

Important Information Provided by Novartis Pharmaceuticals Corporation

Andre F, Fasching PA, Prat A, et al. Pooled analysis of patients treated with 1st-line ribociclib + endocrine therapy in the MONALEESA studies: long-term progression-free survival. Poster presented at: San Antonio Breast Cancer Symposium; December 9-12, 2025; San Antonio, TX. Poster PD5-10.

AI, aromatase inhibitor.

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.

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MONALEESA-2: Study design



Patient portrayal.

MONALEESA-2 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) + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. Patients continued treatment until disease progression or unacceptable toxicity. PFS was the primary end point.[1,2]

BASELINE PATIENT CHARACTERISTICS IN MONALEESA-2[2,*]

	KISQALI + letrozole (n=334)	Placebo + letrozole (n=334)
Age, median, year	62	63
ECOG PS at baseline, %		
0	61.4	60.5
1	38.6	39.5
Disease characteristics, %		
De novo	34.1	33.8
Recurrent	65.9	66.2
DFI ≤12 months	1.2	3
DFI >12 months	64.7	62.9
No. of metastatic sites, %		
0	0.6	0.3
1	29.9	35
2	35.3	30.8
3+	34.1	33.8
Site of metastases, %		
Bone, Any	73.7	73.1
Bone, Only	20.7	23.4
Visceral[†]	59	58.7

*There were no significant differences between the groups.

[†]Visceral involvement included liver, lung, and other visceral metastases.

DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; mBC, metastatic breast cancer; PFS, progression-free survival.

MONALEESA-3: Study design



Patient portrayal.

MONALEESA-3 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) + 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. Patients continued treatment until disease progression or unacceptable toxicity. PFS was the primary end point.[1,3]

BASELINE PATIENT CHARACTERISTICS IN MONALEESA-3[3]

	KISQALI + fulvestrant (n=484)	Placebo + fulvestrant (n=242)
Age, median, year	63	63
ECOG PS at baseline, %		
0	64	65.3
1	35.7	34.3
Missing	0.2	0.4
Disease characteristics, %		
De novo*	20	17.4
Recurrent	80	82.2
DFI ≤12 months	4.5	3.7
DFI >12 months	75.4	78.5
No. of metastatic sites, %		
0	0.4	0
1	31.2	30.2
2	32.2	31.4
3+	36.2	38.0
Site of metastases, %		
Bone, Only	21.3	21.1
Visceral	60.5	60.3
Lung	30.2	29.8
Liver	27.7	26

*De novo includes patients with no first recurrence/progression or with a first recurrence/progression within 90 days of diagnosis with no prior medication. For non-de novo disease, disease-free interval is defined as the time from initial diagnosis to first recurrence/progression.

ET, endocrine therapy.

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MONALEESA-7: Study design



Patient portrayal.

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.** PFS was the primary end point.[1,4,5]

BASELINE PATIENT CHARACTERISTICS IN MONALEESA-7[4]

	KISQALI + NSAI + goserelin (n=335)	Placebo + NSAI + goserelin (n=337)
Age, median, year	43	45
ECOG PS at baseline, %		
0	73	76
1	26	23
2	0	<1
Missing	1	1
Disease characteristics, %		
De novo*	41	40
Recurrent	59	60
DFI ≤12 months	7	4
DFI >12 months	53	56
No. of metastatic sites, %		
0†	<1	0
1	33	35
2	32	29
3+	35	36
Site of metastases, %		
Bone	75	73
Bone, Only	24	23
Visceral‡	58	56

Data are median (range) or number (%). Some percentages do not add up to 100 because of rounding.

*Newly diagnosed disease included patients with no first recurrence or progression, or first recurrence or progression within 90 days of diagnosis with no previous anticancer medication. For patients with existing disease, disease-free interval was the time from initial diagnosis to first recurrence or progression.

†Patients with locoregionally recurrent (non-metastatic) disease were also eligible.

‡Liver, lung, and any other metastatic site except for soft tissue, bone, skin, and lymph nodes.

ITT, intent to treat; NSAI, nonsteroidal aromatase inhibitor.

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Progression-free survival with KISQALI + AI or fulvestrant across the phase III MONALEESA trials

	mPFS in KISQALI group	mPFS in placebo group
MONALEESA-2 **Postmenopausal patients** KISQALI + letrozole vs placebo + letrozole	NR	14.7 months
MONALEESA-3 **Postmenopausal patients** KISQALI + fulvestrant vs placebo + fulvestrant	20.5 months	12.8 months
MONALEESA-7 **Premenopausal patients** KISQALI + NSAI + goserelin vs placebo + NSAI + goserelin	27.5 months	13.8 months

HR, hazard ratio; mPFS, median progression-free survival; NR, not reached.

MONALEESA-2: In the primary analysis at a median follow-up of 15.3 months, mPFS was not reached (95% CI: 19.3-NR) for KISQALI + letrozole vs 14.7 months (95% CI: 13.0-16.5) for placebo + letrozole; HR=0.556 (95% CI: 0.429-0.720); *P*<0.0001.[1,2]

MONALEESA-3: In the primary analysis at a median follow-up of 20 months, mPFS was 20.5 months (95% CI: 18.5-23.5) for KISQALI + fulvestrant vs 12.8 months (95% CI: 10.9-16.3) for placebo + fulvestrant; HR=0.593 (95% CI: 0.480-0.732); *P*<0.0001.[1,3]

MONALEESA-7: Efficacy results are from a prespecified subgroup analysis of 495 patients who received KISQALI (n=248) or placebo (n=247) with an NSAI + goserelin. In the primary analysis at a median follow-up of 19 months, mPFS was 27.5 months (95% CI: 19.1-NR) for KISQALI + NSAI + goserelin vs 13.8 months (95% CI: 12.6-17.4) for placebo + NSAI + goserelin; HR=0.569 (95% CI: 0.436-0.743).[1,4]

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.

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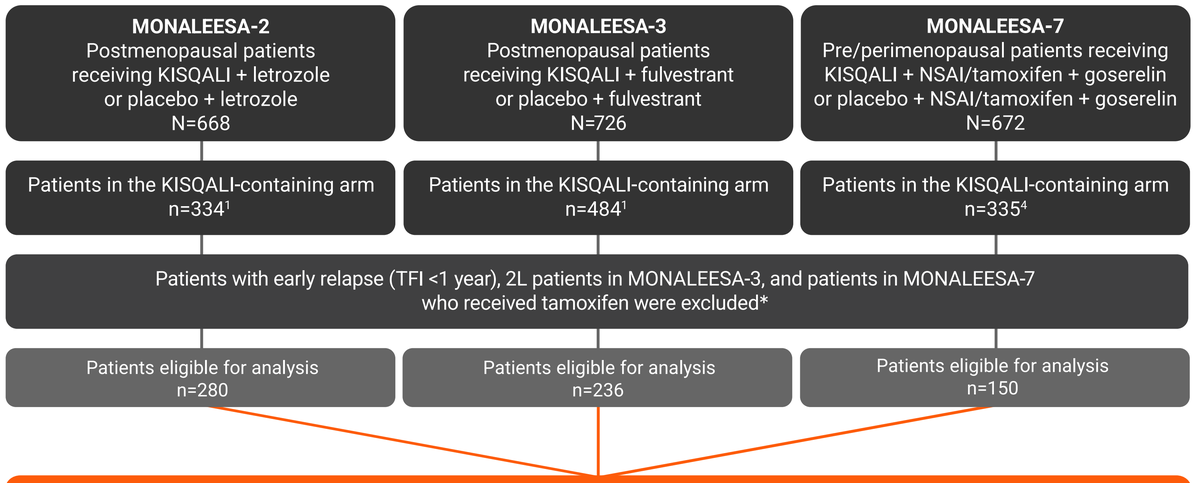
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Post hoc exploratory pooled analysis

Pooled analysis of 1L patients with long-term response with KISQALI + AI or fulvestrant in the MONALEESA studies

IMPORTANT SAFETY INFORMATION

REFERENCES



Methods:

In this descriptive, hypothesis-generating, exploratory pooled analysis of the 3 pivotal trials, investigators studied baseline characteristics and biomarkers of 1L patients in the active treatment arms who achieved long-term response (LTR), defined as progression-free survival of >4 years, in the pooled MONALEESA trials.[6]

The following analysis is descriptive and the outcomes should be interpreted with caution. Results are from the KISQALI-containing arm in 1L patients in the pooled studies and cannot establish causality or comparative efficacy due to the absence of a randomized control group. PFS and other outcomes may be due to chance as this was not a prespecified analysis and there was no control for type 1 error. Variability in study design, patient characteristics, and assessment methods across pooled datasets may introduce bias and limit generalizability.

Median outcome for LTR was defined by the doubling of median PFS outcomes of approximately 2 years for patients treated for 1L mBC. These outcomes should be interpreted with caution.[6]

Safety data were not collected in this post hoc exploratory analysis.

***KISQALI is not indicated for concomitant use with tamoxifen.[1]**

†Patients who did not have a LTR were excluded (n=349). Patients who were censored with no PFS (4 years) event prior to the LTR cutoff time were classified as having "unknown" LTR status (n=164). Censoring reasons included lost to follow-up, ongoing without event, adequate assessment no longer available, event after ≥2 missing assessments, withdrew consent, and new cancer therapy added. Exclusions resulted in a smaller sample size; findings could be biased.[6]

1L, first line; 2L, second line; NE, not estimable; OS, overall survival; TFI, treatment-free interval.

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.

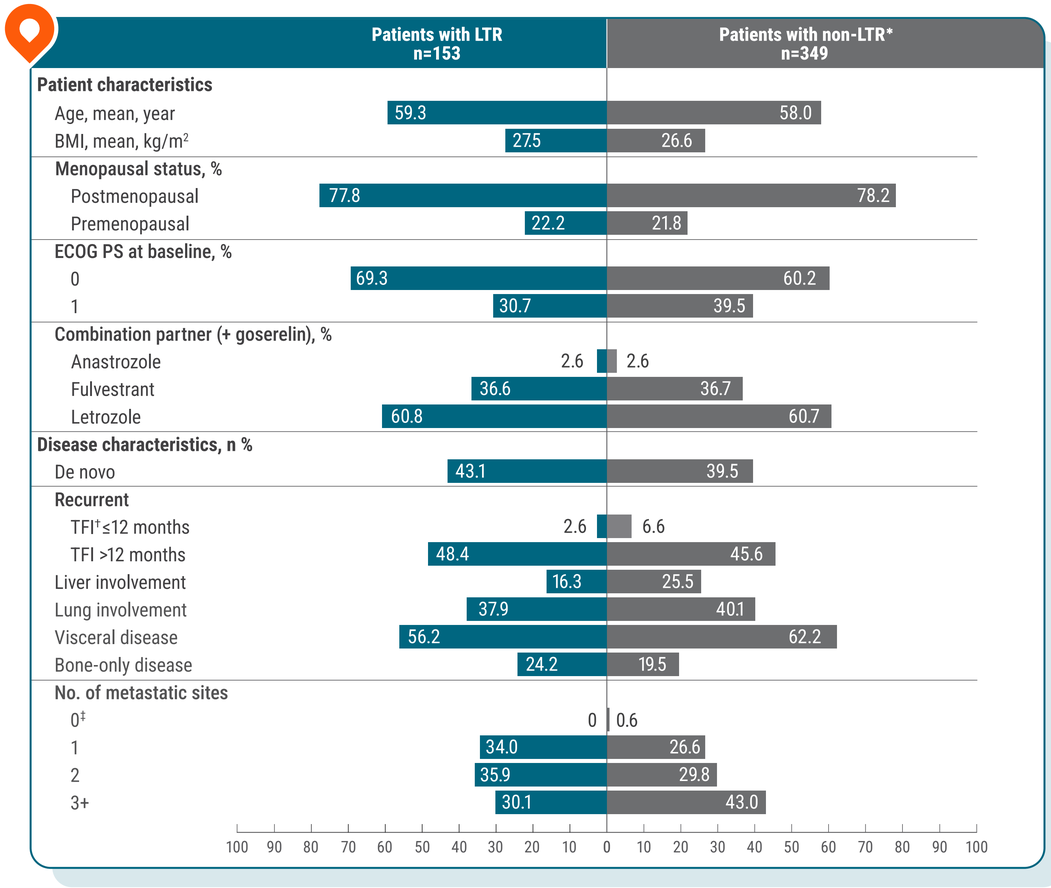
Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

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Post hoc exploratory pooled analysis

Baseline characteristics in patients with long-term responses



*Patients who were censored before LTR cutoff are not included in this table.[6]

†Time from the end of (neo)adjuvant treatment to disease recurrence. All 1L patients have ET-specific TFI >12 months but may have other antineoplastic treatments, resulting in overall TFI ≤12 months.[6]

‡MONALEESA trials included patients with locally advanced disease.[6]

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

BMI, body mass index.

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.

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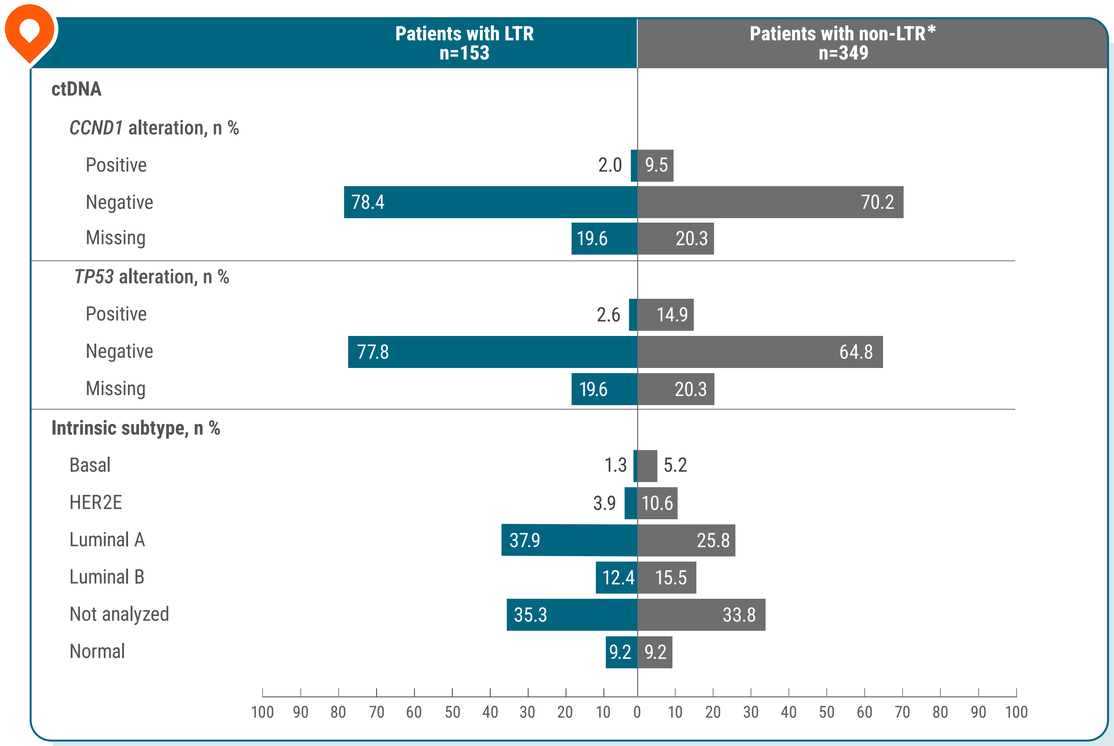
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Post hoc exploratory pooled analysis

Baseline biomarkers in patients with long-term responses

IMPORTANT SAFETY INFORMATION

REFERENCES



	Patients with LTR n=153	Patients with non-LTR* n=349
ctDNA		
ctDNA fraction, mean	0.05	0.13
Tumor mRNA expression		
CCNE1, mean	-0.24	0.13

Long-term responders had[6]:

- Lower ctDNA fraction, lower gene expression of *CCNE1*, and fewer *CCND1/TP53* alterations
- More luminal A disease (37.9% vs 25.8%)

*Patients who were censored before LTR cutoff are not included in this table.[6]

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

CCND1, cyclin D1; CCNE1, cyclin E1; ctDNA, circulating tumor DNA; HER2E, HER2-enriched; mRNA, messenger ribonucleic acid; TP53, tumor protein p53.

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.

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Safety from the MONALEESA clinical trials

IMPORTANT SAFETY INFORMATION

REFERENCES

Select adverse reactions (ARs) in <10% of patients who received KISQALI + ET[1]

Interstitial lung disease/pneumonitis:

- 1.6% of patients had ILD/pneumonitis (any grade, 0.4% had grade 3-4, and 0.1% had a fatal outcome)
- Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis, which may include hypoxia, cough, and dyspnea

SCARs:

- Cases of SJS, TEN, and DiHS/DRESS have been reported. If signs or symptoms of severe cutaneous reactions 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

QT prolongation:

- **Avoid KISQALI in patients who are at significant risk of developing torsades de pointes, 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
- In patients with HR+/HER2- mBC who received KISQALI + AI or fulvestrant
  - 1.4% had a >500 ms post-baseline QTcF value
  - 6% had a >60 ms QTcF increase from baseline
  - There were no reported cases of torsades de pointes
- QTcF prolongation was reversible with dose interruption. The majority of QTcF prolongation occurred within the first 4 weeks of KISQALI
- In MONALEESA-2, in the KISQALI plus 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

QT prolongation increased with concomitant use of tamoxifen. KISQALI is not indicated for concomitant use with tamoxifen.

Embryo-fetal toxicity:

- KISQALI can cause fetal harm when administered to a pregnant woman. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose

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In the MONALEESA-2 trial, fatal ARs occurred in 1.8% of patients who received KISQALI. Fatal ARs in ≥0.1% of patients receiving KISQALI included acute respiratory failure (0.6%), acute myocardial infarction, sudden death (with grade 3 hypokalemia and grade 2 QT prolongation), unknown cause, and pneumonia (0.3% each). In the MONALEESA-3 trial, fatal ARs occurred in 1.2% of patients who received KISQALI. Fatal ARs in ≥0.1% of patients receiving KISQALI included cardiac failure, ventricular arrhythmia, pneumonia, acute respiratory distress, pulmonary embolism, and hemorrhagic shock (0.2% each).

Please see Prescribing Information for a full list of adverse reactions.

AR, adverse reaction; CYP3A, cytochrome P450, family 3, subfamily A; DiHS, drug-induced hypersensitivity syndrome; DRESS, drug reaction with eosinophilia and systemic symptoms; ILD, interstitial lung disease; QTcF, QT interval corrected by Fridericia's formula; SCAR, severe cutaneous adverse reaction; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

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Safety from the MONALEESA clinical trials (continued)

SELECT LABORATORY ABNORMALITIES IN ≥10% OF PATIENTS WHO RECEIVED KISQALI + ET[1]

	MONALEESA-2				MONALEESA-3				MONALEESA-7			
	KISQALI + letrozole (n=334)		Placebo + letrozole (n=330)		KISQALI + fulvestrant (n=483)		Placebo + fulvestrant (n=241)		KISQALI + NSAI + goserelin (n=248)		Placebo + NSAI + goserelin (n=247)	
	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)
Neutrophil count decreased	93	60	24	1.2	92	53	21	0.8	92	63	27	2.4
ALT increased	46	10	36	1.2	44	11	37	1.7	33	6	31	1.6
AST increased	44	7	32	1.5	50	7	43	2.9	37	4.8	35	1.6

Hepatotoxicity:

Across the 3 trials, the median time to onset of grade ≥3 ALT/AST elevation was 92 days for the KISQALI + AI or fulvestrant treatment arms. The median time to resolution to grade ≤2 was 21 days in the KISQALI + AI or fulvestrant treatment arms. In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times 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. Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation.[1]

Neutropenia:

KISQALI causes concentration-dependent neutropenia. Across the 3 trials, 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. Based on the severity of the neutropenia, KISQALI may require dose interruption, reduction, or discontinuation.[1]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

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Safety from the MONALEESA clinical trials (continued)

DOSE MODIFICATIONS DUE TO ARs WITH KISQALI + AI OR FULVESTRANT[1]

	MONALEESA-2	MONALEESA-3	MONALEESA-7
	KISQALI + letrozole (n=334)	KISQALI + fulvestrant (n=483)	KISQALI + NSAI + goserelin (n=248)
Dose interruption due to ARs	71%	72%	73%
Dose reduction due to ARs	45%	32%	33%
Permanent discontinuation due to ARs	7%	8%	3%

In a pooled analysis of the MONALEESA-2, -3, and -7 trials, the most common (≥20%) ARs, including laboratory abnormalities, were leukocytes decreased (95%), neutrophils decreased (93%), hemoglobin decreased (68%), lymphocytes decreased (66%), AST increased (55%), gamma-glutamyl transferase increased (53%), ALT 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%).[1]

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

NCCN CATEGORY 1

National Comprehensive Cancer Network® (NCCN®) **differentiates ribociclib (KISQALI®) as the only Category 1 Preferred 1L treatment option** in combination with an AI for appropriate patients with HR+/HER2- mBC[7]

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.

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor.

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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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.**

Please click here for full Prescribing Information for KISQALI.

KISQALI® ribociclib 200 mg tablets

References

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

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