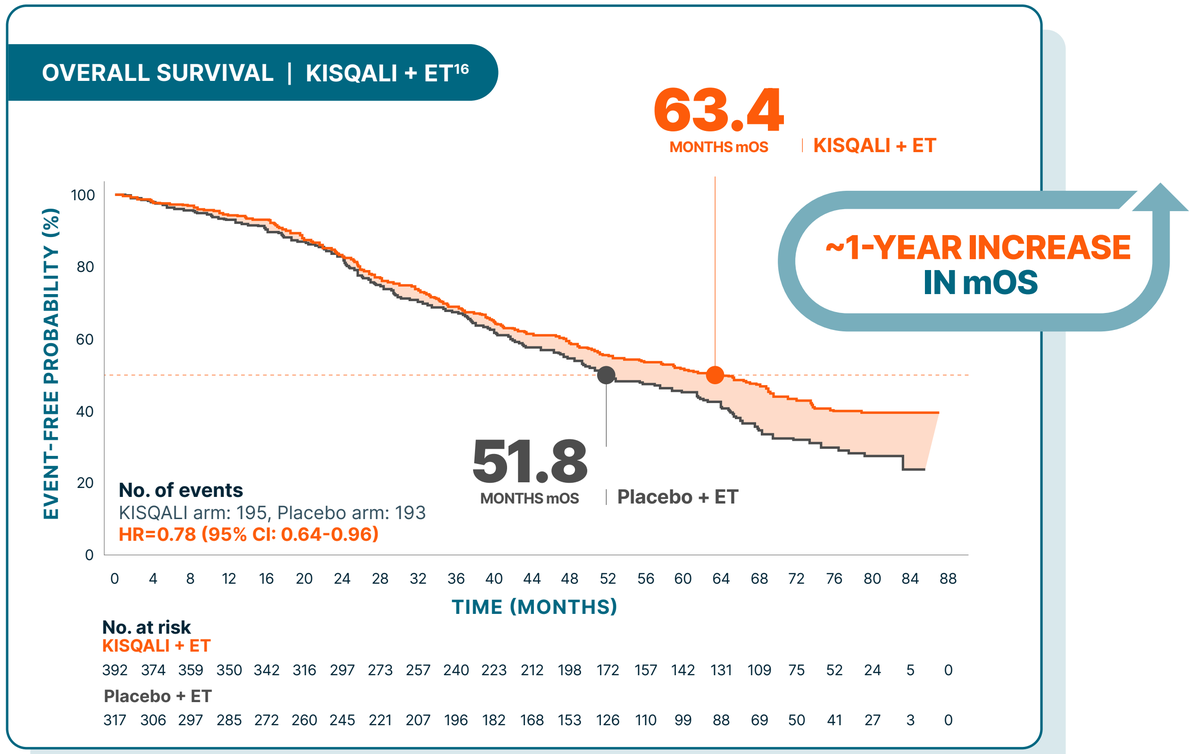
KISQALI® ribociclib 200 mg tablets

KISQALI demonstrated >5 years median overall survival in 1L patients with visceral disease across 3 phase III MONALEESA trials

In an exploratory, pooled subgroup analysis of 1L patients with visceral metastases (n=709) from MONALEESA-2, -3, and -7:
KISQALI increased median OS by ~1 year in 1L pre- and postmenopausal patients with visceral metastases[16]

At a median follow-up of 72 months



- 1L patients were defined as those with de novo disease (no prior exposure to ET) and those with relapse >12 months from the end of (neo)adjuvant ET (late relapse)[16]

PATIENTS IN THE EXPLORATORY POOLED SUBGROUP ANALYSIS[3,5,8,16]

	KISQALI + ET	Placebo + ET
Total patients included from the MONALEESA trials	1066	823
Patients with visceral metastases	640	484
Patients with visceral metastases receiving 1L therapy	392	317

This pooled analysis included 1889 patients from across the MONALEESA trials, of which 59.5% (n=1124) had visceral metastases; of the 1229 patients receiving 1L therapy, 57.7% (n=709) had visceral metastases.[16]

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

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

Only KISQALI offers single-strength tablets for simple dose reductions with a starting dose of 600 mg

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

Starting dose	1st reduction	2nd reduction
3 TABLETS (600 mg)	2 TABLETS (400 mg)	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:
  - 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
- Dose adjustments for adverse reactions should be made in a stepwise order by reducing the number of tablets taken
- If dose reduction below 200 mg/day is required, discontinue treatment
- Dose modification of KISQALI 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

Dr McAndrew has been compensated for his time by Novartis Pharmaceuticals Corporation.

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.

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

KISQALI® ribociclib 200 mg tablets

KISQALI safety profile

RIGHT CHOICE: ADVERSE EVENTS IN ≥20% OF PATIENTS REGARDLESS OF CAUSALITY IN EITHER TREATMENT ARM IN PATIENTS WITHOUT VISCERAL CRISIS[15]

AE GROUPING, n (%)	Without visceral crisis*			
	KISQALI + ET (n=55)		Combo CT (n=55)	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4
HEMATOLOGIC AEs				
Neutropenia†	48 (87.3)	33 (60.0)	29 (52.7)	22 (40.0)
Leukopenia‡	30 (54.5)	17 (30.9)	17 (30.9)	4 (7.3)
Anemia	19 (34.5)	2 (3.6)	24 (43.6)	5 (9.1)
NONHEMATOLOGIC AEs				
Elevated aspartate aminotransferase	6 (10.9)	2 (3.6)	17 (30.9)	3 (5.5)
Elevated alanine aminotransferase	10 (18.2)	1 (1.8)	20 (36.4)	4 (7.3)
Elevated gamma-glutamyl transferase	6 (10.9)	1 (1.8)	5 (9.1)	2 (3.6)
Electrocardiogram QT prolonged	13 (23.6)	2 (3.6)	5 (9.1)	0
Nausea	7 (12.7)	0	16 (29.1)	1 (1.8)
Vomiting	3 (5.5)	0	16 (29.1)	0
Palmar-plantar erythrodysesthesia	1 (1.8)	0	15 (27.3)	2 (3.6)
Fatigue	5 (9.1)	0	16 (29.1)	2 (3.6)
Diarrhea	3 (5.5)	0	13 (23.6)	1 (1.8)
Arthralgia	13 (23.6)	0	6 (10.9)	0
COVID-19	11 (20.0)	0	7 (12.7)	0
Alopecia	8 (14.5)	0	12 (21.8)	0

RIGHT Choice was a randomized, phase II, open-label, multicenter study of KISQALI + AI + goserelin (n=112) vs combination chemotherapy (either docetaxel + capecitabine, paclitaxel + gemcitabine, or capecitabine + vinorelbine) (n=110) in pre- or perimenopausal patients with HR+/HER2- mBC who have aggressive disease. PFS was the primary end point. Efficacy results are from a subgroup analysis of patients with aggressive disease who did not have visceral crisis. **Due to the nature of the study, results should be interpreted with caution. These results from a subgroup analysis of patients with aggressive disease who did not have visceral crisis are exploratory and hypothesis-generating; as such, there was no statistical procedure controlling for type 1 error.**[12,14,15]

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]

* 6 patients in the patients without visceral crisis subgroup randomized to the combo CT arm were not included in the safety set as they did not receive any study treatment after withdrawal of consent following knowledge of randomization to the CT arm or withdrawal based on investigator's decision.

† Neutropenia includes "neutropenia" and "neutrophil count decreased."

‡ Leukopenia includes "leukopenia" and "white blood cell count decreased."

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

OVERALL SURVIVAL

In MONALEESA-2, KISQALI demonstrated an overall survival benefit vs placebo

>1-YEAR INCREASE IN mOS

RESULTS IN PATIENTS WITH AGGRESSIVE DISEASE

Data from a pooled post hoc analysis of patients with visceral metastases in the MONALEESA trials

~1-YEAR INCREASE IN mOS

Data from a subgroup analysis of patients without visceral crisis in RIGHT Choice

~1-YEAR INCREASE IN mPFS

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[17]

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.

Consider KISQALI for your next 1L adult patient with aggressive disease

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. Patients continued treatment until disease progression or unacceptable toxicity. OS was a secondary end point; PFS was the primary end point.[2-4]

An exploratory, pooled, post hoc analysis of the MONALEESA-2, MONALEESA-3, and MONALEESA-7 studies: In 1L patients with visceral metastases, at a median follow-up of 72 months, mOS was 63.4 months with KISQALI + ET vs 51.8 months with placebo + ET; HR=0.78 (95% CI: 0.64-0.96). **These results are exploratory and hypothesis-generating; as such, there was no statistical procedure controlling for type 1 error.**[16]

RIGHT Choice: Efficacy results are from a subgroup analysis of patients with aggressive disease who did not have visceral crisis. In this subgroup, median PFS was 24.0 months with KISQALI + NSAI + goserelin (95% CI: 21.1-NE) vs 12.8 months with combination chemotherapy (95% CI: 8.5-17.5); HR=0.42 (95% CI: 0.25-0.70). **Due to the nature of the study, results should be interpreted with caution. These results from a subgroup analysis of patients with aggressive disease who did not have visceral crisis are exploratory and hypothesis-generating; as such, there was no statistical procedure controlling for type 1 error.**[14,15]

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

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.**

KISQALI® ribociclib 200 mg tablets

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

Abbreviations and references

Abbreviations: 1L, first line; AE, adverse event; AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CT, chemotherapy; ER+, estrogen receptor-positive; ET, endocrine therapy; HR, hazard ratio; ITT, intent to treat; LHRH, luteinizing hormone-releasing hormone; mBC, metastatic breast cancer; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; NR, not reached; NSAI, nonsteroidal aromatase inhibitor; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

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