A Guide for Treating With KISQALI

NCCN CATEGORY 1 UPDATE

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

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

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

Indications

KISQALI is indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer 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 in postmenopausal women or in men.

The KISQALI® (ribociclib) FEMARA® (letrozole) Co-Pack is indicated as initial endocrine-based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

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.

Across clinical trials in patients with advanced or metastatic breast cancer treated with KISQALI in combination with an aromatase inhibitor or fulvestrant ("KISQALI treatment groups"), 1.2% of patients treated with KISQALI had ILD/pneumonitis of any grade, 0.3% had grade 3/4, and 0.1% had a fatal outcome. Additional cases of ILD/pneumonitis have been observed in the postmarketing setting, with fatalities reported.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

KISQALI—the only CDK4/6 inhibitor to achieve statistically significant overall survival in first line in combination with an AI

Majority of patients reported that overall survival is their #1 treatment goal[2]

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

Dee, Patient on KISQALI

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

Lisa, Patient on KISQALI

MONALEESA-2 was a randomized, double-blind, placebo-controlled phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 80 months, median OS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[3-6]

IMPORTANT SAFETY INFORMATION (continued)

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

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KISQALI® ribociclib 200 mg tablets

Help your patients with HR+/HER2- mBC reach their goal of living longer

As part of the health care team, you are instrumental in helping patients achieve their treatment goals with KISQALI and in supporting their overall treatment experience.

Set expectations

- Speak to patients at the beginning of their treatment journey about what to expect
- Discuss adverse reactions they may experience

Proactively educate

- Inform patients that the majority of adverse reactions in clinical trials with KISQALI were transient, manageable, and reversible (please see full safety profile beginning on page 19)[7-9]
- Discuss effective strategies for managing potential adverse reactions
- Reassure patients that, in clinical trials, efficacy was maintained despite dose reductions[10,11]

Follow up

- Maintain regular touchpoints with patients throughout treatment, which may help with adherence

> "…**overall survival is a very important end point** for patients. In fact, it's one of the…most important end points for patients because it represents their expectation of life."

Gabriel Hortobagyi, MD

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.

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KISQALI® ribociclib 200 mg tablets

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.

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, median OS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[3-6]

MONALEESA-3 was a randomized, double-blind, placebo-controlled phase III study of KISQALI + fulvestrant (n=484) vs placebo + fulvestrant (n=242) for the treatment of postmenopausal patients with HR+/HER2- mBC who have received no or only 1 line of prior ET for advanced disease. OS was a secondary end point; PFS was the primary end point. At a median follow-up of 71 months (exploratory analysis), in a 1L subgroup analysis, median OS was 67.6 months (95% CI: 59.6-NR) with KISQALI + fulvestrant 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.[3,8,12,13]

MONALEESA-7 was a randomized, double-blind, placebo-controlled phase III study of KISQALI + ET (NSAI or tamoxifen) + goserelin vs placebo + ET (NSAI or tamoxifen) + goserelin (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), median OS was 58.7 months with KISQALI + NSAI + goserelin (95% CI: 48.5-NR) vs 47.7 months with 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.[3,7,14,15]

> “Overall survival is the hardest end point to achieve in clinical trials. And in many respects, perhaps the most important…we’re trying to improve the survival of a patient; not just the progression-free survival or the time where the tumor is controlled, but **how long they live…**”

Dennis Slamon, MD, PhD
University of California, Los Angeles

IMPORTANT SAFETY INFORMATION (continued)

Severe cutaneous adverse reactions (continued). If signs or symptoms of SCARs occur, interrupt KISQALI until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended.

If SCARs 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 and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

KISQALI—the only CDK4/6 inhibitor to achieve statistically significant overall survival in first line in combination with an AI

Patient portrayal.

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, median OS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004.[3-6]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation. KISQALI® (ribociclib) and the KISQALI® (ribociclib) FEMARA® (letrozole) Co-Pack have been shown to prolong the QT interval in a concentration-dependent manner. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation. In MONALEESA-2 and MONALEESA-7, in patients with advanced or metastatic breast cancer who received the combination of KISQALI plus an aromatase inhibitor, 7 of 574 patients (1%) had >500 ms postbaseline QTcF value, and 29 of 574 patients (5%) had a >60 ms increase from baseline in QTcF intervals. These electrocardiogram (ECG) changes were reversible with dose interruption and most occurred within the first 4 weeks of treatment. No cases of torsades de pointes were reported. In MONALEESA-2, on 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.

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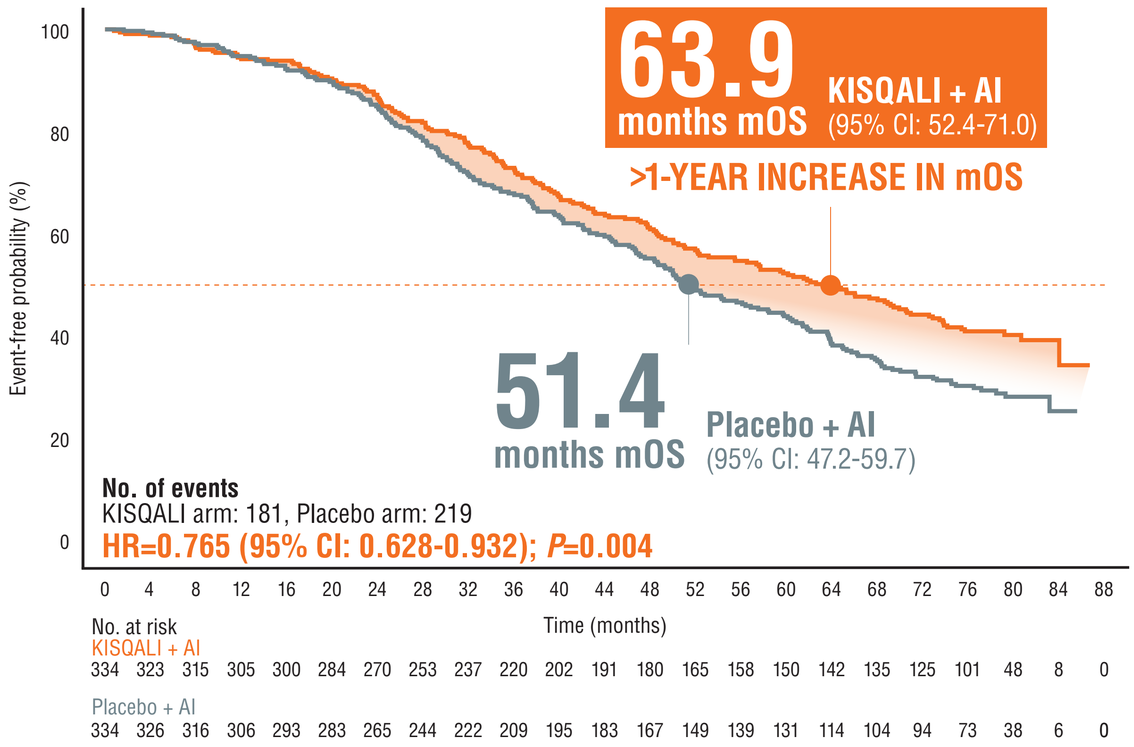
KISQALI® ribociclib 200 mg tablets

Over 5 years median overall survival for first-line postmenopausal patients with an AI

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

At a median follow-up of 80 months

OVERALL SURVIVAL | KISQALI + AI[4,6]



Hazard ratios are based on stratified Cox model.

OS

Patients have cited living longer as their #1 treatment goal. KISQALI can help them reach that goal: In MONALEESA-2, patients experienced a **>1-year increase in median overall survival**.

OVERALL SURVIVAL BENEFIT WITH KISQALI INCREASED OVER TIME

At 6 years, the survival rate of patients receiving KISQALI + letrozole was 44% vs 32% with placebo + letrozole[4]

Study design: MONALEESA-2 was a randomized, double-blind, placebo-controlled phase III study of KISQALI + letrozole (n=334) vs placebo + letrozole (n=334) in postmenopausal patients with HR+/HER2- mBC who received no prior therapy for advanced disease. OS was a secondary end point; PFS was the primary end point.[3-5]

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI or the KISQALI FEMARA Co-Pack only in patients with QTcF values <450 ms. Repeat ECG at approximately Day 14 of the first cycle, at the beginning of the second cycle, and as clinically indicated. Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting therapy with KISQALI or the KISQALI FEMARA Co-Pack therapy.

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KISQALI® ribociclib 200 mg tablets

Patients treated with KISQALI + ET reported similar health-related quality of life outcomes when compared with ET alone

No difference in or delayed time to deterioration (TTD) in health-related quality of life across all 3 phase III trials

Patient-reported outcomes

MONALEESA-2: KISQALI + AI in 1L postmenopausal patients	**NO DIFFERENCE IN TTD** At a median follow-up of 26 months, median TTD ≥10% was 27.7 months vs 27.6 months (HR=0.944 [95% CI: 0.720-1.237])[16]
MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients	**NO DIFFERENCE IN TTD** At a median follow-up of 39 months, median TTD ≥10% was 35.9 months vs 33.1 months (HR=0.81 [95% CI: 0.62-1.06])[17]
MONALEESA-7: KISQALI + AI in 1L premenopausal patients	**DELAYED** At a median follow-up of 35 months, median TTD ≥10% was 34.2 months vs 23.3 months (HR=0.69 [95% CI: 0.52-0.91])[18]

Medians reported as KISQALI vs placebo.

HRQOL was assessed using the EORTC QLQ-C30 questionnaire—a validated tool used worldwide to assess quality of life in patients with cancer.[17-21]

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

IMPORTANT SAFETY INFORMATION (continued)

QT interval prolongation (continued). Avoid the use of KISQALI or the KISQALI FEMARA Co-Pack in patients who already have or who are at significant risk of developing QT prolongation, including patients with:

- long QT syndrome
- uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina, and bradyarrhythmias
- electrolyte abnormalities

Avoid using KISQALI or the KISQALI FEMARA Co-Pack with drugs known to prolong the QT interval and/or strong CYP3A inhibitors, as this may lead to prolongation of the QTcF interval. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

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KISQALI® ribociclib 200 mg tablets

KISQALI means living longer without chemotherapy

Across all 3 phase III trials
Median time to chemotherapy delayed 4 years or more

MONALEESA-2: KISQALI + AI in 1L postmenopausal patients	**OVER 4-YEAR DELAY** At a median follow-up of 80 months, mTTC was 50.6 months with KISQALI + letrozole vs 38.9 months with placebo + letrozole; HR=0.742 (95% CI: 0.606-0.909) [6,22]
MONALEESA-3: KISQALI + fulvestrant in 1L/2L postmenopausal patients	**4-YEAR DELAY** At a median follow-up of 56 months, mTTC was 48.1 months with KISQALI + fulvestrant vs 28.8 months with placebo + fulvestrant; HR=0.704 (95% CI: 0.566-0.876)[23]
MONALEESA-7: KISQALI + AI in 1L premenopausal patients	**OVER 4-YEAR DELAY** At a median follow-up of 54 months, mTTC was 50.9 months with KISQALI + NSAI + goserelin vs 36.0 months with placebo + NSAI + goserelin; HR=0.659 (95% CI: 0.509-0.851)[14]

TTC

Patients fear the side effects of treatment, and chemotherapy in particular. In all trials, those treated with KISQALI + ET had an **increase of ~1 year in time to chemotherapy** compared to patients treated with placebo + ET.

- Time to chemotherapy was an exploratory end point and was defined as the time from randomization to the beginning of the first chemotherapy after discontinuing study treatment[13,15,19]
- There was no prespecified statistical procedure controlling for type 1 error

IMPORTANT SAFETY INFORMATION (continued)

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

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

Only KISQALI offers single-strength tablets for simple dose reductions

With simple dose reductions, eliminate the need for new mid-cycle prescriptions and additional costs[3]

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:
  - An AI once daily (continuously); in premenopausal patients and men, an LHRH agonist should be administered according to current clinical practice guidelines; or[3,24]
  - Fulvestrant 500 mg intramuscularly on Days 1, 15, and 29, and once monthly thereafter for postmenopausal patients or men. In male patients, an LHRH agonist should be administered according to current clinical practice guidelines[3]
- Dose adjustments for adverse reactions should be made in a stepwise order by reducing the number of tablets taken
- Dose modification of KISQALI is recommended based on individual safety and tolerability
- If dose reduction below 200 mg/day is required, discontinue treatment
- KISQALI can be taken with or without food

> "…the single-tablet strength allows for simple dose adjustments, and to me, **that is game changing.**"
>
> Nick McAndrew, MD
> University of California, Los Angeles

IMPORTANT SAFETY INFORMATION (continued)

Hepatobiliary toxicity. Across KISQALI treatment groups, increases in transaminases were observed. In MONALEESA-2 and MONALEESA-7, grade 3/4 increases in alanine aminotransferase (ALT) (11% vs 2%) and aspartate aminotransferase (AST) (8% vs 2%) were reported in the KISQALI and placebo arms, respectively.

Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 111 days and median time to resolution to grade ≤2 was 22 days for the KISQALI treatment groups.

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KISQALI® ribociclib 200 mg tablets

The only CDK4/6 inhibitor to maintain overall survival in patients requiring dose reductions across 3 phase III trials

For patients who had ≥1 dose reduction, overall survival was maintained with KISQALI[10,11,25-27]

	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	**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	**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	**NOT REACHED** (95% CI: NR-NR)	**NOT REACHED** (95% CI: NR-NR)
	HR=0.79 (95% CI: 0.46-1.36)	

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

OS

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

IMPORTANT SAFETY INFORMATION (continued)

Hepatobiliary toxicity (continued). In MONALEESA-2, concurrent elevations in ALT or AST greater than 3 times the upper limit of normal (ULN) and total bilirubin greater than 2 times the ULN, with normal alkaline phosphatase, in the absence of cholestasis occurred in 4 (1%) patients and all patients recovered after discontinuation of KISQALI. No cases occurred in MONALEESA-7.

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KISQALI® ribociclib 200 mg tablets

Flexible dosing with either an AI or fulvestrant

(28-day cycle)[3]	Week 1	Week 2	Week 3	Week 4	Subsequent cycles
KISQALI	✓	✓	✓	—	Repeat 28-day cycle
AI	✓	✓	✓	✓	
or					
KISQALI	✓	✓	✓	—	Repeat 28-day cycle
Fulvestrant	✓ Day 1 injection	—	✓ Day 15 injection (Cycle 1 only)	—	✓ Once monthly

- Please refer to the full Prescribing Information for the recommended dose of the chosen AI
- In premenopausal patients, an LHRH agonist should be administered according to current clinical practice guidelines when given with KISQALI and an AI
- When given with KISQALI, the recommended dose of fulvestrant is 500 mg, administered intramuscularly on Days 1, 15, 29, and once monthly thereafter. In male patients, an LHRH agonist should be administered according to current clinical practice guidelines. Please refer to the full Prescribing Information for fulvestrant

IMPORTANT SAFETY INFORMATION (continued)

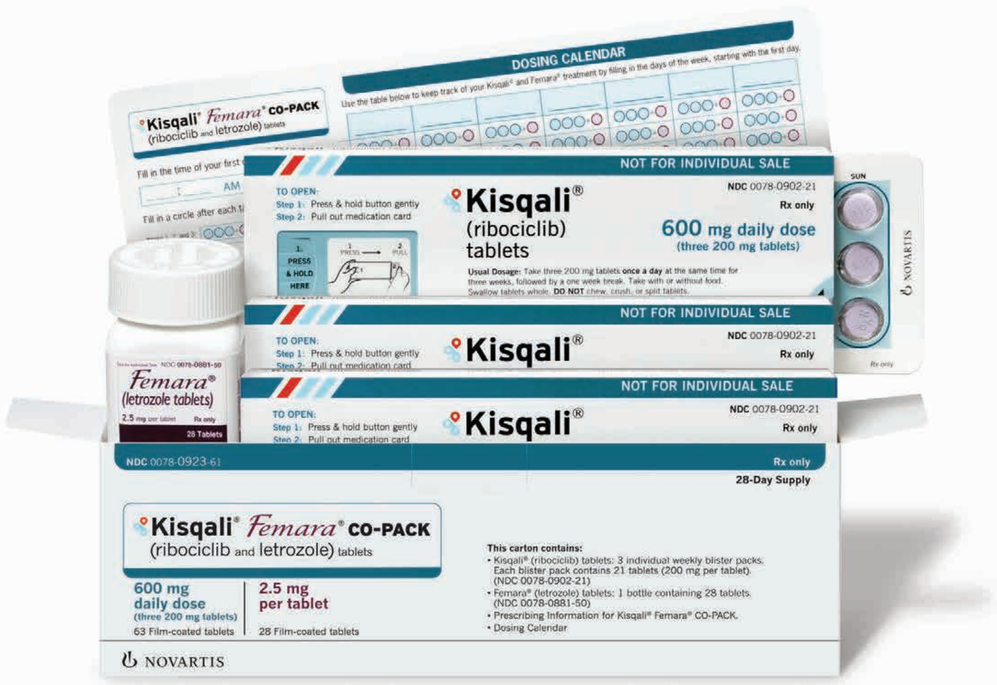
Hepatobiliary toxicity (continued). Perform liver function tests (LFTs) before initiating therapy with KISQALI or the KISQALI FEMARA Co-Pack. Monitor LFTs every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation. Recommendations for patients who have elevated AST/ALT grade ≥3 at baseline have not been established.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

The only CDK4/6 inhibitor available in a convenient co-pack

The KISQALI FEMARA Co-Pack[24]



Available in all 3 approved KISQALI dose options: KISQALI 600 mg (three 200-mg tablets), 400 mg (two 200-mg tablets), and 200 mg (one 200-mg tablet), with FEMARA 2.5 mg (one 2.5-mg tablet).

When prescribing KISQALI and fulvestrant, 2 prescriptions are needed.

A convenient prescription process for you and your patients:

- 1 package containing a 28-day supply of both KISQALI and FEMARA
  — Separate packages not needed
- 1 prescription for convenient prescription writing
- 1 co-pay that covers both KISQALI and FEMARA

The KISQALI FEMARA Co-Pack is indicated as initial endocrine-based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

> “The KISQALI FEMARA Co-Pack…**very helpful for the patients because it’s one easy packaging.**”

Lubna N. Chaudhary, MD
Medical College of Wisconsin

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia. Neutropenia was the most frequently reported adverse reaction (AR) (79%), and a grade 3/4 decrease in neutrophil count (based on laboratory findings) was reported in 66% of patients in the KISQALI treatment groups. Among the patients who had grade 2, 3, or 4 neutropenia, the median time to grade ≥2 was 16 days. The median time to resolution of grade ≥3 (to normalization or grade <3) was 15 days in the KISQALI treatment groups. Febrile neutropenia was reported in 2% of patients in the KISQALI treatment groups. Treatment discontinuation due to neutropenia was 1%.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® Femara® CO-PACK
ribociclib 200 mg tablets and letrozole 2.5 mg tablets

Straightforward dose adjustments

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

ILD=interstitial lung disease.

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

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

BSA=body surface area; IV=intravenous; SCAR=severe cutaneous adverse reaction; SJS=Stevens-Johnson syndrome; TEN=toxic epidermal necrolysis.

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

Straightforward dose adjustments (continued)

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

ANC=absolute neutrophil count; LLN=lower limit of normal.

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

QT PROLONGATION[3]	
ECGs with QTcF >480 ms	Interrupt dose until recovery to <481 ms • If first occurrence, resume at next lower dose level • If QTcF ≥481 ms recurs, interrupt dose until QTcF resolves to <481 ms; then resume at next lower dose level
ECGs with QTcF >500 ms	Interrupt dose if QTcF >500 ms; on recovery to <481 ms, resume at next lower dose level • Permanently discontinue if QTcF interval prolongation is either >500 ms or >60 ms change from baseline AND associated with torsades de pointes, polymorphic ventricular tachycardia, unexplained syncope, or signs/symptoms of serious arrhythmia

ECG=electrocardiogram; QTcF=QT interval corrected by Fridericia's formula.

- ECGs should be assessed prior to initiation of treatment. Repeat ECGs at approximately Day 14 of the first cycle, at the beginning of the second cycle, and as clinically indicated. In case of QTcF prolongation at any given time during treatment, more frequent ECG monitoring is recommended

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

Straightforward dose adjustments (continued)

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

ALT=alanine aminotransferase; AST=aspartate aminotransferase; TB=total bilirubin; ULN=upper limit of normal.

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

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

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

Dosing and administration considerations

SELECT DRUG INTERACTIONS[3]	
Strong CYP3A4 inhibitors	• Avoid concomitant use • If coadministration cannot be avoided, reduce KISQALI dose to 400 mg once daily • Instruct patients to avoid grapefruit and grapefruit juice
Strong CYP3A4 inducers	• Avoid concomitant use
Sensitive CYP3A substrates	• The dose of sensitive CYP3A substrates with narrow therapeutic indices may need to be reduced when given concurrently with KISQALI
Drugs known to prolong QT interval	• Avoid concomitant use of drugs such as antiarrhythmic medicines

CYP3A=cytochrome P450, family 3, subfamily A.

Starting dose modifications for hepatic and renal impairment[3]

- No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh class A). The recommended starting dose is 400 mg KISQALI once daily for patients with moderate (Child-Pugh class B) and severe hepatic impairment (Child-Pugh class C)
- No dose adjustment is necessary in patients with mild or moderate renal impairment. The recommended starting dose is 200 mg KISQALI once daily for patients with severe renal impairment

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KISQALI® ribociclib 200 mg tablets

Upfront ECG monitoring

ECG MONITORING[3]		
Baseline		✓
Cycle 1	Day 14	✓
Cycle 2	Day 1	✓ (final scheduled)

- KISQALI should only be initiated in patients with QTcF <450 ms. In case of QTcF prolongation during therapy, more frequent monitoring is recommended
- Any additional monitoring should be performed as clinically indicated
- Monitoring requirements based on a 28-day treatment cycle

ECG **Only 3 ECGs are required**—and all are completed within the **first 30 days of treatment**.

Low incidence of QT prolongation across all KISQALI clinical trials, and most cases were moderate in nature[3]

In a pooled analysis across 3 phase III trials of 1054 premenopausal and postmenopausal patients treated with KISQALI + an AI or fulvestrant:

1% had a >500 ms postbaseline QTcF value

6% experienced a >60 ms increase from baseline in QTcF interval

- There were no reported cases of torsades de pointes

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

IMPORTANT SAFETY INFORMATION (continued)

Neutropenia (continued). Perform complete blood count (CBC) before initiating therapy with KISQALI or the KISQALI FEMARA Co-Pack. 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.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

> "I think it's time to come out of that comfort zone and really start using ribociclib."
>
> Lubna N. Chaudhary, MD
> Medical College of Wisconsin

KISQALI® ribociclib 200 mg tablets

Routine laboratory monitoring

		CBC/LFT[3]	Electrolytes[3]
Baseline		✓	✓
Cycle 1	Day 14	✓	
Cycle 2	Day 1	✓	✓
	Day 14	✓	
Cycle 3-6	Day 1	✓	✓

CBC=complete blood count; LFT=liver function test.

- For LFTs, if grade ≥2 abnormalities are noted, more frequent monitoring is recommended
- Correct any electrolyte abnormalities prior to treatment
- Additional monitoring may be required as clinically indicated
- Monitoring requirements based on a 28-day treatment cycle

LAB

The majority of scheduled monitoring occurs **within the first 2 cycles of therapy** and there is **no scheduled monitoring beyond Cycle 6**.

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. In animal reproduction studies, administration of KISQALI to pregnant rats and rabbits during organogenesis caused embryo-fetal toxicities at maternal exposures that were 0.6 and 1.5 times the human clinical exposure, respectively, based on area under the curve. Letrozole caused embryo-fetal toxicities in rats and rabbits at maternal exposures that were below the maximum recommended human dose on a milligrams-per-square-meter basis. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI or the KISQALI FEMARA Co-Pack 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 and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

KISQALI + letrozole safety profile

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

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[3]

	KISQALI + LETROZOLE n=334		PLACEBO + LETROZOLE n=330	
	Grade 3 or 4	All grades	Grade 3 or 4	All grades
Vomiting	3.6%	29%	0.9%	16%
Decreased appetite	1.5%	19%	0.3%	15%
Back pain	2.1%	20%	0.3%	18%
Nausea	2.4%	52%	0.6%	29%
Fatigue	2.4%	37%	0.9%	30%
Urinary tract infection	0.6%	11%	0%	8%
Headache	0.3%	22%	0.3%	19%
Insomnia	0.3%	12%	0%	9%
Dyspnea	1.2%	12%	0.6%	9%
Diarrhea	1.2%	35%	0.9%	22%
Constipation	1.2%	25%	0%	19%
Stomatitis	0.3%	12%	0%	7%
Abdominal pain	1.2%	11%	0%	8%
Rash	0.6%	17%	0%	8%
Pruritus	0.6%	14%	0%	6%
Pyrexia	0.3%	13%	0%	6%
Alopecia	0%	33%	0%	16%
Edema peripheral	0%	12%	0%	10%

- Dose reductions due to ARs occurred in 45% of patients receiving KISQALI plus letrozole
- Permanent discontinuations: 7% with KISQALI + letrozole

AR The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

KISQALI + letrozole safety profile (continued)

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

LABORATORY ABNORMALITIES OCCURRING IN ≥10% OF PATIENTS[3]

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

- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include: pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatobiliary toxicity, neutropenia, and embryo-fetal toxicity
- The most common (≥20% on the KISQALI arm and ≥2% higher than placebo) adverse reactions, including laboratory abnormalities, were neutrophils decreased, leukocytes decreased, hemoglobin decreased, nausea, lymphocytes decreased, alanine aminotransferase increased, aspartate aminotransferase increased, fatigue, diarrhea, alopecia, vomiting, platelets decreased, constipation, headache, and back pain
- The most common grade 3/4 ARs (reported at a frequency ≥5%): neutropenia, leukopenia, abnormal liver function tests, and lymphopenia

AR The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

KISQALI + fulvestrant safety profile

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

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[3]

	KISQALI + FULVESTRANT n=483		PLACEBO + FULVESTRANT n=241	
	Grade 3 or 4	All grades	Grade 3 or 4	All grades
Infections	4.6%	42%	1.7%	30%
Dyspnea	1.4%	15%	1.7%	12%
Nausea	1.4%	45%	0.8%	28%
Vomiting	1.4%	27%	0%	13%
Abdominal pain	1.4%	17%	0.8%	13%
Diarrhea	0.6%	29%	0.8%	20%
Constipation	0.8%	25%	0%	12%
Rash	0.8%	23%	0%	8%
Pruritus	0.2%	20%	0%	7%
Decreased appetite	0.2%	16%	0%	13%
Dizziness	0.2%	13%	0%	8%
Pyrexia	0.2%	11%	0%	7%
Cough	0%	22%	0%	15%
Alopecia	0%	19%	0%	5%
Edema peripheral	0%	15%	0%	7%

- Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (1%)
- Dose reductions due to ARs: 32% with KISQALI + fulvestrant
- Permanent discontinuations: 8% with KISQALI + fulvestrant
- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include: pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatobiliary toxicity, neutropenia, and embryo-fetal toxicity

AR

The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

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KISQALI® ribociclib 200 mg tablets

KISQALI + fulvestrant safety profile (continued)

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

LABORATORY ABNORMALITIES[3]

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

GGT=gamma-glutamyl transferase.

- The most common (≥20% on the KISQALI arm and ≥2% higher than placebo) adverse reactions, including laboratory abnormalities, were leukocytes decreased, neutrophils decreased, lymphocytes decreased, creatinine increased, hemoglobin decreased, gamma-glutamyl transferase increased, aspartate aminotransferase increased, nausea, alanine aminotransferase increased, infections, platelets decreased, diarrhea, vomiting, constipation, glucose serum decreased, cough, rash, and pruritus
- Most common grade 3/4 ARs (reported at a frequency ≥5%): neutropenia, leukopenia, infections, and abnormal liver function tests

AR The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

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KISQALI® ribociclib 200 mg tablets

KISQALI + NSAI + goserelin safety profile

MONALEESA-7: KISQALI + AI in 1L premenopausal patients

ADVERSE REACTIONS OCCURRING IN ≥10% AND ≥2% HIGHER THAN PLACEBO[3]

	KISQALI + NSAI + GOSERELIN n=248		PLACEBO + NSAI + GOSERELIN n=247	
	Grade 3 or 4	All grades	Grade 3 or 4	All grades
Infections	1.6%	36%	0.4%	24%
Arthralgia	0.8%	34%	1.2%	29%
Rash	0.4%	17%	0%	9%
Pyrexia	0.8%	17%	0%	7%
Nausea	0%	32%	0%	20%
Alopecia	0%	21%	0%	13%
Constipation	0%	16%	0%	12%
Cough	0%	15%	0%	10%
Pain in extremity	0%	10%	1.2%	8%
Stomatitis	0%	10%	0.4%	8%
Pruritus	0%	11%	0%	4%

- Infections included urinary and respiratory tract infections, gastroenteritis, and sepsis (<1%)
- Dose reductions due to ARs: 33% for patients taking KISQALI + NSAI + goserelin
- Permanent discontinuations: 3% for patients taking KISQALI + NSAI + goserelin
- Patients may require dose interruption, reduction, or discontinuation for ARs. Monitoring should include: pulmonary symptoms, ECGs, serum electrolytes, LFTs, and CBCs. See Warnings and Precautions for risk of ILD/pneumonitis, SCARs, QT prolongation, hepatobiliary toxicity, neutropenia, and embryo-fetal toxicity

AR

The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

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KISQALI® ribociclib 200 mg tablets

KISQALI + NSAI + goserelin safety profile (continued)

MONALEESA-7: KISQALI + AI in 1L premenopausal patients

LABORATORY ABNORMALITIES[3]

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

GGT=gamma-glutamyl transferase.

- The most common (≥20% on the KISQALI arm and ≥2% higher than placebo) adverse reactions, including laboratory abnormalities, were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, gamma-glutamyl transferase increased, aspartate aminotransferase increased, infections, arthralgia, alanine aminotransferase increased, nausea, platelets decreased, and alopecia
- Most common grade 3/4 ARs (reported at a frequency ≥5%): neutropenia, leukopenia, and abnormal liver function tests

AR The majority of adverse reactions with KISQALI were **transient, manageable, and reversible**.

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KISQALI® ribociclib 200 mg tablets

The support you need to help your patients start and stay on therapy

Novartis is committed to helping patients who have been prescribed KISQALI receive all the support they need on their treatment journey

Access assistance

Patients may be eligible to receive:

- ✓ **$0** co-pay
- ✓ Voucher or sample for **1 free** treatment cycle to get started
- ✓ Up to **5 free** treatment cycles

See terms and conditions on next page.

Patient support

- ✓ Benefits investigation and information is available through dedicated specialists from **Patient Assistance Now Oncology (PANO)**
- ✓ The **Novartis Patient Navigator Program** offers support and education for eligible patients during their treatment journey

9 out of 10 patients have favorable coverage for KISQALI for all approved indications[28]

Unrestricted or single-step edit coverage from MMIT data as of July 2023.

INFO For more information about patient support programs visit:
HCP.Novartis.com/Access

$0 co-pay for your eligible patients

NOVARTIS

Universal Co-pay Card

Eligible patients save on out-of-pocket costs

Tell your patients to visit
Copay.NovartisOncology.com
or call **1-877-577-7756**.

Patients may be eligible for immediate co-pay savings on their next prescription of KISQALI tablets, FEMARA tablets, the KISQALI FEMARA Co-Pack tablets, and/or generic letrozole.

- Eligible patients with private insurance may pay $0 per month
- Novartis will pay the remaining co-pay, up to $15,000 per calendar year, per product*

***Limitations apply.** This offer is only available to patients with private insurance. The program is not available for patients who are enrolled in Medicare, Medicaid, or any other federal or state healthcare program. Use of this offer for FEMARA (or generic letrozole) does not require a KISQALI prescription. Offer is NOT valid for purchases of FEMARA only by Massachusetts patients or California patients that do not meet additional eligibility criteria. Novartis reserves the right to rescind, revoke, or amend this program without notice. For full Terms and Conditions, visit CoPay.NovartisOncology.com or call 1-877-577-7756.

Encourage your patients to find out if they are eligible to enroll in the Novartis Universal Co-pay Program by visiting **CoPay.NovartisOncology.com** or calling **1-877-577-7756**.

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets *Femara*® and letrozole 2.5 mg tablets CO-PACK

Access assistance

One free treatment cycle to get started

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

Please see your sales representative for vouchers. You can also visit **www.FreeTreatmentVoucher.com** or call **1-800-282-7630**.

Up to 5 free treatment cycles for uninterrupted access

- Through the **KISQALI Access Program**, commercially insured patients waiting for their coverage to take effect for KISQALI, FEMARA, the KISQALI FEMARA Co-Pack, and/or generic letrozole may be eligible for an additional supply of KISQALI that could continue for up to 5 treatment cycles
- To enroll your eligible patient in this patient support service, submit a completed Novartis Patient Assistance Now Oncology (PANO) Service Request Form and select the KISQALI Access Program check box
- Limitations apply. Eligible patients must have commercial insurance, a completed Service Request Form, and be experiencing a delay in obtaining coverage for KISQALI. Program is not available to patients whose medications are reimbursed in whole or in part by Medicare, Medicaid, TRICARE, or any other federal or state program. No purchase necessary. Participation is not a guarantee of insurance coverage. Once coverage is approved, patients will no longer be eligible. Novartis Pharmaceuticals Corporation reserves the right to rescind, revoke, or amend this program without notice

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KISQALI® ribociclib 200 mg tablets

Patient support

Novartis Patient Navigator Program for personalized support and education

The Novartis Patient Navigator Program is staffed by a dedicated team of specialists who support eligible patients during their treatment journey.* Patients who enroll in the program receive a series of phone calls from a specially trained navigator who will support and guide them through various aspects of initiating their prescribed therapy.

Novartis Patient Navigators provide:

- Access to disease and product education materials
- Information about lifestyle support
- Access to Novartis products via assistance with benefits investigation and other financial support
- Support to help improve adherence to therapy and patient outcomes
- Collaboration and coordination with other Novartis Oncology Patient Support programs

*The Novartis Patient Navigator Program is available for select Novartis Oncology products. Patient Navigator services do not involve the practice of nursing or provide clinical advice and counseling.

To learn more about the Patient Navigator Program and obtain information about enrollment, contact Patient Assistance Now Oncology at **1-800-282-7630, prompt 3**.

Specialized support is brought to you by Novartis Patient Assistance Now Oncology

Patient Assistance Now Oncology
Assistance. Access. Answers.

- Patient Assistance Now Oncology (PANO) is a support center consisting of insurance specialists and case managers who provide access to information regarding an array of services. Consider PANO your first stop for information about Novartis Oncology Patient Support services. Dedicated support specialists help direct callers to the services that best fit their needs. To learn more, call **1-800-282-7630** or visit **HCP.Novartis.com/Access**

IMPORTANT SAFETY INFORMATION (continued)

Adverse reactions. In the pooled safety population of MONALEESA-2 and MONALEESA-7, most common (incidence ≥20%) ARs include infections, nausea, fatigue, diarrhea, headache, alopecia, vomiting, back pain, constipation, cough, rash, and abdominal pain.

Laboratory abnormalities. In the pooled safety population of MONALEESA-2 and MONALEESA-7, the most common laboratory abnormalities reported in the KISQALI arm (all grades, pooled incidence ≥20%) **were leukocytes decreased, neutrophils decreased, hemoglobin decreased, lymphocytes decreased, ALT increased, AST increased, platelets decreased, and creatinine increased.**

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KISQALI® ribociclib 200 mg tablets

KISQALI—more life for living

Talk to your patients
about KISQALI today.

MONALEESA-2: At a median follow-up of 80 months, median OS was 63.9 months with KISQALI + letrozole (95% CI: 52.4-71.0) vs 51.4 months with letrozole (95% CI: 47.2-59.7); HR=0.765 (95% CI: 0.628-0.932); *P*=0.004. PFS was the primary end point.[4-6]

IMPORTANT SAFETY INFORMATION

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

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

Please see additional Important Safety Information throughout and click here for full Prescribing Information for KISQALI and click here for full Prescribing Information for the KISQALI FEMARA Co-Pack.

KISQALI® ribociclib 200 mg tablets

Indications

KISQALI is indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer 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 in postmenopausal women or in men.

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.

Across clinical trials in patients with advanced or metastatic breast cancer treated with KISQALI in combination with an aromatase inhibitor or fulvestrant ("KISQALI treatment groups"), 1.6% of patients treated with KISQALI 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 been observed in the postmarketing setting, with fatalities reported.

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 treatment with KISQALI immediately and evaluate the patient. Permanently discontinue treatment with KISQALI in patients with recurrent symptomatic or severe 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. Consultation with a dermatologist is recommended.

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. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation. Across KISQALI treatment groups, 15 of 1054 patients (1.4%) had >500 ms postbaseline QTcF value, and 61 of 1054 (6%) had a >60 ms increase from baseline in QTcF intervals. These electrocardiogram (ECG) changes were reversible with dose interruption and most occurred within the first 4 weeks of treatment. No cases of torsades de pointes were reported.

In MONALEESA-2, on 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.

Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI only in patients with QTcF values <450 ms. Repeat ECG at approximately Day 14 of the first cycle, at the beginning of the second cycle, and as clinically indicated. Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting therapy with KISQALI.

Avoid the use of KISQALI in patients who already have or who are at significant risk of developing QT prolongation, including patients with:

- long QT syndrome
- uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina, and bradyarrhythmias
- electrolyte abnormalities

Avoid using KISQALI with drugs known to prolong the QT interval and/or strong CYP3A inhibitors, as this may lead to prolongation of the QTcF interval.

Increased QT prolongation with concomitant use of tamoxifen. KISQALI is not indicated for concomitant use with tamoxifen. In MONALEESA-7, the observed mean QTcF increase from baseline was ≥10 ms higher in the tamoxifen + placebo subgroup compared with the non-steroidal 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.

Hepatobiliary toxicity. Across KISQALI treatment groups, increases in transaminases were observed. Across all trials, grade 3/4 increases in alanine aminotransferase (ALT) (11% vs 2.1%) and aspartate aminotransferase (AST) (8% vs 2%) were reported in the KISQALI and placebo arms, respectively.

Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 92 days and median time to resolution to grade ≤2 was 21 days for the KISQALI treatment groups.

In MONALEESA-2 and MONALEESA-3, concurrent elevations in ALT or AST greater than 3 times the upper limit of normal (ULN) and total bilirubin greater than 2 times the ULN, with normal alkaline phosphatase, in the absence of cholestasis occurred in 6 (1%) patients and all patients recovered after discontinuation of KISQALI. No cases occurred in MONALEESA-7.

Perform liver function tests (LFTs) before initiating therapy with 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. Recommendations for patients who have elevated AST/ALT grade ≥3 at baseline have not been established.

Neutropenia. Across KISQALI treatment groups neutropenia was the most frequently reported adverse reaction (AR) (75%), and a grade 3/4 decrease in neutrophil count (based on laboratory findings) was reported in 62% of patients in the KISQALI treatment groups. Among the patients who had grade 2, 3, or 4 neutropenia, the median time to grade ≥2 was 17 days. The median time to resolution of grade ≥3 (to normalization or grade <3) was 12 days in the KISQALI treatment groups. Febrile neutropenia was reported in 1.7% of patients in the KISQALI treatment groups. Treatment discontinuation due to neutropenia was 1%.

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. In animal reproduction studies, administration of KISQALI to pregnant rats and rabbits during organogenesis caused embryo-fetal toxicities at maternal exposures that were 0.6 and 1.5 times the human clinical exposure, respectively, based on area under the curve. 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

References

1L=first line; 2L=second line; AI=aromatase inhibitor; AR=adverse reaction; CDK=cyclin-dependent kinase; CTCAE=Common Terminology Criteria for Adverse Events; EORTC QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ET=endocrine therapy; HR=hazard ratio; HRQOL=health-related quality of life; ITT=intent to treat; LHRH=luteinizing hormone-releasing hormone; mBC=metastatic breast cancer; mOS=median overall survival; mTTC=median time to chemotherapy; NR=not reached; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PFS=progression-free survival; QOL=quality of life; TTD=time to deterioration.

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